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Medical Geology in Mining

Health Hazards Due to Metal Toxicity

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ISSN 2197-9545 ISSN 2197-9553 (electronic)
Springer Geology
ISBN 978-3-030-99494-5 ISBN 978-3-030-99495-2 (eBook)
https://doi.org/10.1007/978-3-030-99495-2

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

The occupational health hazard is a major area of concern since industrial growth is demand-driven and therefore, a particular type of work environment is inevitable. This has given rise to several health-related issues such as direct exposure to pathogens to the workers in butcheries, continuous exposure to particular types of chemicals in several manufacturing industries, and particular postures in which the workers such as crane operators work.

This book specifically deals with the occupational health hazards in the mines. The National Institute of Miners' Health (NIMH), which is now a part of the Indian Council of Medical Research (ICMR), has done pioneering work on health hazards caused to the mine workers. Nevertheless, the compilation presented in this book covers a wide range of topics, including health hazards due to metal toxicity, dust, noise, ergonomics, and postural injuries. Furthermore, some of the topics such as noise exposures and postural injuries were not addressed adequately by the previous researchers. This book, therefore, provides an impetus in these hitherto ignored areas. On the whole, this compilation is a unique collection of very useful articles written by eminent workers in this field. The editors of the book are reputed and revered in their respective domains of knowledge. Moreover, the book is being published by a highly reputed and renowned publishing house—Springer Nature. I, therefore, have no doubt that this book will become a compulsory reference to all those who are working in this field. I congratulate the editors for bringing out this valuable publication.

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Preface

Mining plays a pivotal role in the development of modern civilization. By providing the essential raw materials, mining ensures progress, safety, and comfort of people. However, this essential activity comes with several woes, the most important of which being the occupational health hazards. Mines act as sources of constant danger and risk to the miners irrespective of the scale of mining, such as large-scale industrial mining or small-scale artisanal mining. Not only are there accidents, but continuous exposure to dust, metal toxicity, hazardous gases and fumes, and loud noises, giving rise to a variety of diseases to mine workers. This book discusses a wide range of health-related issues pertaining to mining, with particular reference to occupational diseases, metal toxicity, postural injuries in miners, modern fire safety controls, noise-induced hearing loss prevention, and noise mapping.

Medical Geology is an important discipline in earth sciences; unfortunately, not much literature is available on this subject. This book is, therefore, intended for the practicing engineers and supervisors in mines, health and safety professionals, researchers, as well as students of the mining industry. The range of topics covered in this book are written by eminent authors who are active workers in their respective domains. The first chapter by **Sishodiya** is on the problem of silicosis to mine workers and industrial workers. He proposed a case study of silica dust in Rajasthan, India, and presented several statistics depicting the hazard potential. **Sherekar et al**. discussed the role of pyrite in aggravating pneumoconiosis caused to coal mining workers. Another common disease observed in miners is tuberculosis (TB), which is not much discussed in published literature. In this book, **Husain et al**. have provided a thorough review on TB which is a worthy addition to existing knowledge in medical geology. Similar to TB, the chronic obstructive pulmonary disease (COPD), which is also not much discussed in the literature, has been brought forth by **Pingle et al**., **Somayaji and Trivedi** have presented an overview of skin diseases to the miners. **Tiwari and Sarangi** presented the potentiality of specific plant species for phytoremediation of arsenic, which is a deleterious environmental constituent and hazardous to human health. **Burnase et al**. presented an overview of health hazards caused due to metal toxicity. This is one of the best and most detailed accounts of metal toxicity available in the literature. Noise pollution is also one of the potential hazards, which was a little

bit ignored in the literature. However, in this book, there are two papers dealing with this topic. The paper by **Thakkar et al**. presents a case study of noise-induced hearing loss (NIHL) in the active mining area, whereas **Manwar and Pal** emphasized on noise mapping as a potential monitoring tool for the prevention of NIHL. Ergonomics is related to work-space management which helps the miners to reduce stress caused due to improper postures and wrong space management. **Kulkarni et al**. presented an overview of postural injuries to mine workers, whereas **Salve and Paul** discussed the critical issues in ergonomics of mining areas. Injuries are also caused due to different types of accidents in active mines. **Shrawankar et al**. give a strategy to combat such disasters. **Randive et al**. presented an interesting study on health hazards due to silica pebbles in the soil, which is a new potential source of geogenic health hazard. **Tumane et al**. discussed the effects and environmental health hazards of coal fly ash (CFA), with special emphasis on sustainability and management of industrial mining CFA. The book has 14 chapters including 74 figures and 37 tables. We did our best to cover almost all known, potential, and possible health hazards in mining. We believe this book will provide a useful reference to the students as well as researchers working in these areas.

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Bengaluru, India — Shubhangi Pingle
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Acknowledgements

First and foremost, we thank Alexis Vizcaino who read our proposal thoroughly and lend his helping hand throughout the book project. We are also thankful to our project coordinators Dinesh Natarajan and Jivitha, who followed up with timely reminders. We are thankful to all reviewers who spared their valuable time for scrutinizing the manuscript and offering comments, criticism, and helpful suggestion; which greatly helped in the improvement of the manuscript. We are also thankful to all the authors for contributing their valuable research work for this book and also for their patience and cooperation throughout the book project. We are also indebted to Sanjeevani Jawadand for the editorial assistance; without her help it would not have been possible to complete this work in time. Finally, we thank Dr. R. S. Dhariwal, Scientist G and Head, Non-Communicable Diseases, Indian Council of Medical Research, for writing an elaborate forward for this book. We also thank all those who were directly or indirectly involved in this work.

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Silicosis Detection and Relief Programme: A Case Study of Rajasthan, India

P. K. Sishodiya

1 Introduction

Silicosis is an incurable, debilitating and invariably fatal occupational disease caused by inhalation of silica dust. The disease is responsible for considerable morbidity and mortality among workers employed in dusty occupations all over the world. Studies in India and other countries have shown the high prevalence in mining and mineral processing, construction, glass making, cement, granite, slate quarrying and dressing, metal grinding, iron and steel foundries, silica milling, flint crushing, manufacture of abrasive soaps and many other industries where exposure to silica dust is prevalent. The occurrence of silicosis has been reported from almost all states in India though very few cases are notified to the authority despite the fact that it is a notifiable disease under various health and safety legislation. National Human Rights Commission has identified Andhra Pradesh, Gujarat, Haryana, Jharkhand, Madhya Pradesh, Rajasthan and West Bengal as endemic states for the prevalence of silicosis (National Human rights Commission 2017).

Silicosis is a notified disease under section 25of Mines Act, 1952, section 89 of Factories Act 1948 and Rule 273 of Rajasthan Building and Other Construction Workers (Regulation of Employment and Conditions of Service) Rules, 2009. It is also a compensable disease under section 3 of the Employees Compensation Act, 1923 and section 52 (ii) of Employee State Insurance Act, 1948.

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_1

2 Silicosis Prone Industries in Rajasthan

Rajasthan is one of the western states in India famous for marble mining and the sandstone carving industry. However, the name and fame in stone carving have extracted a heavy price on the health of workers due to the occurrence of silicosis in this industry.

2.1 Mining and Mineral Processing

Rajasthan is rich in minerals and has the largest geographical area under mining with 2587 leases for major minerals, 10,851 for minor minerals and 19,251 quarry licenses. The majority of leases of sandstone mines and quarries are in the unorganized and small-scale sector. Sandstone is available in several districts and in 19 out of 33 districts, mining and mineral processing is an important industry providing direct and indirect employment to about 3 million persons (Rajasthan State Human Rights Commission 2014).

The working in most sandstone mines is wholly manual with little or no mechanization. After removal of overburden, the rock is manually cut in blocks of stone by making holes with chisels and hammer (Fig. 1a). The block of stone so separated is split into stone slabs of various thickness depending on natural stratification. The stone slabs are sold as such or cut into smaller slabs and cobblestones depending on the nature of the stone and commercial requirements. With the development of new technology, value addition in the form of polishing is also being done.

The majority of mines employ less than 50 persons and do not use power or explosives, hence are not covered by the definition of "Mine" under the Mines Act, 1952, the central act for enforcement of health and safety in mines. The mine owners and mine workers are ignorant of health and safety requirements and the occurrence of diseases due to general lack of education and awareness.

2.2 Construction and Stone Carving Industry

The construction industry is another major employer in the state. Though no reliable statistics are available, it is estimated that more than 3.0 million persons are employed in the industry. Of these, 2.7 million are registered with Rajasthan Building and Other Construction Workers (BOCW) Welfare Board (Building and Other Construction Workers Welfare Board, Rajasthan 2020). BOCWs constitute one of the most numerous and vulnerable segments of the unorganized sector in the state. Their work is seasonal in nature, the relationship between employer and employee is temporary, working hours are uncertain, basic amenities and welfare facilities are negligible and awareness for occupational health hazards is non-existent. Studies have shown that

Fig. 1 **a** Chiseling a block of sandstone for extraction by manual mining, **b** Electric Hand Cutter being used in stone cutting, **c** Manual Chiseling, **d** Chiseling Operation with Electric Chisel, **e** Typical Stone carving Workshop in a large unit, **f** Manual rubbing and polishing

the building and construction industry has the highest rate of accidents after mining, Therefore, the risk to life and limb is inherent to working in this sector. Very little scientific information is available on the prevalence of occupational diseases among these workers.

Stone carving has a unique place in the building and construction industry, more so in Rajasthan where sandstone is widely used as construction material and stone carving is inherent to the culture. While an exact number of stone carving units are difficult to get, it is estimated that there are thousands of small and unorganized stone carving units employing more than 100,000 persons. The stone carving work involves designing, cutting stone blocks, chiseling, grinding, polishing and other processes (Fig. 1 b–f). Recently, mechanization and use of powered tools without dust control devices for grinding and cutting have significantly increased dust exposure and consequently the risk of silicosis.

2.3 Quartz and Feldspar Milling

Processing of quartz and feldspar by milling to make powder for supply to glass and other industries is an important industry in mineral-rich districts. The process is inherently dusty involves the crushing of boulders of mineral ore, milling, sieving with vibrating screens and bagging in plastic or jute bags leading to extremely high exposure to dust in the absence of dust control systems.

2.4 Stone Crushing

Stone crushing to make grit for road and other construction is another important source of dust exposure among workers. Invariably, the large number of stone crushers are located in a small area. The process involves crushing large boulders of stone in jaw crushers, sieving, and size separation in the open area causing heavy environmental and workplace pollution.

Most of the 3 million workers engaged in mining and mineral processing industries and more than 3 million workers in the construction industry are potentially exposed to silica dust and are at the risk of developing silicosis and other dust diseases.

3 Prevalence of Silicosis

3.1 The Indian Scenario

The first enquiry about the occurrence of silicosis in India was made by the Royal Commission of Indian Labour in 1929 who did not find any incidence of silicosis. However, a detailed investigation in Kolar Gold Fields from 1940–1946 by Chief Advisor of Factories involving 7653 mine workers found that 3402 (43.7%) workers were suffering from silicosis. Subsequently, silicosis was recognized as an important occupational disease in mines. Many studies have been conducted in the past to determine the prevalence of silicosis amongst stone quarry and quartz milling industry in the country. Sikand and Pamra (1949) were the first to report cases of silicosis in stone workers in India. They recorded 52.4% cases of silicosis among stone cutters and 12.5% among stone breakers. They also reported a higher prevalence of tuberculosis among workers (Sikand and Pamra 1964). A study conducted by Desert Medicine Research Center, Jodhpur (1994), to find out the pattern and predictors of mortality amongst the sandstone workers showed that the radiological opacities suggestive of silicosis were seen in 9.9% of radiographs, and radiological signs of

pulmonary tuberculosis were seen in 15.6% radiographs. The prevalence of both conditions increased with the duration of work (Mathur 1996). Another medical survey of 125 stone cutters in sandstone mines located in the Lalitpur district of Uttar Pradesh revealed the prevalence of silicosis and tuberculosis was 22% and 48% respectively. The average duration of dust exposure for the development of silicosis was 12 to 15 years (Kashyap 1994). A study of Jodhpur sandstone mine workers in 1994, found that about 10% of the mineworkers examined suffered from silicosis. The second study conducted in 1996, in the sandstone mines in Jodhpur, also showed that out of the 288 workers examined, 14% were found to be suffering from severe silicosis and 28% were found to be suffering from silicosis of less severity. A study in Lal-Kuan, New Delhi to assess the health status of the resident who worked on stone crushers and in quarries revealed that approximately 39% of the subjects examined were suspected to be suffering from silicosis, or silico-tuberculosis. The prevalence of pulmonary tuberculosis among subjects was 29% (OK International 2005). In a review article Saiyed and Tiwari suggested that the prevalence of silicosis among stone quarry workers was 21% and among stone crushers 12% (Saiyed and Tiwari 2004). In a study based on the evaluation of medical records of stone mine workers with respiratory morbidity in the Karauli district, the prevalence of silicosis was found to be 78.4% (Aravali 2013).

3.2 International Scenario

There are numerous studies on the prevalence of silicosis among sandstone mine workers and stone processing work from all over the world. National Institute of Occupational Safety and Health (NIOSH), USA (2001) published the first consolidated report on occupational injuries, illness and hazardous exposure in the mining industry and reported that silicosis prevalence was about 12% amongst 1170 stone operators. A study of stone carvers in Brazil reported that the prevalence of silicosis was 53.7% and High-Resolution Computed Tomography (HRCT) characterized Silicotic nodules better than chest X-ray. Early coalescence of small opacities was associated with lung function impairment (Antao and Pinheiro 2004).In one study from Thailand, the prevalence of silicosis among stone cutting workers was 36.1% and an association between silicosis and tuberculosis was also observed (Silanun and Chaiear 2017). A cross-sectional study of 180 workers of stone-cutting factories in Malayer-Azandarian, Iran during 2008–2009 demonstrated that 16 (8.9%) had silicosis, lung function test was abnormal in 35 (19.4%) workers and 16 (8.9%) had respiratory symptoms (Aghilinejad et al. 2012).

4 Development of Silicosis Relief and Rehabilitation Programme in Rajasthan

Though silicosis had been reported from Mica Mines in Bhilwara and Lead and Zinc Mines in Zawar, Udaipur as early as 1964, there were no reports of silicosis from sandstone mines till 1994. The problem was first highlighted in 2009–10, by National Human Rights Commission (NHRC) when 48 cases of silicosis including 22 cases of death were given relief by the state government.

The attention to the prevalence of silicosis in stone mines and the stone carving industry in Rajasthan was drawn only after series of reports from the National Institute of Miners' Health (NIMH). The reports indicated a high prevalence of silicosis varying from 38.4% to 78.5% in the Karauli district among stone mine workers and 100% prevalence among workers who worked for more than 20 years in stone mines (Aravali (2013). Silicosis was also reported from workers as young as 22 years of age among persons engaged in stone carving work.

On the basis of reports from the National Institute of Miners' Health (NIMH), Rajasthan State Human Rights Commission (RSHRC), took suo-moto cognizance in 2013 and recommended detection and rehabilitation of silicosis affected persons. The commission also submitted a **"Special Report on Silicosis"** to the government with comprehensive recommendations (Rajasthan State Human Rights Commission 2014). Following the Commission's recommendation, the state government decided to give ex gratia payment of INR 100,000 to silicosis/asbestosis patients and INR 300,000 to the dependents of the deceased. Rajasthan Employees' Compensation (Occupational Diseases) Rules 1965 were suitably amended to set up Pneumoconiosis Boards in every district and Appellate Pneumoconiosis Boards in 5 government medical colleges consisting of Radiologist, Chest Physician and General Physician. Mobile Silicosis Surveillance Units were commissioned for the detection of silicosis and silicosis detection camps were organized in "hotspots" areas. The systematic relief and rehabilitation programme was started for mine and BOCW workers. In October 2019, the government of Rajasthan formulated and adopted a comprehensive "Rajasthan Policy on Pneumoconiosis including Silicosis Detection, Prevention, Control and Rehabilitation" (Department of Specially Abled Persons, Government of Rajasthan 2019).

5 Detection and Certification System for Silicosis in Rajasthan

Rajasthan has instituted a systematic programme for the detection and certification of silicosis and other pneumoconiosis. The certificate of silicosis from the District Pneumoconiosis Board is mandatory for obtaining monetary relief from the government.

5.1 Silicosis Grant Disbursement Portal of Rajasthan

Any person who wishes to be certified for silicosis can register on the online Rajasthan Silicosis Portal through internet kiosks called e-Mitra or through the internet. His application is forwarded by the District Nodal Officer to the nearest Primary or Community Health Center for an initial medical examination consisting of a general physical examination and chest radiograph. If suspected to be suffering from silicosis or pneumoconiosis, he is referred to the District Pneumoconiosis Board where detailed medical examination and investigations are conducted. If found suffering from silicosis, an online silicosis certificate is issued and sent to the nodal district authority. The authority then forwards it to the Mining or Labour Department depending on the worker's registration and nature of work. The department disburses entitled monetary relief directly to the bank account of the victim through the Silicosis Grant Disbursement Portal of the state government. The system is accessible to the public to ensure transparency. The beneficiary also becomes entitled to benefits under various other welfare schemes of the state including monthly pension.

6 Rajasthan Policy on "Pneumoconiosis Including Silicosis Detection, Prevention, Control and Rehabilitation" (Department of Specially Abled Persons, Government of Rajasthan 2019)

The government of Rajasthan has formulated and adopted a state pneumoconiosis policy for silicosis detection, prevention, control and rehabilitation as a flagship programme of the state government. The salient features of the policy include:

- The policy covers any worker/person suffering from Pneumoconiosis including silicosis and certified by the Competent Authority notified by the State Government
- The policy also covers Migrant Workers from outside the State, who has worked in any industry, mines or any other establishment in the State
- A comprehensive programme for detection, health surveillance, prevention, control and rehabilitation for Pneumoconiosis and other dust-related diseases.
- Monetary relief for every person certified to be suffering from pneumoconiosis from centralized Pneumoconiosis Fund through Direct Bank Transfer.
- Free treatment, investigations and medicines by the State Government
- Pension equivalent to persons with disability and family pension to the dependents in event of death of the victim.
- Training of medical doctors engaged in screening for pneumoconiosis and members of Pneumoconiosis Boards in the detection of Pneumoconiosis.
- Improving framework for prevention and control of pneumoconiosis by strict enforcement of legislative requirements and guidelines.

- Monitoring implementation of the policy and annual social audit of the implementation of the policy as per the Auditing Standards of Social Audit.
- Constitution of the standing committee under the chairmanship of Chief Secretary to monitor and periodically review the progress of implementation of the policy.

Following features of policy have been implemented for all persons suffering from silicosis/pneumoconiosis;

- The online registration portal for screening and certification of cases of pneumoconiosis
- One-time financial assistance of INR 300,000 to the person suffering from silicosis/pneumoconiosis and INR 200,000 to the dependent in the event of death of the silicosis victim.
- Disability Pension of INR 1500 per month for the victim.
- Free treatment and medicines for victims.
- Constitution of Working Group for Prevention and Control of Pneumoconiosis
- Monitoring and review committee under the chairmanship of Chief Secretary, Rajasthan.
- Providing benefits under various welfare schemes of the state government similar to the Below Poverty Limit (BPL) scheme.

Some of the difficulties in implementation being faced in the implementation of the policy include;

- A large number of registered workers for screening and certification and delay in initial screening and certification.
- Most mines and stone processing units are in the unorganized and small-scale sector, there is difficulty in the implementation of prevention and control measures.
- Lack of adequate manpower for enforcement of legislative measures.
- Difficulties in the development and implementation of sustainable prevention and control strategies in mines and stone carving units.

7 Status of Silicosis Among BOCWs and Inferences from the Case Study

While only very few cases of silicosis have been reported from other states in India and no other state has formulated and implemented a comprehensive policy on silicosis, more than 22,000 cases have been detected and certified in Rajasthan since 2011. The Building and Other Construction Workers (BOCW) Welfare Board is implementing a relief scheme for silicosis affected beneficiaries since August 2015 which include conducting health screening camps for detection of cases of silicosis, referring to district Pneumoconiosis Boards for online certification and providing monetary relief to affected workers. As of March 2020, in 101 health screening camps organized in Rajasthan, 6911 beneficiaries were examined and 2750 cases of suspected silicosis were referred to District Pneumoconiosis Boards for confirmation

and certification. A higher number of camps were organized in areas where stone carving work is carried out and the prevalence of silicosis was higher such as Sirohi, Dausa, Nagaur, Pali, Jodhpur, etc. Figure 2 shows the detection rate of suspected cases of silicosis in health screening camps varying from 0 to 69.4% with an average of 39.8% among beneficiaries reporting for medical examination.

The BOCW Board provided monetary relief of INR 837.5 Million to 4977 cases of silicosis including 741 cases of death due to silicosis. Figure 3 shows the year-wise distribution of relief to beneficiaries.

Detailed analysis of records shows that 1906 of 4977 (38.3%) silicosis cases and 300 of 741 (40.5%) of deaths occurred in the age group of 31–40 years with a peak of 19.2% and 21.2% respectively in the age group of 36–40 years. Table 1 gives an age-wise distribution of cases of silicosis and deaths due to silicosis.

The youngest case of silicosis was 18 years old. Three workers below the age of 20 years died of silicosis and all 14 deaths due to silicosis below the age of 25 years occurred in the Sirohi district. The median and mean age for occurrence of silicosis

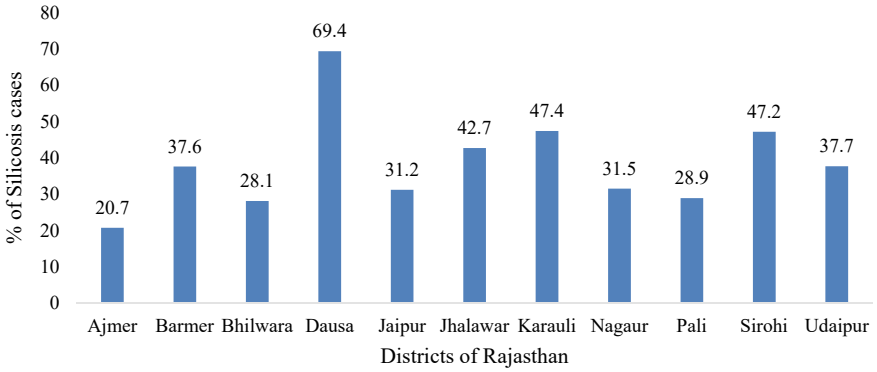

Fig. 2 Detection rate of silicosis in worst-affected districts during health screening camps

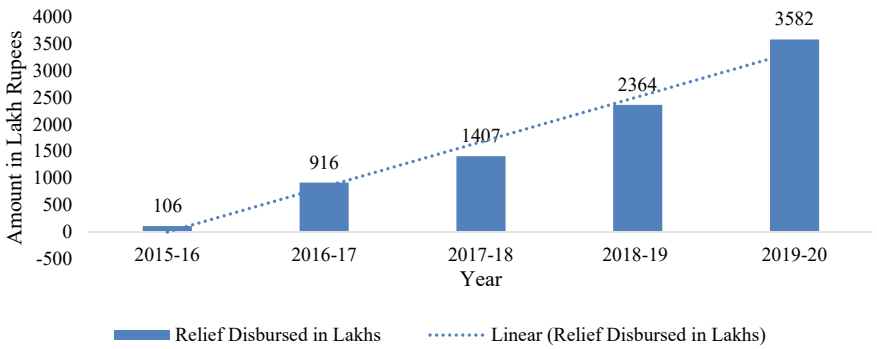

Fig. 3 Year-wise disbursement of relief by BOCW Board

Table 1 Age Group distribution of cases of Silicosis and Deaths

Age distribution of silicosis cases and deaths			
Age groups	Silicosis cases	Deaths Cases	Total
<20	11	3	14
21–30	644	120	764
31–40	1605	300	1905
41–50	1339	214	1553
51–60	634	102	736
60 +	3	2	5
Grand total	**4236**	**741**	**4977**

was 40 years and 40.7 years respectively while the median and mean age for death due to silicosis was 38 years and39.6 years respectively.

The comparison of morbidity and mortality trends due to silicosis among districts with predominantly mining and stone carving industries is shown in Figs. 4 and 5. There is a significant difference in the age distribution of workers for the occurrence of silicosis and death due to silicosis in districts with predominantly mining and stone carving industries. While in the case of mining districts the incidence of silicosis and deaths due to silicosis increases with age and peaking in the age group of 46–50 and 51 to 55 years respectively, in the case of stone carving districts, the incidence of silicosis reaches its peak in the age group of 31 to 35 and deaths in the age group of 36 to 40 respectively. The prevalence of silicosis among BOCW beneficiaries in the stone carving industry is also higher than mine workers. Table 2 shows comparative age groups distribution of cases of silicosis and deaths due to silicosis and their percentage in stone carving and mining districts.

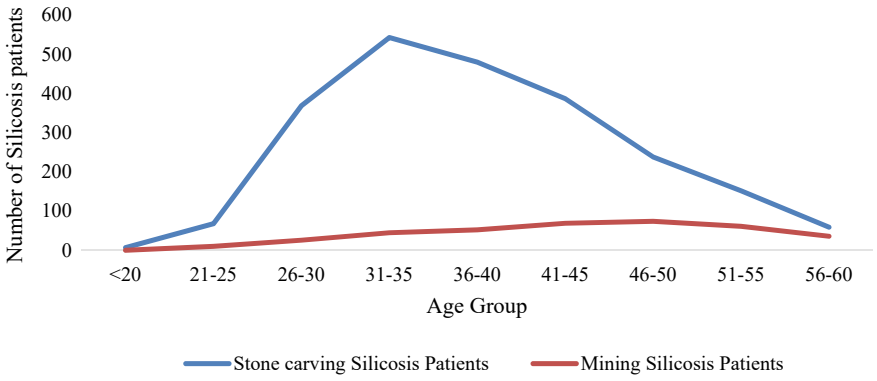

Fig. 4 The comparative trend of Silicosis patients in Stone carving and Mining districts

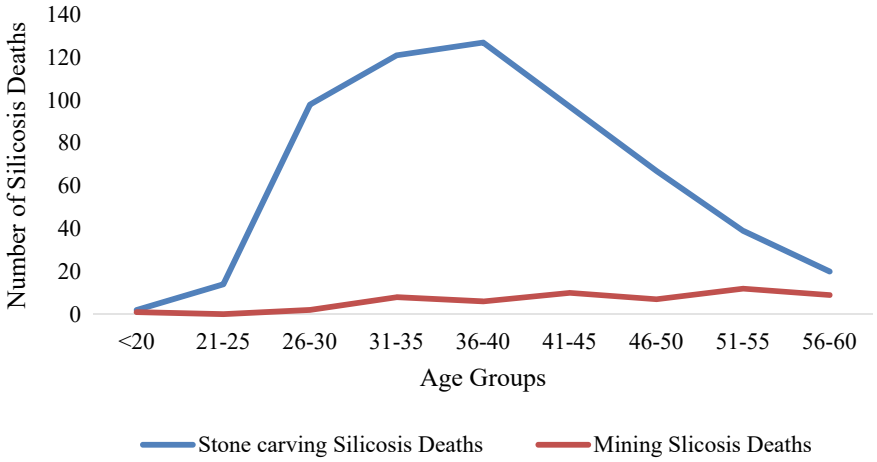

Fig. 5 The comparative trend of Silicosis deaths in Stone carving and Mining districts

Table 2 Distribution of cases of silicosis and deaths in mining and stone carving districts (Figures in parenthesis show values in percentage)

Age groups	Stone carving		Mining	
	Silicosis cases	Silicosis deaths	Silicosis cases	Silicosis deaths
<20	7 (0.3)	2 (0.5)	0 (0)	1 (1.8)
21–25	68 (3)	14 (2.4)	10 (2.7)	0 (0)
26–30	369 (16)	98 (16.8)	26 (7.2)	2 (3.6)
31–35	543 (23.6)	121 (20.7)	45 (12.1)	8 (14.6)
36–40	480 (20.8)	127 (21.7)	52 (13.9)	6 (10.9)
41–45	387 (16.8)	97 (14.9)	69 (18.5)	10 (18.2)
46–50	238 (10.3)	67 (11.5)	74 (19.8)	7 (12.7)
51–55	152 (6.6)	39 (6.7)	61 (16.4)	12 (21.8)
56–60	59 (2.6)	20 (3.4)	36 (10)	9 (16.4)

8 Summary

Silicosis is an incurable, debilitating and invariably fatal occupational disease caused by inhalation of silica dust. The occurrence of silicosis has been reported from almost all states of India though very few cases of silicosis are notified to the authority. National Human Rights Commission has identified Andhra Pradesh, Gujarat, Haryana, Jharkhand, Madhya Pradesh, Rajasthan and West Bengal as endemic states for the prevalence of silicosis.

In Rajasthan, a large number of persons are employed in small scale and unorganized sectors in the mining and construction industry and are at the risk of developing

silicosis. The state government has formulated a comprehensive "Rajasthan Policy on Pneumoconiosis including Silicosis Detection, Prevention, Control and Rehabilitation" for detection, certification and rehabilitation of persons suffering from silicosis. It has also instituted a systematic programme for detection and certification of silicosis and providing monetary relief to the affected persons. More than 22,000 cases of silicosis have been certified and more than INR 2500 Million disbursed as a relief to silicosis victims by March 2020.

The analysis of data of 4978 BOCW beneficiaries including 741 cases of death, showed that the occurrence of silicosis and deaths due to silicosis is much higher in districts with stone carving industry than the mining industry. The mean age for silicosis among stone carving workers was 40.7 years with the highest prevalence in the age group of 31–35 years. Similarly, the mean age for death due to silicosis was 39.6 years with a peak in the age group of 36–40 years. There is also a significant difference in morbidity and mortality trends among mining and stone carving districts in the occurrence of silicosis and death due to silicosis.

In conclusion, it can be said that prevention, control and rehabilitation in silicosis will remain a challenge for years to come in Rajasthan despite considerable efforts by the state government. With increasing awareness among workers and affected persons and better health screening facilities, the number of cases of silicosis detected is likely to increase substantially. The state government of Rajasthan has taken the bold decision to recognize silicosis as an endemic problem that had been ignored earlier. Adoption and implementation of state policy on silicosis detection, prevention, control and rehabilitation and the start of an online Silicosis Grant Disbursement Portal have provided great relief to silicosis victims and is a step in the right direction. The policy addresses the poorest of the poor segment of the population in the unorganized sector of the economy suffering from dust-related occupational diseases.

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Role of Pyrite in Aggravating Coal Worker's Pneumoconiosis

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1 Introduction

The mining industry plays an important role in the industrial development of almost all countries in the world. The occupational risks associated with coal minerals mining are well-documented in mining structures to health problems associated with chronic exposure to mining dust (Cohn et al. 2006). Constant intake of the occupational doses of mineral-rich dust is dangerous, often leading to diseases such as asthma, silicosis, asbestosis, and pneumoconiosis (Moitra et al. 2015). Pneumoconiosis refers to a group of fibrotic lung diseases includes; fibrosis or asbestosis (inhalation of fibrous minerals such as asbestos), silicosis (mineralized silica), coal workers' pneumoconiosis (CWP) or 'black lung' (coal dust), berylliosis (mineral beryl, though rare) and talcosis (inhalation of soft minerals talc or steatite) (Moitra et al. 2015; Zosky et al. 2016). Coal is prime fossil fuel mined globally for energy production. Also, there are millions of workers from coal-producing countries that are associated with different coal mining operations and transportations (Mukherjee et al. 2005). These occupational activities are responsible to produce a high density of fine respirable coal dust in the working environment. Long term inhalation of coal dust by exposed workers and its retention in the lung parenchyma leads to diffuse fibrosis of lung tissue, which refers to a kind of chronic systemic disease known as

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_2

CWP (Karkhanis and Joshi 2013; Han et al. 2017). The disease has been divided into two major forms; Simple form which is called Simple Coal Workers' Pneumoconiosis (SCWP). Another form is complicated or Progressive Massive Fibrosis (PMF) (Zheng et al. 2017). The global prevalence of the disease varies with countries and responsible factors are discussed in the following sections.

1.1 Global Scenario of CWP Associated with Coal Industries

The CWP is the most common occupational disease encountered among coal miners (Cohn et al. 2006). As one of the oldest lung diseases, the first case of CWP was recognized in 1822 as 'miner's asthma' and the first case report was reported by Gregory in 1831 (Moitra et al. 2015). After that several studies have been confirmed the cases of CWP and also reported its prevalence in different countries. In addition, significant variation in the prevalence of CWP has been found between countries over time.

The Coal Mine Safety Act (CMSA) of 1969 has been introduced in the United States (US) to compensate the miners and lessen the dust permissible limit. In consequence, the prevalence of CWP has been reduced to 2%; 1995–1999 from 11.2%; 1970–1974 (Moitra et al. 2015). Since CMSA was imposed in the US in 1969, a similar reduction of CWP prevalence from 6.5%; 1970 to 2.1%; 1990, was reported. However, the increased prevalence of CWP 3.2% in 2000 along with PMF 0.31%; 2000 from 0.14%; 1990 was reported in US (Zosky et al. 2016). In the same years, the study conducted by the Centers for Disease Control (CDC) showed 46 (2.0%) of 2257 miners had CWP (Moitra et al. 2015). Coal Industry Ministry of China conducted the national Chinese epidemiological cross-sectional survey in 1992 and reported a 6.49% overall prevalence of CWP among the total of 1,839,456 surveyed coal miners (Li et al. 2007). Systemic analysis of CWP prevalence in China has been estimated using data from 11 studies conducted from 2001 to 2011 on different geographical coal mining locations. The pulled number of dust exposed miners' population was 173,646 from which 10,821 has been confirmed for CWP with 6.23% of prevalence (Mo et al. 2014). Moreover, the prevalence of CWP (60.28%) was shown by the China National Institute of Occupational Health and Poison Control (CNIOHPC) amongst a total of 23,152 diagnosed cases of pneumoconiosis in 2013 (Han et al. 2015). Another study was showed a comparative analysis of CWP prevalence in China, the USA and Australia. In detail, the data presented by the Chinese Center for Disease Control and Prevention (CCDC) and National Health and Family Planning Commission (NHFPC) was stated that 127,368 cases of CWP have been diagnosed against the total of 249,864 pneumoconiosis cases with a 50.98% prevalence from 2003 to 2016. National Institute for Occupational Safety and Health (NIOSH) was reported 37,965 confirmed cases of CWP of International Labour Office (ILO) category from 1968 to 2015. Whereas in Australia, a 24-year mortality surveillance study reported that <10% CWP fatalities accounted against 1000 cases of pneumoconiosis between 1979 and 2002, while, only 26 cases were reported by the Queensland government

from 1986 to 2018 (Han et al. 2018). The overall average CWP prevalence in other countries including United Kingdom (UK) for the year 1959 to 2000 was 4.07%, India for the year 1986 to 1988 was 15.4%, Turkey for the year 1985 to 2004 was 4.01% and Brazil for the year 1988 was 5.6% has been reported (Mo et al. 2014).

Despite the variation in reported CWP cases throughout the globe, the prevalence of CWP is usually found higher in developing countries than in developed countries (Zheng et al. 2017). Coal rank, geographical locations of coal mines, major mining activities, rules and regulations regarding occupational hygiene and dust permissible limits, years of working, age, personnel safety measure and advancement in disease diagnostic parameters, etc., are major accountable as well variable factors associated with the global scenario of CWP.

1.2 Types of Coal and CWP

Coal is a mixture of heterogeneous substances made up of inorganic and organic materials. Coal rank is defined as the extent to which organic materials have matured during a geological time, which refers to the quality of the coal. Anthracite, bituminous, sub-bituminous and lignite are the four major coal types ranks based on fixed carbon, volatile matter, heating and gross-calorific value shown in Table 1 (Huang et al. 2005; Gamble et al. 2012; McCunney et al. 2009). Regional differences in CWP prevalence have historically been understood to be related to coal rank. The prevalence of CWP spans an order of magnitude from anthracite to low volatile coal (Gamble et al. 2012; Zhang et al. 2002; Antao et al. 2005).

A systematic meta-analysis study in china showed a 5.88%, 5.38% and 0.15% prevalence rate of CWP for coal workers exposed to bituminous, anthracite and lignite coals respectively (Mo et al. 2014). China has 75% bituminous, 13% lignite and 12% anthracite coal reserves and reported 6.23% CWP prevalence against total coal mining workers from 2003 to 2017. While the USA has 89.73% reserve coal including bituminous and sub-bituminous, 10.04% lignite and only 0.23% anthracite

Table 1 Major coal ranks/types with carbon, oxygen and hydrogen content

Rank		Coal type/Description	Approximate content (%) (dry mineral matter–free basis)		
			Carbon	Oxygen	Hydrogen
(High) ↑	100	Anthracite	95–93	2–4	2–4
	200–300	Semi-bituminous	93–87	4–5	4.5–5.9
(Intermediate) ↑	400–900	Bituminous	87–77	5–15	4.9–5.7
		Sub-Bituminous	77–70	13–20	5–6
(Low)	NA	Lignite	70–60	20–30	5–6
		Peat	Less than 60	30–40	5–7

coal which can be associated with a lower CWP prevalence of 3.2% than China. Moreover, a negligible 0.5% CWP prevalence rate has been accounted for in Australia; the country has 48.56% black and 51.44% brown coal reserve (Han et al. 2018). Interestingly, a report from the UK mentioned the relationship between the period of exposure such as 8, 16 and 36 years and coal rank viz; highest, intermediate and lowest respectively were required for developing 20% prevalence of CWP. Moreover, a study in South Wales confirmed the highest number of radiological abnormalities in anthracite mines and intermediate in steam coal with the lowest in bituminous coal mines (Gamble et al. 2012).

1.2.1 Diagnosed Cases of CWP

Earlier reported global picture of CWP prevalence will simply alleviate the number of confirmed CWP cases from coal-producing countries. In brief, major coal-producing countries including China have 119,380 diagnosed cases up to the end of the year 1992 and 127,368 cases for the year 2003 to 2016. Whereas 37,965 confirmed CWP cases have been reported from the USA for the period of the year 1968 to 2015 and from the year 1986 to 2018, Queensland has reported 26 cases (Li et al. 2007; Han et al. 2018). In 1997, a study has been undertaken to find the CWP prevalence in 10 coal mines regions of Madhya Pradesh and Orissa states of India by re-reading of chest x-ray plates taken during the Periodical Medical Examination over 5 years and confirmed the total of 1,317 cases for CWP from 43,504 x-ray film read (Parihar et al. 1997). Although several studies have been commenced in different coal mining regions of various countries to elucidate the prevalence of CWP, the prevalence of CWP could not be identified precisely.

1.2.2 Death Rate

Chronic doses of respirable coal dust particles for the whole duration of service leads to the condition of CWP; which may transform into PMF and can be lethal (Zosky et al. 2016). A study on mortality probability from state-owned mines in the east of China from 1963 to 2014 explained the mortality rate of 19.19% amongst a total of 495 diagnosed cases of CWP including 12.1 and 57.4 years of average life span and death age respectively (Han et al. 2017). In 2003, NIOSH proposed an average 50% death rate for CWP attributed to the total death accounted for pneumoconiosis for the period of 10 years from 1990 to 1999 (Huang et al. 2005). Besides that, the Global Burden of Disease (GBD) Study 2013 on the cause of specific mortality demonstrated the global deaths for diseases encountered under chronic respiratory disease for years 1990 and 2013. The overall deaths accounted for chronic respiratory diseases in 1990 were 3,490,200 and in 2013 the number went to 4,267,500 with a median percent change of 21.9. Also, the reported deaths for CWP were 28,900 and 25,200 in 1990 and 2013 respectively showing –13.7% of median. From this data the global percent death rate for CWP was calculated at 0.82; 1990 and 0.59; 2013 with

respect to total death accounted for chronic respiratory diseases along with 35.6% of margin for median percent change from 1990 to 2013 (GBD 2015).

1.2.3 Importance of Geographic Locations

The progressive geological alteration or coalification can be specifying the coal rank from lignite to anthracite (Gamble et al. 2012). The higher geological age of coal resulted in the coalification of high-rank coal. In West Germany, maximum pneumoconiosis occurrence was reported in high ranked coal mines which, eventually has a high mass-number index (MNI: the mass in mg/m^3 per 1000 particles/cm^3 of dust in respirable range) besides, the similar MNI and comparable mineral content associated with low-rank coal. Also, the cytotoxicity studies signified the more damage to cells exposed with respirable dust of coal had maximum geological age (Bennett et al. 2015). Despite the coal rank, coal mine type (underground and opencast), structural geology of mines, size diversity in the coal seam, the geographical distribution of coal with mineral contents, varieties in mining technique and dust controlling measures or enforcement of permissible exposure limits are the cumulative factors may also participate in the progression of CWP (Han et al. 2018; Huang et al. 2005; Antao et al. 2005). Moreover, the maximum CWP incident has been observed with underground coal miners than open-cast due to the denser dust concentration and confined ventilation circuits in underground environments (Han et al. 2018). Principal working locations and periods of underground exposure are the relative factors responsible for CWP prevalence. Coalface > Miscellaneous > Maintenance > Transportation > Surface are the working environment having higher to lower CWP prevalence rate with increasing years of exposure (Huang et al. 2006). Geographical locations having a large proportion of high-rank coal, the maximum number of underground coal mines and structural geology including complex fold and faults with thin-medium coal seam width and increased collision of rock during coal extraction activities have resulted in increased MNI which was further associated with prevalent CWP episodes.

1.2.4 Compensation Schemes

Many diseases are associated with occupational exposure and are clinically indistinguishable from non-occupational diseases. Evolution in diagnostic parameters for respiratory lung diseases facilitates the eligibility determination for compensation and benefits. Most of the coal-producing countries has evolved the disease diagnostic criteria and their compensation scheme for victims of CWP. Lung tissue examination from biopsy, autopsy specimen or by the chest x-ray film developed and interpreted according to an international convention developed under the auspices of the ILO has been accepted for the benefits. Based on x-ray film interpretations, the positive CWP miners have been allowed to transfer their job from dusty to least dusty workplaces (Weeks and Wagner 1986). The benefit has been provided to survivor miners (disabled), or dependants in case of death due to CWP by the U.S. Department of

Labor, Division of Coal Mine Workers' Compensation (DOL) operated, Title IV of Federal Black Lung Program and administered claims filed under the Black Lung Benefits Act of 1969 with time to time amendments (Whitaker 1981; Almberg et al. 2018). The Department of Natural Resources Mines and Energy (DNRME), Queensland offers the free respiratory assessment through the Coal Mine Workers' Health Scheme. Depending upon the degree of permanent lung impairment, the victim has been entitled with lump-sum compensation of $330,240 and additionally he/she will be eligible for an amount of $123,700 in cases diagnosed with CWP (Queensland 2020). In India, a compensation policy for CWP and other occupational diseases has been established under Mines Act- 1952 & Employee Compensation Act–2009. Occupational disease board, constituted by Coal India Limited, Ministry of Coal examines the suspected CWP cases, detected during Periodic Medical Examination to confirm the disease and compensation to be paid to the employee and rehabilitation by change of job. Also, the disease progression has been reviewed by the board in retired coal workers (Fourteenth Report 2015).

This portion reveals the cover on circumstances of CWP and associated global fatalities. Geographic seating, coal rank and mining activities are key factors for the production of toxic dust which are found to be dealing with the worldwide variation in the prevalence of CWP. Even though, it is needed to locate the actual component associated with coal mine dust and what role it plays in the buildup of CWP.

2 Factors Contributing to the Development of CWP

In the past 3–5 decades, CWP; the most common disease encountered among coal miners (Cohn et al. 2006) has received more attention due to its clear occupational association than other respiratory diseases (Huang et al. 2002). Predominant exposure of airborne (Han et al. 2015) respirable mixed coal dust has a strong relationship with the prevalence of CWP (Mukherjee et al. 2005; Mo et al. 2014; Zhang et al. 2002; Huang et al. 2002) while its rate of progression is related to the mass of exposed dust during working lifetime (Antao et al. 2005). Initially, silica or quartz content was thought to be a major potential confounding risk factor until CWP was found to occur when there was minimal silica in the coal mine dust (Gamble et al. 2012; McCunney et al. 2009). Likewise, quartz composition does not emerge to account wholly for alteration in CWP prevalence. However, the contribution of coal rank in the development of CWP has been confirmed by epidemiological studies and also suggested that the carbon content of coal is a vital factor to assess CWP risk (McCunney et al. 2009). A different, modern epidemiological (Huang et al. 2005; McCunney et al. 2009) in vivo animal (Aladdin et al. 2013) in vitro cell line (Zhang et al. 2002; Huang et al. 2002; Aladdin et al. 2013) and experimental laboratory studies (Cohn et al. 2006; Dalal et al. 1995) investigated and proved the constructive role of iron which, released from pyrite fraction present in the coal as a strong contributing factor in the prevalence of CWP (McCunney et al. 2009).

2.1 Coal Dust

Though organic carbon is the predominant constituent, a wide range of inorganic minerals is also present in coal, including carbonates (calcite and siderite), sulfide ores (pyrite), clays (kaolinite and illite), oxide ores, quartz, phosphates and other elements including metals, nonmetals and metalloids shown in Table 3 (Cohn et al. 2006; Zosky et al. 2016; Huang et al. 2005; Gamble et al. 2012; Zhang et al. 2002; McCunney et al. 2009; IARC 1997). The proportion of minerals (general range; Table 2) in coal varies broadly along with the type of coal and from coal seam to seam (Gamble et al. 2012; IARC 1997). Numerous activities are involved in the process of coal excavation, primarily responsible for the production of heterogeneous fine particulate matter, known as coal dust. Along with coal cutting, roof bolting, fractured rock or distribution of rock dust (low-silica limestone dust) to prevent explosions and diesel exhausts (> 1 micron) are other major sources associated with an elevated level of mixed respirable (> 10-micron aerodynamic diameter) dust density in coal mines (IARC 1997).

2.1.1 Composition of Coal Dust

The complex and heterogeneous nature of coal mine dust acts as a main environmental factor in the development of simple CWP (McCunney et al. 2009; IARC 1997). More than 50 different elements, their oxides (Table 2) and minerals (Table 3) at variable concentrations are ancillary components involved in the formation of coal dust with carbon as the primary component (IARC 1997).

Most information on coal mine dust composition has been raised from industrial hygiene studies in coal mines of different countries. Additionally, coal dust sampling in coal mines focused on the components associated with lung diseases, which includes mixed coal dust, oxides, silicates and mineral metals and non-metals. Earlier studies eventually reported the composition of oxides (Quartz or silica) and silicates (Kaolinite and Sericite/Illite) in coal dust. In contrast, the composition of toxic elements has been started to report in several recent industrial hygiene studies. The average composition of these elements from different mines and countries is shown in Table 4 with the year of the study conducted (Mukherjee et al. 2005; IARC 1997; Aladdin et al. 2013; Dalal et al. 1995). Percent content of elements (Fe, Ca, S, Al) was represented amongst the total element composition in coal dust.

Knowing the amount of diversity in coal dust compositions and concentrations of various coal mines with periods of exposure throughout miners' populations can be considered as collective measures to establish statistics of CWP prevalence. However, the identification of crucial components and bioavailability from coal with exposure doses through inhalation of respirable coal dust will provide strong evidence-based data on CWP.

Table 2 A general range of various elements and trace elements including metals, non-metal and metalloids reported in coal varieties

Metals	Range (percent/ppm)	Non-metals	Range (percent/ppm)
Aluminum	0.43–3.04%	Chlorine	0.01–0.54%
Calcium	0.05–2.67%	Organic sulfur	0.31–3.09%
Iron	0.34–4.32%	Pyritic sulfur	0.06–3.78%
Potassium	0.02–0.43%	Sulfate sulfur	0.01–1.06%
Magnesium	0.01–0.25%	Total sulfur	0.42–6.47%
Sodium	0–0.2%	Sulfur by X-ray fluorescence	0.54–5.4%
Titanium	0.02–0.15%	Boron	5–224 ppm
Beryllium	0.2–4 ppm	Bromine	4–52 ppm
Cadmium	0.1–65 ppm	Fluorine	25–143 ppm
Cobalt	1–43 ppm	Phosphorus	5–400 ppm
Chromium	4–54 ppm	Selenium	0.45–7.7 ppm
Copper	5–61 ppm	*Metalloids*	*Range (percent/ppm)*
Gallium	1.1–7.5 ppm		
Mercury	0.02–1.6 ppm	Silicon	0.58–6.09%
Manganese	6–1 8 1 ppm	Arsenic	0.5–93 ppm
Molybdenum	1–30 ppm	Germanium	1–43 ppm
Nickel	3–80 ppm	Antimony	0.2–8.9 ppm
Lead	4–218 ppm		
Tin	1–51 ppm		
Vanadium	11–78 ppm		
Zinc	6–5350 ppm		
Zirconium	8–133 ppm		

Table 3 Composition of mineral matter in coal ash

Mineral constituents	Representative percentage
Silicon dioxide / silica (SiO_2)	40–90
Aluminum oxide (Al_2O_3)	20–60
Iron or ferric oxide (Fe_2O_3)	5–25
Calcium oxide (CaO)	1–15
Magnesium oxide (MgO)	0.5–4
Sodium oxide (Na_2O)	0.5–3
Potassium oxide (K_2O)	0.5–3
Sulfur oxide (SO_2)	0.5–10
Phosphorus pentoxide (P_2O_5)	0–1
Titanium oxide (TiO_2)	0–2

Table 4 Average amount of toxic elements reported in coal mine dust and occupations

Description of studies with location and year	Average/mean (%) content in coal mine dust							
	Oxides	Silicates			Elements			
	Quartz/Silica	Kaolin and Mica	Kaolinite	Sericite/Illite	Fe	Ca	S	Al
Compositional data for airborne dusts in British coal mines before 1970	4.1	14.1	ND		ND			
Quartz content in dust for various underground occupations in United States mines, 1985–92	4.7	ND			ND			
Oxides and silicates content in the dust of anthracite, bituminous and gas coal type of size < 5 μm & < 3 μm in German coal mines, 1971	3.5	ND	5.7	14.51	ND			
Quartz content in the return air of coal faces in different coal seams and coal rank in Ruhr, Germany, 1953, 1963 – 71	2.4	ND			ND			
Free silica content in different coal mines/methods of Eastern India, 2004	3.1	ND			ND			

(continued)

Table 4 (continued)

Description of studies with location and year	Average/mean (%) content in coal mine dust							
	Oxides	Silicates			Elements			
	Quartz/Silica	Kaolin and Mica	Kaolinite	Sericite/Illite	Fe	Ca	S	Al
Spectroscopic determination of mineral content in coal mine dust from Utah and West Virginia, 1995	2.22	ND			0.6	ND		
X-ray Fluorescence detection of major elements in coal mine dust of Pennsylvania and Utah, 2013	ND	ND			21	38.5	23	18

ND: Not Determined

2.1.2 Release of Toxic Elements from Coal

Excavation of coal, transportation, washing or purification and final industrial and other utilizations are the activities and occupations firmly involved in coal processing and use. These coal processing activities release several toxic pollutants along with heavy metals and harmful trace elements into water bodies (mineralized water) which channelize as "Mine drainage" and often elevate the mineral contents in groundwater and soil (Khan et al. 2017) causing environmental pollution. The ordinary route of emission for toxic trace pollutants, organic and inorganic compounds goes through the natural geochemical process of hydration and oxidation of coal. Oxidation reactions take place in iron pyrite (FeS_2) present in coal seam eventually produce sulphuric acid and emit the ferrous (Fe^{2+}) ions (Jaishankar et al. 2014). Another process of toxic components (As, Cd, Co, Cr, Cu, Hg, Fe, Mn, Ni, Pb, Se, and Zn) emission is discharging of fly ash via direct combustion of coal and fuel oil from coal-fired power generation plants (Reddy et al. 2005). Moreover, pyrolysis is a critical initial reaction stage of coal combustion also responsible for the release of heavy metal elements including Hg, Cd, As and Pb via increased volatility with increasing the temperature (Zhou et al. 2019).

Major inorganic constituents such as silicon, aluminium, sulfur and oxides of Fe, Ca, Mg, Na, K, Ti and other trace elements including Ni, Zn, Cd, Hg, Li, Cr etc. analyzed as ash are necessary to remove from coal to retain its calorific value. Various chemical processes including step-wise acid leaching (HCl, H_2SO_4), use of oxidizing and chelating agents (H_2O_2, $K_2Cr_2O_7$, NaOCl, $Fe_2(SO_4)_3$ and EDTA, citric acid), alkali-acid leaching treatments (NaOH, caustic-HCl–HNO_3 and caustic-HCl–H_2SO_4, aq. KOH or aq. Ca $(OH)_2$) (Dhawan and Sharma 2019; Praharaja et al. 2002) and bioleaching using *Acidithiobacillus ferrooxidans* (Hong et al. 2013) prove 80%–90% demineralization and desulfurization of coal varieties. Releasing of such toxic elemental pollutants from coal has been accumulated in the environment and prevalently acts as a health threat for workers along with local populations living near coal processing industries.

2.2 Pyrite Associated with Coals and Liberation Mechanism of Allied Trace Elements

Coal formation has taken place in a reduced environment with an irregular oxidation process (Zhao et al. 2020; Elsetinow et al. 2001). Various stages of coal development from peat to coal are associated with the formation of pyrite (FeS_2) by enrichment of sulfur (S) and iron (Fe) content. In detail, disseminated sulfate from seawater into peat converted in hydrogen sulfide, polysulfides and elemental sulfur by the bacterial reduction process. The reaction between ferrous iron and hydrogen sulfide resulted

in the generation of pyrite crystal and mackinawite ($FeS_{0.9}$) which further reacts with elemental sulfur to form greigite (Fe_3S_4) and finally converted to framboidal pyrite (FeS_2). Pyrite in coal commonly appears in microscopic or macroscopic form as a massive, disseminated and thin layer deposited in cleats/fractures, cell fillings and pyrite veins through circulating underground water or from basinal fluids after the solidification of coal (Hong et al. 2013; Elsetinow et al. 2001; Chou 2012). Megascopic and microscopic analysis of coal lumps of sub-bituminous coal samples of Padhrar coal mine region of Pakistan further clarifies the presence of pyrites in thick and thin bands and nodules forms. Quartz masses and clay materials were also observed closely associated with the organic coal matter shown in Fig. 1a and b (Shahzad et al. 2016).

Pyrite is the major iron sulfides mineral contributed as an inorganic part of coal with the association of some trace elements including As, Cd, Fe, Hg etc. Moreover,

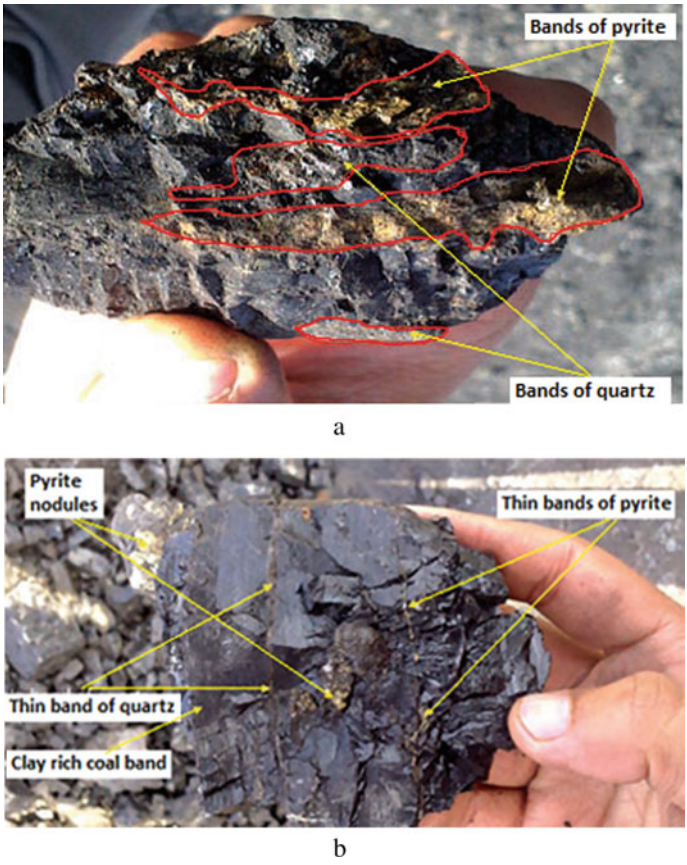


Fig. 1 **a** Pyrite and quartz bands of medium thickness in the coal, **b** Pyrite nodules, thin bands of pyrite and quartz and clay-rich band in the coal lump

iron is present in the coal predominantly associated with sulfur in the form of iron disulfide or pyrite (Cohn et al. 2006; Zhou et al. 2019; Elsetinow et al. 2001; Rezaee and Honaker 2020). Some weathering products of pyrites including szomolnokite, rosenite, melanterite, coquimbite, roemerite, jarosite, and halotrichite, all are majorly composed of ferric sulfide. Oxidation of pyrite started through the adsorption of oxygen and water at the surface of pyrite resulting in the release of ferrous iron (Fe^{2+}), sulfate (SO_4^{2-}) and hydrogen (H^+), leading to the development of acidic conditions in coal. Low pH (pH ~ 3) condition in medium further responsible to release the associated elements (Elsetinow et al. 2001; Rezaee and Honaker 2020). Also, the bioleaching process of coal by *A. ferrooxidans* has been involved in the oxidation of pyrite to release the sulfur (S) and Fe^{2+} associated with pyrite and released S can further oxidize to form SO_4^{2-} (Hong et al. 2013). The earlier mentioned techniques of demineralization and desulfurization of coal are ultimately associated with the oxidation of pyrite and resulting in the release of allied trace elements (Dhawan and Sharma 2019; Praharaja et al. 2002; Hong et al. 2013). The oxidative condition of pyrite associated with coal has the potential to increase total dissolved solids (TDS) and promote the degradation of water quality (Rezaee and Honaker 2020).

Recent epidemiological and experimental studies have demonstrated the concrete role of bioavailable iron (both ferrous and ferric), an oxidation product of pyrite present in coal mine dust in the generation of reactive oxygen species (ROS), a key component in the inflammatory response associated with CWP. Additionally, the findings of these studies stated that the CWP can be correlated with the amount of pyrite present in the coals (Cohn et al. 2006; Zhang et al. 2002; Huang et al. 2002; McCunney et al. 2009; Dalal et al. 1995).

2.3 Bioavailable Iron (BAI)

Formerly, CWP was considered to be an alteration of silicosis, caused due to the inhalation of a crystalline form of silica or quartz associated with coal dust. Now, several evidence-based studies reverse the former understanding of silica exposure and CWP prevalence by validating the role of iron-containing coal dust in the associated evolutionary mechanism of CWP. In general, iron is well-known transition metal present in coal having redox potential, which participates in most of the reversible one-electron oxidation–reduction reactions by switching between the two oxidation states, i.e. ferrous (Fe^{2+}) and ferric (Fe^{3+}) which are further accountable for the production of oxidants (Huang et al. 2005). Free iron radicals present in the inhaled coal dust, Fe^{2+} and Fe^{3+}, are mainly associated with increased hydroxyl radical, ROS and deoxyribonucleic acid (DNA) oxidation product production through the Fenton reaction (Cohn et al. 2006; Huang et al. 2005; Dalal et al. 1995; Elsetinow et al. 2001; Schins and Borm 1999) given as follows:

$$\mathbf{Fe^{2+} + O_2 \rightarrow Fe^{3+} + O_2^*}$$
$$\mathbf{Fe^{2+} + O_2^* + 2H^+ \rightarrow Fe^{3+} + H_2O_2}$$
$$\mathbf{Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} +^* OH + OH^-}$$
$$\mathbf{Fe_{3+} + H_2O_2 \rightarrow Fe^{2+} +^* \mathit{OOH} + \mathit{H}^+}$$

Fenton reaction-based evolution of such toxic radicals is found to be a chief component in inflammatory responses and biochemical as well as immunological alterations associated with CWP and positively correlated to the iron content of inhaled coal dust (Cohn et al. 2006; Huang et al. 2005, 2002; Zhang et al. 2002; Dalal et al. 1995; Schins and Borm 1999). Moreover, using electron spin resonance and the spin-trapping agent DMPO, scientists show that, Fe^{2+} can reduce oxygen molecule (O_2) in an aqueous medium (O_2 solubility in water: 3%, v/v) to produce oxidants. The abundance of O_2 and hydrogen peroxide (H_2O_2) in the pulmonary medium makes smoother the progress of production of hydroxyl (*OH) radicals after inhalation of Fe^{2+-}containing coal particles, ultimately resulting in lung injury (Huang et al. 1998). The potential to generate *OH radicals and induce lipid peroxidation by the bituminous coal samples from a different source of origin (Utah and West Virginia) were reported which was correlated with the available surface iron and further suggested its role in the development of CWP in different coal mining areas (Dalal et al. 1995). Effects of coal dust from Pennsylvania (PA) (high CWP prevalence) and Utah (UT) (low CWP prevalence) coal mine region on JB6 mouse epidermal cells were studied. Activator protein-1 (AP-1) and nuclear factor of activated T cells (NFAT) which are transcription factors associated with regulation of cytokines were activated by PA coal while UT coal did not show any activation in JB6 mouse epidermal cells. For comparison, cells were also treated with ferrous sulfate and found that iron transactivated both AP-1 and NFAT. The observed results showed that a high amount of bioavailable iron present in PA coal is responsible for the activation of AP-1 and NFAT which are the mediator for inflammation associated with CWP (Huang et al. 2002). Another study reported clear regional differences in the prevalence of CWP and correlated with the predicted amount of BAI present in coal samples of seven US state coal mining regions shown in Fig. 2. The highest CWP prevalence commonly observed in bituminous coal miners of PA (cumulated prevalence of 45.4%) and least common in miners of Colorado (CO) i.e. 4.6%, showed a positive correlation with predicted BAI 11.82 and 0.15 mmol/100 gm dry coal from studied coal samples of PA and CO respectively after adjusting for age and years spent in underground mining shown in Table 5 (Huang et al. 2005).

Correlations between pyrite content of coal and generation of H_2O_2 and *OH radicals were reported, which further led to degradation of RNA. The possible mechanism behind oxidation of biomolecules shows in (Fig. 3), dissolved O_2 reacts with either Fe^{2+} at the pyrite surface or dissolved Fe^{2+} to form H_2O_2 through the Haber–Weiss reactions (1), which may further react with dissolved Fe^{2+} to form *OH through the Fenton reaction (2). The study concluded that the size, shape, exposed surface area, exposure period along with pyrite content of coal will be cumulative factors determining the prevalence of CWP among coal miners (Cohn et al. 2006).

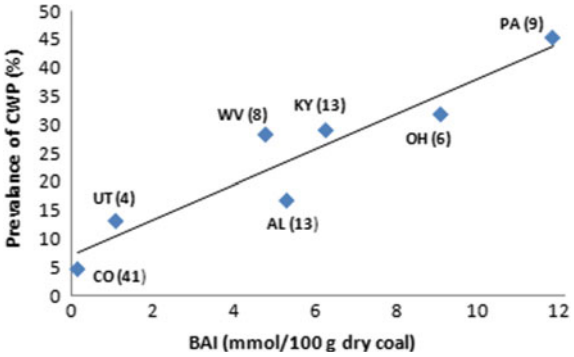
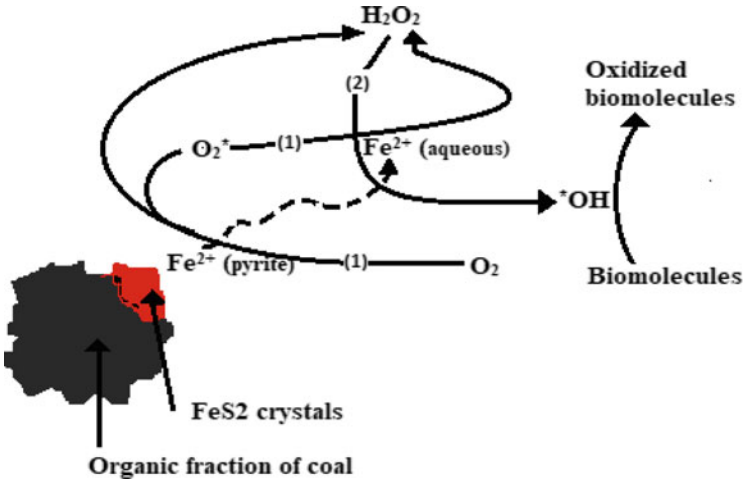


Fig. 2 Correlation between the prevalence of CWP and BAI in seven US state coal mine regions

Table 5 Average levels (mmol/100 g dry coal) of total H_2SO_4 (1/2 S_{py} + SO_4), available amount of acid (1/2 S_{py} + SO_4–CaO), total iron, and predicted BAI

State	No. of mines	CWP (%)	½ S_{py} + SO_4	½ S_{py} + SO_4–CaO	Fe_2O_3	BAI
Pennsylvania (PA)	9	45.35	18.61	14.63	12.48	11.82
Ohio (OH)	6	31.80	19.91	14.69	12.83	9.07
Kentucky (KY)	13	29.00	13.17	7.49	9.78	6.25
West Virginia (WV)	8	28.25	9.15	4.57	7.27	4.77
Alabama (AL)	13	16.70	9.65	6.77	8.85	5.29
Utah (UT)	4	13.10	4.14	−3.19	2.69	1.09
Colorado (CO)	41	4.60	1.92	−2.69	3.68	0.15

Amount of BAI (both Fe^{2+} and Fe^{3+}) released in medium (pH 4.5, 3 days incubation period; which mimicking lysosomes condition) from coal dust samples of three known CWP prevalence (Utah; UT, West Virginia; WV and Pennsylvania; PA) mining regions established good correlation ($r = 0.92$) between BAI and prevalence of CWP. Moreover, the released amount of Ca^{2+} associated with calcite ($CaCO_3$); known as an inhibitory factor for iron bioavailability was found to inversely correlate with CWP prevalence shown in Table 6. The percent release of bioavailable metals (Fe and Ca) was calculated by dividing the amount of metal released under acidic conditions (10 mM phosphate, pH 4.5) with the total amounts of that metal present in the coal × 100 shown in Table 7. The results were further confirmed by measuring cellular iron and lipid peroxidation in human lung epithelial Type II A549 cells exposed with coal dust samples against control, which showed the active role of BAI in the generation of oxidative stress; promoting lipid peroxidation and promising inference in CWP prevalence (Zhang et al. 2002).



$$(1)\ O_2 + Fe^{2+} \rightarrow Fe^{3+} + (O_2^*) \qquad (2)\ H_2O_2 + Fe^{2+} \rightarrow Fe^{3+} + OH^- + {}^*OH$$

$$Fe^{2+} + (O_2^*) + 2H^+ \rightarrow Fe^{3+} + H_2O_2$$

Fig. 3 Mechanisms associated with coal that contains pyrite reacts with dissolved oxygen to generate H_2O_2 and *OH, with *OH leading to biomolecules degradation

Table 6 Average levels of bioavailable iron (ferrous and ferric) and calcium in the coal mine region with different prevalence of CWP*

Region	No. of samples	CWP prevalence (%)	Fe^{2+}	Fe^{3+}	Ca^{2+}
UT	10	4	1.95	7.62	717.5
WV	10	10	1963.14	2695.7	498.83
PA	8	26	7288.2	4860.8	662.9

* Metal concentrations were parts per million (ppm) of coal (w / w)

Table 7 Bioavailability of metals as a percentage released under acidic conditions mimicking phagolysosomes of cells

Coal region	Fe % release	Ca % release
UT	0.45	13.95
WA	24.66	20.33
PA	42.28	52.34

However, there was also noted that the accumulation of iron could result in part from its coordination by humic-like substances (HLS), which comprise up to 30% of dust weight in certain coals. Scientists suggested that HLS in coal dust with iron cladions subsequently catalyze oxidant generation and the accumulation of this metal in the lungs. The relevance of iron coordination by HLS in lung injury after exposure

to coal dust can assist in the understanding of certain clinical features of CWP (Ghio and Quigley 1994). Hence, the efficacy of coal-bearing dust in CWP multiplies due to the addition of iron. Despite all, it is important to understand the mechanism of iron bioavailability from coal dust.

Iron released in 10 mM phosphate solution of pH 4.5, which mimics the phagolysosomes of cells are defined as bioavailable iron (BAI). The amount of BAI can be calculated according to the chemical interactions of pyrite, sulfuric acid, calcite, and total iron. BAI mainly consists of water-soluble iron including ferrous and ferric sulfate released from coal via oxidation of pyrite by the following equation:

$$\mathbf{2FeS_2 + 7O_2 + 2H_2O \rightarrow 2FeSO_4 + 2H_2SO_4}$$

One mole FeS_2 will produce 1 mol BAI as ferrous sulfate ($FeSO_4$) and 1 mol sulfuric acid (H_2 SO_4) i.e. iron present in coals can become bioavailable by pyrite oxidation, which produces ferrous sulfate and sulfuric acid. However, calcite ($CaCO_3$) is the major component in coals that neutralizes the available acid and inhibits iron bioavailability. Therefore, levels of BAI in the coals are determined by the available amounts of acid after neutralization by calcite and the amount of total iron in the coals. If $CaCO_3$ is present in the coal, it will consume the acid and neutralize the pH as follows:

$$\mathbf{CaCO_3 + H_2SO_4 \rightarrow CaSO_4 + H_2O + CO_2}$$

The consumption of acid will accelerate the oxidation of bioavailable iron to non-bioavailable forms of iron. Therefore, no BAI will accumulate when $CaCO_3$ is present (Huang et al. 2005, 1998; Zhang et al. 2002). If $CaCO_3$ is absent in the coals, acid solubilization (H_2SO_4 earlier produced from oxidation reaction of pyrite) of another iron-containing compound, i.e. siderite ($FeCO_3$) would take place and release more BAI as per the following reaction (Huang et al. 2005):

$$\mathbf{FeCO_3 + H_2SO_4 \rightarrow FeSO_4 + H_2O + CO_2}$$

2.3.1 Physicochemical Factors Associated with Iron Bioavailability

Pyrite mineral oxidation is the central and well-known process for releasing iron from coal. Consequently, multiple physicochemical factors responsible for pyrite oxidation including oxygen partial pressure, temperature, and relative humidity along with the amount of calcite, pH and buffering capacity of coal are found to be associated with iron bioavailability (Cohn et al. 2006; Huang et al. 2005, 1998, 1994; Zhang et al. 2002; Elsetinow et al. 2001; Rezaee and Honaker 2020; Santos et al. 2016). However, the physicochemical conditions of coal are likely to vary in different coal mines due to variable amounts of sulfur and other minerals content in the coal (Huang et al. 1994). A limited amount of BAI released from the coal having higher

$CaCO_3$ and $FeSO_3$ content was observed because the acidic condition of coal simply neutralized by available $CaCO_3$ leading to less acid available for iron solubilization and cannot become bioavailable (Huang et al. 2005; Zhang et al. 2002; Aladdin et al. 2013). Also, it was observed that, released Fe^{2+} in acidic pH conditions, acted as the primary oxidant thus escalating the pyrite oxidation process (Huang et al. 1998) followed by maximum bioavailability of iron. Furthermore, higher pH (Huang et al. 2005) and low-temperature oxidation of coal (Elsetinow et al. 2001; Sen et al. 2009) would facilitate ferrous and ferric ion oxidation and leads to the formation of goethite (FeOOH), which is water-insoluble and thus limited the more iron bioavailability. Other factors such as humidity, ageing period and grinding duration of coal (pyrite particle size) and pH were also manipulating the formation and stability of BAI (hydrated FeSO4) which resulted in oxidation of pyrite. Briefly, 15- and 30-min air grinded pyrite powder divided and allowed to age (to be oxidized with oxygen) in saturated solution further these saturated solutions allowed to establish relative humidities of 5.7%, 57.6% and 89.8% respectively. Aged pyrite particles of 15 and 30 min grinding and respective humidities mixed with three coal samples and oxidizing activity of suspension filtrated of pyrite-coal mixtures (Gardanne suspension, Escarpelles suspension, La Mure suspension) were evaluated. Results showed the highest oxidizing activity measured through electron spin resonance (ESR) in Escarpelles and La Mure suspensions compared to Gardanne suspension containing equal aged pyrite. Moreover, the pyrite oxidation activity as a function of relative humidity and time were reported higher for 30 min grinding and 89.8% of relative humidity while it was decreased for 15 min grinding and decreasing humidity (57.6% and 5.7%). Whereas the maximum change in pH from 7.18 to 3.05 and 6.53 to 3.04 were observed in high oxidizing pyrite-coal suspensions (Elsetinow et al. 2001; Huang et al. 1994). All such physiochemical conditions of coal were reported as influencing factors for the bioavailability of iron from coal.

2.3.2 Environmental Stability of BAI

The stability of iron once released as a result of pyrite oxidation depends upon the pH and air exposure in the coal dust (Huang et al. 1994). Stability of BAI i.e. Fe^{2+} was also influenced by the rate of oxygenation (Singer and Stumm 1970) of Fe^{2+} to Fe^{3+} which was higher and immediate in the high pH condition where $CaCO_3$ neutralizes the acid (Cohn et al. 2006; Huang et al. 2005; Zhang et al. 2002) available from the initial steps of Fe_2S oxidation. Besides that, a half-life of 3 years was reported for BAI at pH 3 i.e. $pH < 4.5$ has been optimum for BAI stability while BAI gets precipitated at $pH < 4.5$ and 8 min of half-life was reported at neutral pH 7 (Aladdin et al. 2013; Huang et al. 1994). Again, the study showed maximum stability of Fe^{2+} in low buffering capacity coal which release Fe^{2+} from the exposed coal dust in the phagolysosomes of macrophages and subsequent phagocytosis due to the acidic environment of macrophages (Huang et al. 1998). The environmental, as well as biological stability of BAI, facilitates its involvement in the mechanism of coal dust induced lung impairment in the mining workers. This is one of the concerning health

factors associated with coal mine dust and acid mine drainage which needs to be overcome at the mine level.

3 Pathophysiology of CWP

The CWP is a slowly progressive parenchymal lung disease comprising a variety of pulmonary radiological and pathological changes caused by the inhalation of toxic coal mine dust (Zosky et al. 2016; Lassalle et al. 1989). A strong relationship has been associated between inhaled doses of respirable toxic coal dust for working lifetime by miners' and the risk of developing various forms of CWP with its rate of progression i.e. simple CWP and complicated CWP or PMF (Zosky et al. 2016; Zheng et al. 2017; Antao et al. 2005; Lassalle et al. 1989; Fujimura 2000). The mechanism of pathophysiology in the occurrence of CWP was well studied and dominated by the preceding oxidative potential of inhaled toxic coal dust and subsequent implications of the inflammatory processes (Zhang et al. 2002; Dalal et al. 1995; Lassalle et al. 1989; Fujimura 2000; Huang 2011; Lee et al. 2002). However, the characteristics and inhalation course of toxic dust are required to understand the scenery system of disease.

3.1 Characteristics of Toxic Dust and Inhalation Mechanism

In coal mining, especially in underground coal mines, emission of dust and density is much higher in coal working segments or front galleries and its level decrease to coal extraction galleries. Whereas, higher dust dispersion has been found in open-cut mines. The impact on human health (lung diseases) of coal dust varies with the size, morphology and mineralogical composition of inhaled particulate matter. Respirable dust fraction < 4 μm has been accepted widely, as finer dust particles easily entered the pulmonary system causing higher penetration at alveolar space (Trechera et al. 2020) and able to stimulate ROS which can create oxidative cellular damage and initiate pulmonary inflammation (Valavanidis et al. 2008). A review study on CWP and coal rank mentioned the maximum surface oxygen content, higher electrostatic charge and smaller particle size with larger surface area usually associated with fresh fractured high-rank coal. The charging characteristics of coal dust showed enhanced respiratory deposition and toxicity of airborne respirable particles and the increased incidence of CWP (Gamble et al. 2012). Maximum depletion of ascorbic acid (AA) and reduced glutathione (GSH); an important antioxidant found within respiratory tract lining fluid (RTLF) were recorded for the coal dust has a higher composition of particulate matter (PM) < 4 μm than the dust with more PM > 4. The amount of oxidants generated by coal dust or PM is associated with the size of particles; fine particles having a larger surface area for oxidation reactions compare to bigger PM (Trechera et al. 2020). An appropriate relationship between particle size and the

toxicity mechanism of coal dust was proven by the in vitro study conducted on the A549 cell line. Size segregated coal fly ash (CFA) fractions (<1 μm, <2.5 μm, 2.5–10 μm and >10 μm) from three different mining regions (Utah, Illinois, and North Dakota) were tested on A549 cell line for induction and synthesis of inflammatory cytokine, interleukin-8 (IL-8) and amount of ferritin concentration in cells. In results, ferritin concentrations were recorded 1.4, 1.3 and 1.3 fold higher for the CFA fraction of <1 μm exposed cells than <2.5 μm fraction treated cells of Utah, Illinois, and North Dakota CFA, respectively. Moreover, the level of IL-8 in cell growth mediums exposed with CFA fraction of Utah, Illinois, and North Dakota were found to be 1.6, 1.9, 1.4 fold higher than the levels of IL-8 with the <2.5 μm fractions of the same coal type. Results have summarized that the amount of IL-8 secretion and ferritin concentration induced by CFA were reliant on the type of coal bioavailability of iron from the particles, with utmost response to smaller size fractions which released maximum amount of iron (Smith et al. 2000). The characteristics of coal mine dust samples including its ash content, the size distribution of particles, type of dust, clay mineral content, trace element content, wettability, surface carbon and oxygen content, explosion tendency, specific surface area were examined and showed its possible health impact. Two underground coal dust samples collected from return airways locations of mines namely JLS-3 and LTS from Jiulishan and Lutaishan coal mines located in China respectively contain high amounts of ash, whereas the relation between dust particles was agglomeration and adhesive type. Both the samples also had higher clay minerals and the greatest wettability. The surface carbon and oxygen element content of LTS was lowest, 53.76% and the highest 43.75% were recorded. The specific surface area for LTS was highest i.e. >400m^3/kg and for JLS-3 was 350–400m^3/kg which indicates both the dust samples had higher explosion tendency. Moreover, the particle size distribution proportions of PM10 were 58.95 and 60.09% respectively for JLS-3 and LTS samples which were fine types and highest among the all studied samples. These characteristic measures of dust particles are indicating their toxicity, however, the proportion of fine particles >10 μm in both samples were highest, indicating more harm by directly entering the respiratory tract and alveoli causing permanent lung injury (Su et al. 2020).

Miners exposed continuously to high-density dust concentrations with the maximum composition of respirable PM are prone to getting chronic inhalation doses and the greatest dust deposition in the lung parenchyma. The inhalation mechanism associated with this dust mostly depends upon the particle size and its density in the exposed environment (Mukherjee et al. 2005; Huang et al. 2005; Lee et al. 2002). The US Environmental Protection Agency and other agencies in the air pollution regulation proposed two main categories of PM such as $PM_{2.5}$ which refer to particles with an aerodynamic diameter (a.d.) <2.5 μm and PM_{10}. The human respiratory system is divided into an extrathoracic (oro- or nasopharyngeal) region where the PM_{10} has been deposited, the tracheobronchial tree (cylindrical airways) where the particle with a.d. between $PM_{2.5}$–PM_{10} has been restricted while the last acinar (alveoli, gas-exchange section) region which is most important for $PM_{2.5}$ and ultrafine (<0.05 μm) particle retention and disease progression (Trechera et al. 2020; Valavanidis et al. 2008; Su et al. 2020). Some important factors are associated with

the inhalation mechanism and particle toxicity which includes the chemical and morphological properties of the dust, particle durability and leaching, particle deposition and translocation. Also, the host factors such as lung volume, breathing rate and depth, and particle clearance via mucociliary and interstitial "lymph nodes" clearance routes are deliberating with the severity status of toxicity induced with inhaled dust (Schins RPF and Borm PJA 1999). Such inhalation mechanism and amount of dust deposited at each pulmonary region can be correlated with the histopathological alteration or biopsy evidence of confirmed CWP cases. Moreover, the dust permissible limit in mines of coal-producing countries is varying from 1–3 mg/m^3 and somewhere 4 mg/m^3 which influenced the dust inhalation pattern and frequency of CWP cases in the globe (Fourteenth Report 2015; IARC 1997). However, the biochemical and molecular changes of CWP come into the picture at letter stages of exposure which strongly facilitate the understanding of definite pathophysiological mechanisms linked with CWP.

3.2 Biochemical and Immunological Aspects

The CWP is considered as one of the human lung pathologies related to oxidative stress (Gamble et al. 2012; Fujimura 2000; Huang 2011; Lee et al. 2002; Valavanidis et al. 2008). Oxidative stress and inflammation are reported to be the most important part of the development of fibrotic damage to the lung tissue in coal dust-induced CWP (Schins RPF and Borm PJA 1999; Lassalle et al. 1989; Fujimura 2000; Huang 2011; Valavanidis et al. 2008). There is an acceptance of the concept of the implication of the inflammatory process in the development of pneumoconiosis. The iron present in the coal reacts with the O_2/H_2O_2 (Cohn et al. 2006; Gamble et al. 2012) when inhaled by the lung to form ROS. These ROS are the mediators which stimulate the activation of alveolar macrophage (AM) and other immune cells (Schins and Borm 1999; Fujimura 2000; Huang 2011). In turn, the activated macrophages are either clear by the lysosomal enzymes or tend to release cytokines. The secretion of these cytokines by the AM as well as lung epithelial cells exposed to coal dust mediate the pathogenesis of CWP. Moreover, oxygen radicals, lysosomal enzymes, inflammatory cytokines, and other pro-inflammatory and pro-fibrotic mediators initiate the process of alveolitis and followed by reparative and fibrotic phase, which stimulates the growth factor and overproduction of fibronectin and collagen, resulting in the development of fibrosis (Zheng et al. 2017; Huang et al. 2002; Aladdin et al. 2013; Schins and Borm 1999; Fujimura 2000; Huang 2011). Thus, oxidative stress and inflammation are the most important parts associated with the pathophysiology of CWP.

The oxidative degradation of RNA molecules was reported by the action of *OH molecules which were generated as a result of H_2O_2 oxidation through soluble Fe^{2+} released from the pyrite crystal associated with coal (Cohn et al. 2006). High BAI containing coal dust induced activation of transcription factors (AP-1 and NFA) which regulates inflammatory cytokines secretion were found to be associated with the high level of oxidative stress generation (Huang et al. 2002). The author reviewed

the possible intracellular or biological mechanisms involved in the progression of CWP and PMF. They proposed that reaction of coal dust with macrophages cells eventually resulted in the membrane lipid peroxidation and releasing the intracellular enzymes which effectively obliterate the alveolar septa of lung tissue. Another step is the secretion of fibrogenic factors from AMs and epithelial cells exposed to coal dust. These fibrogenic factors are responsible for the development of lung fibrosis (PMF) via fibroblast proliferation and collagen deposition. Also, the pulmonary phagocytosis of coal dust by AMs stimulates cytokine secretion leading to the production of oxidant species, which destroy antioxidant defences mechanism resulting in lipid peroxidation and lung scarring (McCunney et al. 2009).

The biochemical and immunological changes and concerned mediators involved in the pathology of CWP and PMF induced by coal dust were studied by several scientists and proposed the mechanism of associated inflammation. In brief, inhaled coal dust particles stimulates the activation of phagocytes, leads to generation of $O_2{}^{*-}$ and ROS (Huang et al. 2005; Schins and Borm 1999) which further shown to induce the proinflammatory cytokines, tumor necrosis factor-alpha (TNF-α) (Schins and Borm 1999, 1995; Smith et al. 2000; Zhai et al. 1998, 2002; Lassalle et al. 1990), interleukin-1beta (IL-1β) (Schins and Borm 1999; Lassalle et al. 1990), interleukin-6 (IL-6) (Schins and Borm 1999; Zhai et al. 2002), interleukin-8 (IL-8) (Schins and Borm 1999; Smith et al. 2000), monocyte chemotactic protein-1 (MCP-1), transforming growth factor-beta (TGF-β) and intercellular adhesion molecule-1 (ICAM-1) (Schins and Borm 1999) and finally resulted into fibrotic tissue. Specific roles of these molecules in the pathophysiology of disease are shown in Table 8 and the networking of cytokines in Fig. 4.

3.3 Lung Burden and Histopathological Alterations

The CWP is a major inflammatory disease caused by activation of challenged macrophages and effectors molecule in response to coal mining dust. There is experimental evidence on the correlation between silica content in coal and fibrogenic activity in the lungs. Irrespective of silica, pyrite content in coal releases BAI and induced ROS production, which worsens the condition of miners and epidemiologically defined the dose–response relationship between coal dust exposure and CWP prevalence (Cohn et al. 2006; Huang et al. 2005; Zhang et al. 2002). The proposed dust transport mechanism in the lung parenchyma is through erosion of the bronchiolar wall and rupture of the lymph node capsule. Laboratory in vivo studies (King et al. 1958; Kolling et al. 2011; Green et al. 2007; Pinho et al. 2004; Caballero-Gallardo and Olivero-Verbel 2016) was reported the pathological changes in animal lungs exposed to different doses of respirable coal dust.

An acute dose of pure saline (control) or coal dust (iron 2.48% and silica 27.3%) at 3 mg/0.5 ml saline directly exposed by intratracheal instillation in rats, were showed peribronchial tissue and interstitial septa without important alteration in a control group, Fig. 5a1 and a2. Peribronchial and perivascular inflammatory infiltration with

Table 8 Coal dust induced inflammatory mediators/cytokines, their source of origin and role in pathophysiology in pulmonary diseases

Mediators/Cytokines	Source/Origin	Role in pulmonary diseases
TNF-α	Alveolar macrophages Monocytes	Primary mediator of lung inflammation, Alter cell migration and permeability, Production of secondary mediator IL-6 and IL-8, MCP-1and ICAM-1, Chemoattractant, Associated with fibroblast growth and collagen gene expression
IL-1β	Alveolar macrophages Epithelial cells Monocytes	Proinflammatory mediator, Induced secretion of TNF-α and increase the level of mRNA of IL-8, Associated with fibroblast growth and collagen gene expression
IL-6	Alveolar macrophages	Secondary mediator of lung inflammation, Induces T-cell activation and proliferation, ICAM-1
IL-8	Alveolar macrophages	Secondary mediator of lung inflammation, Chemotactic for eosinophils, neutrophils, T-lymphocytes, and basophils
MCP-1	Alveolar macrophages Epithelial cells Fibroblasts cells Monocytes,	Induce IL-6 secretion, Chemoattractant for monocytes
TGF-β	Alveolar macrophages Monocytes Neutrophils	Induced fibroblast growth and proliferation Production of collagen and fibronectin
ICAM-1	Endothelial cells Bronchial and alveolar epithelium Alveolar macrophages	Leukocyte recruiting factor, involved in fibrosis

macrophages in alveolar space at 7th day of (3 mg coal/ 0.5 saline) installation shown in Fig. 5b1 and b2, while at the 30th day, infiltration of alveolar giant cell and macrophage were observed shown in Fig. 5c1 and c2 (Pinho et al. 2004).

Scientists have different opinions in association to parenchymal changes and the magnitude of coal dust induced lung pathologies. However, exposure history and respiratory symptoms with lung imagining, computed tomography scan and pulmonary function testing could be clinical basics for the diagnosis of simple CWP and other coal dust-related fibrotic lung diseases (PMF and DDF: Dust-related diffuse fibrosis) (Petsonk et al. 2013; Gorman and Cagle 2018).

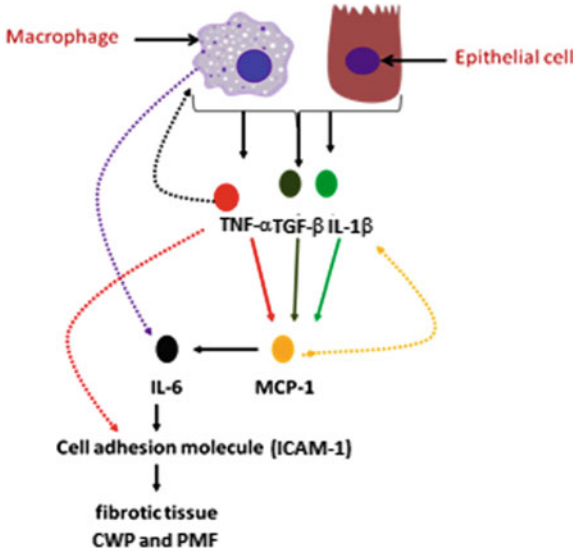


Fig. 4 Pulmonary networking of cytokine in coal dust induced CWP and PMF

The inflammatory and fibrotic lesions with emphysema to be found in the lining of a respiratory bronchiole in biopsy spacemen of lung shown in Fig. 6a, which have been proposed specific histopathological alterations for CWP. Whereas, coal nodule associated scar and prominent fibrosis associated with collagen bundle and abundant infiltration of macrophages shown in Fig. 6b were noted for complicated CWP. The study also reported focal emphysema; enlarged air spaces adjacent to coal nodule in lung parenchyma shown in Fig. 6c which also found to be associated with all types of CWP pathologies (PMF and DDF) (Gorman and Cagle 2018). The possible reason behind emphysematous lesions in lung parenchyma is the uncontrolled proteolysis of lung tissue by the elevated level of trypsin. The inactivation of α1-antitrypsin (α1-AT) through oxidative stress generated as a result of pyrite containing coal dust exposure and generation of oxidant species was the basics associated with the proposed reason of lung emphysema in CWP suggested in an experimental research study (Huang et al. 1994).

4 Possible Diagnostic Biomarkers for CWP

Several incurable diseases are associated with older workers having a prolonged history of respirable air-borne dust exposure. Some diseases of coal miners such as CWP and PMF are non-reversible and prevention is supposed to be the best remedial step. Biomarkers play a great role to improve the early identification of risk assessment and disease prevention in the mining environment. The Committee on Biological Markers of the National Research Council (NRC) in the United States of America

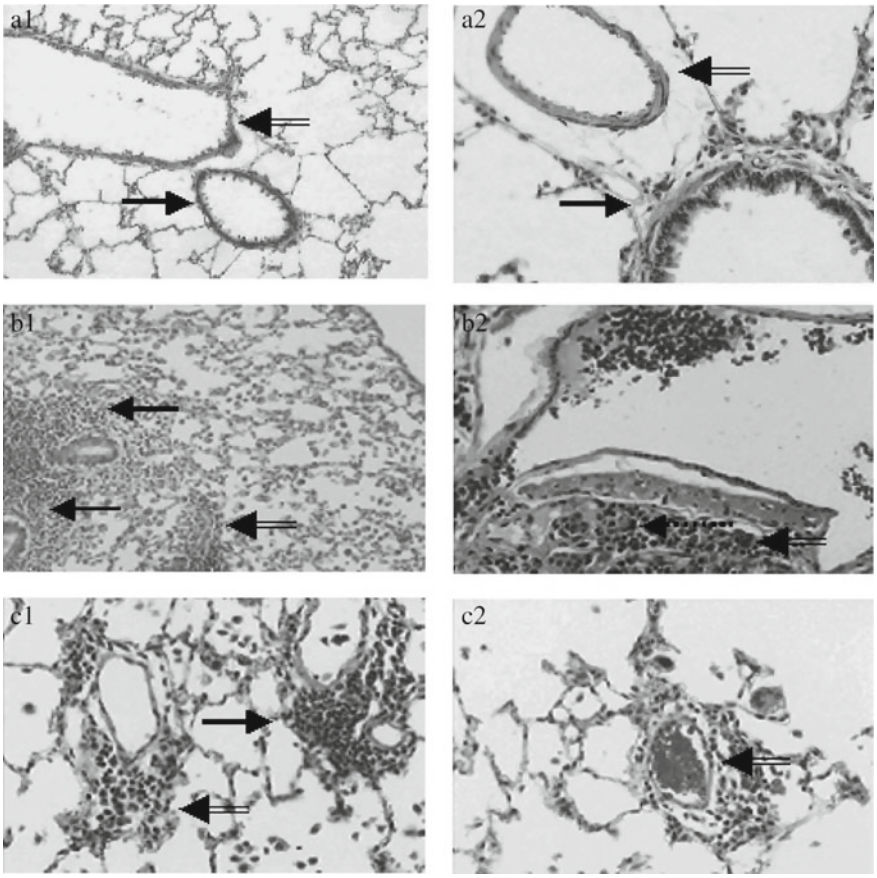


Fig. 5 Histopathological alterations in animal lungs exposed with normal saline or iron-containing coal dust

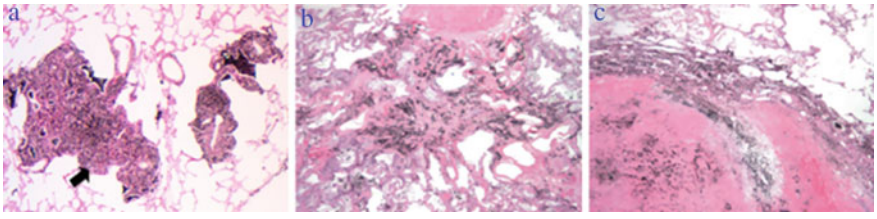


Fig. 6 Human lung histopathological illustrations noted for simple and complicated CWP, PMF and DDF

has defined biomarkers as "Indicators of variation in cellular or biochemical components or processes, structure or function that are measurable in biologic systems or samples" (NRC 1989). Several epidemiological human studies and in vivo animals as well as in vitro cell line experimental studies proposed the utilization of biomarkers for early diagnosis and validation of CWP and PMF. Moreover, biomarkers may indicate the principal steps between exposure of coal dust and resultant lung pathologies in miners (Gulumian et al. 2006; Ayaaba et al. 2017).

In detail, coal dust induces the oxidation process resulting in the production of varieties of oxidants. To scavenge these oxidants, the activity of several antioxidant enzymes such as glutathione peroxidase (GPx), superoxide dismutase (SOD), has been elevated. The level of lipid peroxidation has also increased with respect to increased oxidants. Estimation of these enzymes would act as a biomarker for early diagnosis of CWP in pyrite or bioavailable iron-containing coal dust exposed populations (Zhang et al. 2002; McCunney et al. 2009; Dalal et al. 1995; Gulumian et al. 2006). Bioavailable iron ($FeSO_4$) induced activation of AP-1 and NFAT were reported in the coal dust exposure in vitro JB6 mouse epidermal cell line. Increased levels of these transcription factors in the cell growth medium can translate it as a human serum biomarker for CWP. Moreover, increased ferritin levels in serum can confirm the role of iron in CWP (Huang et al. 2002). TNF-α and IL-1β are proinflammatory cytokines, expressed in the early onset of lung inflammation induced by coal dust. Several studies confirmed the validity of both cytokines as a biomarker in coal miners having CWP (Schins and Borm 1995; Zhai et al. 2002; Lassalle et al. 1990; Gulumian et al. 2006). IL-8 and IL-6 act as a secondary mediators of lung inflammation. Increased level of IL-8 in human lung epithelial cells (A549) induced by high BAI containing coal dust was reported and positively correlated with the higher prevalence of CWP in the same coal mine region (Smith et al. 2000). Another case–control study showed a significantly elevated level of IL-6 in retired coal miners classified with CWP (Zhai et al. 2002). Both IL-8 and IL-6 were proposed as attractive additional serum markers for CWP especially when measured along with TNF-α and IL-1 (Gulumian et al. 2006). Other biomarkers such as platelet-derived growth factor (PDGF) and transforming growth factor (TGF) which showed their role in collagen deposition and fibrosis in the lung. The expression of these biomarkers has been associated with late inflammatory responses and can be utilized as a diagnostic marker for pulmonary fibrotic diseases (Schins and Borm 1999; Gulumian et al. 2006). These stage-specific biomarkers are found to be associated with the prognosis of CWP and PMF. Though several epidemiological and experimental results proved the possible role of such biomarkers in the early diagnosis of these diseases, more adequate data on human studies are necessary to confirm the use of these peripheral blood biomarkers in non-invasive routine medical examinations in dust exposed workers.

5 Preventive Measures

The mining operations are inevitable; these cannot be stopped as long as mining is active and workers are supposed to work in the active mining areas, where dust is constantly generated. Chronic exposure to mining dust often leads to untreatable pulmonary diseases amongst active mining workers and surrounding populations located near mining areas. Therefore, different preventive measures are needed to be taken at several mining stages and activities. However, identification of significant risk factors associated with coal workers lung diseases and their relevant medical understanding is a must to assist reduce the mining hazards. Following are the various preventive approaches proposed to counter the coal mine dust-related occupational health hazards.

Preventive measures at beginning of active mining

- Geographic locations and related biodiversity should be taken into account before mine planning.
- Identification of toxic components i.e. traces metals and their concentration in coal or associated with coal seams.
- Grading of mine according to associated toxic components in coal. i.e. pyrite or BAI.
- Involvement of innovative engineering approaches in mine design and progression which minimize mining hazards.

Preventive measures during active mining

- Effective guidelines to use mechanical equipment as a replacement for human workers at mining activities associated with high levels of dust generation.
- Dilution of dust density with proper circulating aeration and ventilation in underground mining.
- Use of vigorous dust suppressing interventions in mining regions e.g. continuous water spraying over active coal harvesting phase, haulage road, coal transportation route, coal storage and other dusty areas.
- Calcite present in certain coals can prevent acid solubilization of iron compounds. Spraying with an aqueous mixture of calcium (active element in calcite) and water may actively reduce iron bioavailability from coal dust before inhalation and thus, may play a protective role in CWP.
- Chemical and biological leaching of toxic metal from coal before its industrial use and combustions, also reduce the emission of toxic pollutants in the environment.
- Neutralizing the acidic mine water and leaching of toxic components before drainage into surrounding water bodies.

Preventive measures regarding occupational safety and hygiene

- Organizing brainstorming sessions for mineworkers towards encouragement for personnel hygiene and safety with eliminations of poor hygienic practices.

- Research innovations in the development of authentic and handy protective equipment/accessories against dust exposure.

Clinical measure to mitigate incidence and severity of respiratory diseases of coal workers'

- Identifying the key risk factors, their role in disease mechanism, pathophysiological assessment of diseases, use of early responded diagnostic biomarkers and routines medical checkup of disease suspects are the whole cascade that may prevent the disease incidence and prevalence.
- Mine rules and regulations associated with mining hazards should be improvised with results of several epidemiological and experimental researches conducted on mining populations.
- Periodic medical examinations frequency should be increased in high CWP prevalence regions.
- Identification of disease-prone workers using early diagnostic non-invasive biomarkers is one of the promising approaches toward the development of a reliable medical management plan.
- Following the international rules and criteria for CWP diagnostic using reliable tools (e.g. lung spirometry, radiography, test in BAL fluids etc.) which assist the disease discrimination with other related diseases.

With the identification of the crucial role of pyrite in aggravating CWP, further research studies need to conduct a more reliable quantitative analysis of coal and associated components with their correlation in chronic lung diseases. Primary health measures and enactment of laws and regulations determined by various mine safety acts of different countries should be properly employed in coal mines. Also, disease surveillance, dust exposure control and compensations to miners are important aspects related to the control of CWP (Ayaaba et al. 2017). Moreover, the disease prevention program in the mining population should involve national and international co-operations, government bodies, research communities and social organizations along with health compensations and insurances under judiciary, healthcare and physicians.

6 Summary

Coal workers' pneumoconiosis (CWP) is an untreatable but preventable lung disease commonly encountered in coal miners. It is one of the oldest occupational lung diseases where the first case of CWP was recognized in 1822 as 'miner's asthma' and the first case report was reported by Gregory in 1831. Earlier epidemiological studies and surveys including active coal workers as well as retired workers as subjects concluded that the quartz or silica fractions present in coal seams is the key risk factor associated with CWP. These findings were also supported by several experimental laboratory and autopsy studies. Many scientists had studied the coal composition and

associated hazardous components which were found to be responsible for dust-related diseases. These occupational health-related investigations have mainly focused on the quartz, clay mineral and some silicates concentrations in coal. The research published in the last 3–4 decades from different countries clarified the uncertainty associated with coal components responsible for the development of CWP. These studies reported the high prevalence of CWP in coal miners working in coal regions where negligible quartz concentration is present in coal. In recent decades, some experimental and epidemiological data on coal miners' lung diseases and associated risk factors proposed the significant correlation between iron content in coal and the higher prevalence of CWP.

Chronic inhalation of coal dust is the utmost cause of CWP occurrence in coal miners. However, its pathological and biochemical mechanisms were not known earlier. At the end of the twentieth century, the reported evidence showed the bioavailable iron (BAI) present in coal dust and ash has been associated with the generation of oxidant radicals in an aqueous medium. Later, at the beginning of the twenty-first century, several epidemiological studies confirmed the high prevalence of CWP in coal mine regions having maximum bioavailability of iron from coal. Iron is a redox metal mostly combined with sulfur to form pyrite which is an iron sulfide mineral contributed as an inorganic part of coal. Oxidation of pyrite (FeS_2) resulting in the release of water-soluble iron which participates in most of the reversible one-electron oxidation–reduction reactions by switching between the two oxidation states i.e. ferrous (Fe^{2+}) and ferric (Fe^{3+}), also known as BAI. Inhaled coal dust particles have been settled in alveolar spaces where its phagocytosis by macrophages further resulted in the release of BAI from pyrite in an acidic phagolysosomal environment. The redox potential of BAI contributed to the development of oxidative stress which eventually triggered the inflammatory processes in the lung. As a result of inflammation, the pulmonary structure got hampered and showed normal i.e. simple CWP to severe (complicated CWP or progressive massive fibrosis) pathological alterations in the lung. The severity of CWP has been also associated with the number of inhalable coal doses throughout the working professional, the composition of the inhaled coal dust and the lifestyle of coal workers.

The prevalence of CWP varies according to coal rank, geological locations of mines and working occupation of miners at mining workplace along with pyrite content in coal. The data published by various government and occupational health-related agencies of coal-producing countries can be accounted for in estimating the global burden of CWP and the death rate. Such global data on death, caused due to CWP has been published in one of the highly reputed medical journals; Lancet which showed more than 28,000 deaths up to 1990 and 25,000 up to 2013 reported for CWP. The top coal producing countries including China have reported 127,368, USA; 37,965, Australia (Queensland); 26 and India; 1,317 confirmed CWP cases of International Labor Organization (ILO) category from 1980 to 2015. Several studies and health surveys have been commenced in different coal mining regions of various countries to elucidate the prevalence of CWP, but the actual prevalence of CWP could not be obtained precisely, which is the drawback for health care programs and

miners safety. The lack of implementation of diagnostic criteria and the burden of heavy compensation benefits might be the reasons behind this drawback.

The CWP is a worldwide concern for the occupational health of miners working in coal industries. Prevention is the primary means to tackle this incurable lung disease. Proper implementation of occupational safety rules and laws, dust management controls, utilization of respiratory equipment for minimizing dust inhalation, and removal of toxic components from coal before its final utilization are some preventive measures that can be taken at the mining workplace. Whereas, awareness about personal hygiene and skill improvement for safe mining along with consistent training for miners will also reduce the CWP scenario at the mine level. Despite these preventive approaches, conventional periodic health examinations which have been designed and conducted for mining populations should be modernized. It could be updated with the addition of early diagnostic biomarkers and trustworthy medical diagnostic parameters of ILO standard, which will advance the efforts taken for CWP delineation. However, identification of important risk factors allied with CWP prevalence and understanding the disease progression mechanism are key aspects to develop a reliable medical management plan to counter this problem. Further, the execution of compensation rules with appropriate regulations and free health care plans will improve the economic as well as the living status of coal miners.

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Tuberculosis in Mine Workers: Advances in Current Diagnostic Landscape

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1 Statement of Problem

India is regarded as the highest TB burden country accounting quarter of all worldwide TB cases. One of the major reasons for high TB incidences includes a lack of adequate tools for diagnosis of TB especially in high-risk populations from TB endemic settings. Mine workers in India constitute a significant part of the global workforce but are associated with considerable risk for the development of TB due to poor living and working conditions along with the high prevalence of occupational diseases. Lack of health surveillance combined with high associated risk factors makes miners as one of the most vulnerable populations for TB infection. Identification of novel diagnostic biomarkers for early prediction of latent and active TB infection along with monitoring disease progression and treatment outcomes have been endorsed by WHO in its current TB diagnostic landscape and End TB strategy millennium goals. In the present chapter, we highlight the diagnostic utility of existing diagnostic tools along with newer biomarkers for diagnosis of TB infection.

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_3

2 Introduction

Tuberculosis (TB) is a global infectious disease of significant public health importance. TB is caused by the bacterium ***Mycobacterium tuberculosis*** (MTB) which is aerobic, non-motile, non-spore-forming, road shaped bacilli and belongs to the group of closely related mycobacterium species (***M. bovis.*** **M.** ***africanum, M. microti, M. caprae, M. pinnipedii, M. canetti and M. mungi***) known as Mycobacterium TB complex (MTBC) (Delogu et al. 2013). TB is an airborne disease and is often carried in airborne particles (1–5 microns size) referred to as droplet nuclei generated by coughing or sneezing from the infected individual. MTB typically infects the lungs also known as pulmonary TB (PTB) (Jilani et al. 2020). Although PTB is the most common manifestation of TB, in certain cases bacteria can spread to other sites of the body via the bloodstream and establish infection leading to a condition known as extra pulmonary TB (EPTB). In India, around 15–20% of all TB infections are contributed by EPTB (Purohit and Mustafa 2015). Episodes of EPTB infection are more frequent in people living with human immunodeficiency virus (PLHIV), where it accounts for 50–60% of TB infections (Prakasha et al. 2013). Among the various EPTB forms, infection of meninges in the central nervous system (CNS) also known as Tuberculosis Meningitis (TBM) or miliary TB has been regarded as most fatal and is often associated with high neurological morbidity and mortality rates (Husain et al. 2017). Other common EPTB infections reported include Bone TB, Spine TB, Ocular TB, Pleural TB, Genital TB, lymph node TB, Skin TB, Adrenal TB (Addison's disease).

Globally MTB has been regarded as the major etiological pathogen for a majority of human TB infections except in West African countries where ***M. africanum*** is commonly found (Sharma et al. 2016). In recent times, with the advent of the newer diagnostic tools, other species of mycobacteria such as *M. bovis* has been recognized as an emerging pathogen responsible for causing zoonotic-TB in humans (Bapat et al. 2017). Group of Non-Tuberculous mycobacteria (NTM) species also known as environmental mycobacteria are also among other emerging pathogens that have been reported in PTB and EPTB infection among both immunocompromised and immunocompetent populations especially in high TB burden countries (Maurya et al. 2015).

3 Historical Perspective

TB is regarded as the oldest known human disease with some reports postulating its origins dating back to 150 million years (Barberis et al. 2017). The earliest evidence of TB infection dates back to 2400 BC in Egypt, where the remains of mummies with deformities typical of TB disease was found. (Barberis et al. 2017). TB has also reference in early biblical books as "*schachepheth"* (Daniel and Daniel 1999). In the middle ages, TB illness was known as "Kings Evil" in England and France

(Murray et al. 2016). In the early days, TB was also known by "Consumption" (Greek term "phthisis") (Barberis et al. 2017). In India, the earliest documentation regarding TB dates back to 3300 years ago (Kashyap et al. 2013a). In early Vedic medicine, TB was described as Yakshma, which was subsequently renamed in Ayurveda as 'Rajayakshma' meaning king of the diseases (Debnath et al. 2012). In the seventeenth century, the first anatomical and pathological description of TB illness was provided by Francis Sylvius (Barberis et al. 2017). The word "Tuberculosis" was coined in the late 19th Century by Johann Lukas Schönlein (Pioneers 2000). In 1882, the causative pathogen responsible for TB was isolated by German physician Robert Koch, who termed it MTB, hence MTB is also known as Koch's bacillus or Tubercle bacilli (Barberis et al. 2017). MTB has been regarded as an evolutionary specialized form of ***M. bovis*** which is believed to be transmitted by TB infected cattle to migratory Indo-Europeans in Western Europe and Eurasia (Kashyap et al. 2013a).

4 Global Epidemiology of TB

Despite available vaccine and drug treatment, an estimated quarter of the world's population is believed to be harbouring TB infection (Husain et al. 2016). In 1993, TB became the only disease to be declared a global health emergency by the World health organization (WHO). As per the WHO Global TB report 2020, an estimated 10 million people were infected with MTB in 2019 accounting for over 1.2 million deaths (WHO Global tuberculosis report 2020). TB has also been regarded as a major cause of death in PLHIV. In 2019, estimated 8.2% of overall TB infection was documented in PLHIV with 28,000 deaths (WHO Global Tuberculosis Report 2020). Geographically, three WHO regions namely South-East Asia (44%), East-Africa (25%) and Western Pacific (18%) accounted for almost 87% of all TB infections in 2019 (TB facts.org. 2020). Eight high burden countries namely India, Indonesia, China, Philippines, Pakistan, Nigeria, Bangladesh and South Africa accounted for two-thirds of the global total (Fig. 1) (WHO Global Tuberculosis Report 2020). In the fight against TB, members of states of WHO and the United nation (UN) developed the WHO end TB strategy and UN-sustainable development goals (SDG) in 2014–15 which were further reaffirmed and revised in 2018. The current WHO end TB strategy and UN-SDG are committed to end TB by 2030 which includes global reduction % TB related incidences and deaths by 80% and 90 till 2030.

Drug resistance (DR) in TB represents a formidable obstacle to TB care and prevention and a significant hurdle in global targets of TB elimination. In 2019, an estimated 0.5 million people developed rifampicin-resistant TB (RR-TB) [drug resistance observed to frontline drug rifampicin], out of which 78% had multidrug-resistant TB (MDR-TB) [resistance to two or more front line drugs] (WHO 2020). Out of 500,000 DR cases, an estimated 206,030 were detected and notified in 2019 (WHO Global Tuberculosis Report 2020). The incidence of MDR-TB among high burden countries is presented in Fig. 2. Among the high burden countries, India, China and Russian Federation accounts for almost 50% of all estimated MDR-TB

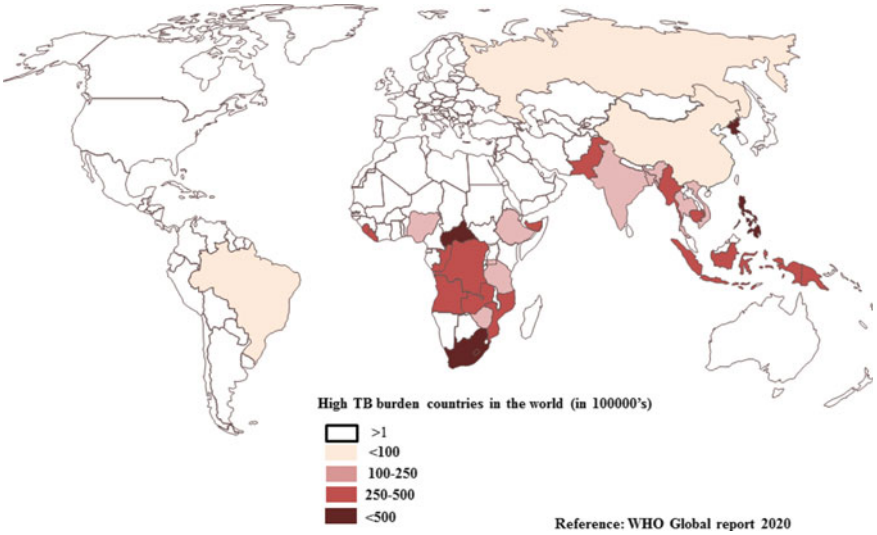

Fig. 1 Global incidence of TB (per 100,000 populations) among high TB burden countries

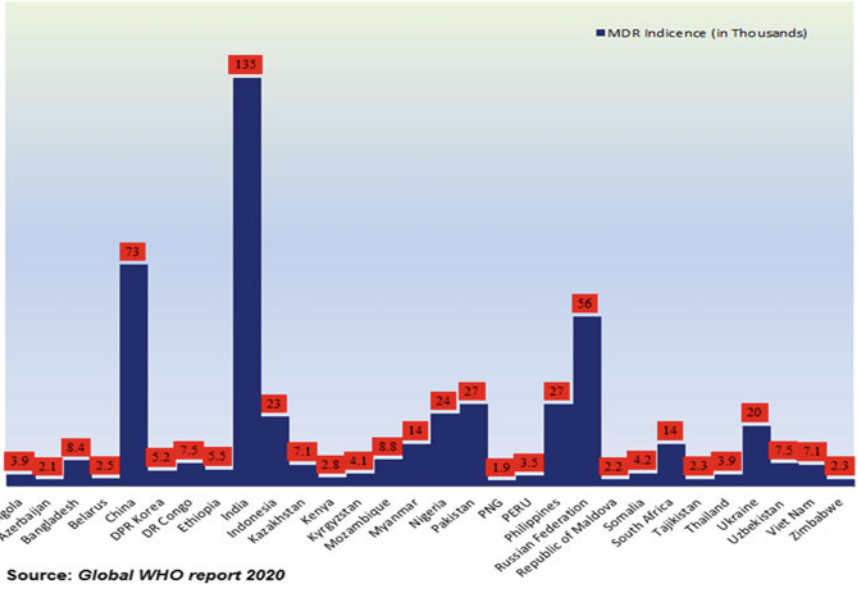

Fig. 2 Global MDR-TB incidence (in 1000) among high TB burden countries

cases (TB facts.org. 2020). The overall incidence of RR/MDR observed was 17.7% in TB relapse cases and 3.3% in freshly detected cases (WHO 2020).

5 TB-India

India is regarded as the highest TB burden Country in the world (Kashyap et al. 2013b). In 2019, an estimated incidence case of TB in India was 2.69 million accounting quarter of all global TB cases (Central Tuberculosis Division 2020). An estimated 79,000 deaths were reported by India in 2019 much lower than WHO estimates of 4.4 million (HIV and in India 2020). India is also the third-largest HIV burden country and globally ranked second in terms of HIV associated TB (HIV-TB) cases (The Times of India 2020). In 2019, an estimated 92,000 TB cases were reported by India, in PLHIV with 9700 deaths accounting for 9% of the global burden (WHO Global Tuberculosis Report 2020). India also accounts for the highest incidence of DR-TB cases. In 2019, India reported 130,000 cases of DR-TB cases accounting for a quarter of all global burden (Central Tuberculosis Division, Government of India 2020). Recent DR epidemiological surveys from India shows a high incidence of RR/MDR-TB of 12–17% among previously treated cases compared to 3% detected among new cases (Fig. 3a) (Chatterjee et al. 2018). Six states namely Uttar Pradesh (18%), Maharashtra (8.7%), Gujarat (6.12%), Rajasthan (6.73%), Madhya Pradesh (6.80%), Bihar (4.70%) contribute half of the overall TB cases in India (Fig. 3b) (TB facts.org: TB India Statistics 2020). TB in India is managed by the central TB division under its National TB elimination programme (NTEP) (formerly, Revised National TB Control Programme (RNCTP). Since its implementation in 1997, the programme has achieved remarkable success in TB care with pan-India coverage

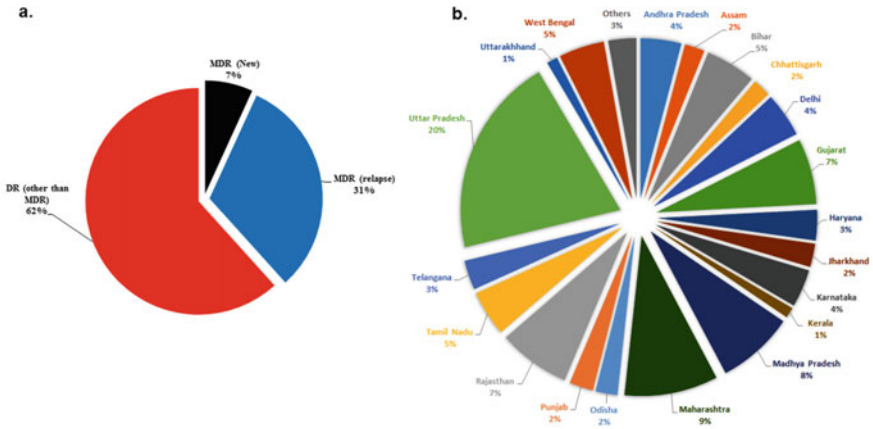

Fig. 3 **a** Incidence of drug-resistant TB in India. **b** state-wise incidence of TB in India based on TB notification rates

accomplished by 2006 (Kashyap et al. 2013a). In 2007, the programmatic management of DR-TB (PMDT, formerly DOTS-Plus) was launched to boost DR-TB care in India, update guidelines for which were release in 2017. In 2014, standards of TB care in India were released which comprised of universal guidelines for TB care for both public and private sectors (WHO 2014). In 2017, India set up its revised national strategic plan (NSP) to eliminate TB by 2025, five years before 2030 set by WHO end TB strategy and UN-SDG. Under the revised NSP goal, India needs to reduce its TB cases by at least 10% every year in comparison with the global target of 2%. Despite significant efforts, a decline in the incidence of TB has remained below the national target. India still contributes around 25% of missing cases globally (WHO Global Tuberculosis Report 2020) despite mandatory notification envisaged by NTEP in 2012. In India, TB has been often regarded as a disease of poverty linked to vulnerable populations living in densely populated high endemic zones. One of the critical challenges influencing the outcome of NSP in India include lack of management and diagnosis of latent TB infection (LTBI) in vulnerable and marginalized populations at risk (PLHIV, malnourished and occupationally exposed). In addition, the emergence of drug resistance represents a significant hurdle in TB elimination, especially with respect to diagnosis and treatment outcome. People with drug resistance requires profound changes in drug regimens compared to drug-sensitive TB cases which are associated with poor treatment adherence impacting the treatment outcome. As a result, the overall treatment success of MDR TB stands significant low (48%) compared to the success rate of drug-sensitive TB as per the national TB report (Yadavar 2019).

6 Active and Latent TB Infection (LTBI) in India

Good host immunity is paramount for the control of TB infection. Upon infection with MTB bacilli, a successfully mounted T-cell immunity can control infection, wherein bacilli remained arrested in a meshwork of various immune activated cells known as granuloma (Ahmad 2011). In this stage, bacteria can be destroyed (~10% cases) and granuloma eventually shrinks leading to calcified lesions in the lung. Alternatively, viable bacteria can remain arrested inside granuloma by surviving host-mediated killing in a latent state for a prolonged period (may be years). This condition is known as LTBI until impairment of host immune response leads to break down of granuloma allowing reactivation of LTBI. Under this stage, bacteria can also immediately disseminate to lungs and other organs establishing active infection with full clinical illness (Salgame et al. 2015) (Fig. 4). The majority outcome (~90%) of MTB infection is the development of latent TB, wherein individual harbours TB bacilli but is usually asymptomatic (Ahmad 2011). Globally estimated 33% of the population is believed to have LTBI (Saha et al. 2019). While there are no exact estimates of LTBI prevalence in India, according to national statistics, roughly 40% of the Indian population harbours TB bacilli in the latent form (TB facts.org: TB India statistics 2020). These statistics represent highly compromised figures possibly due

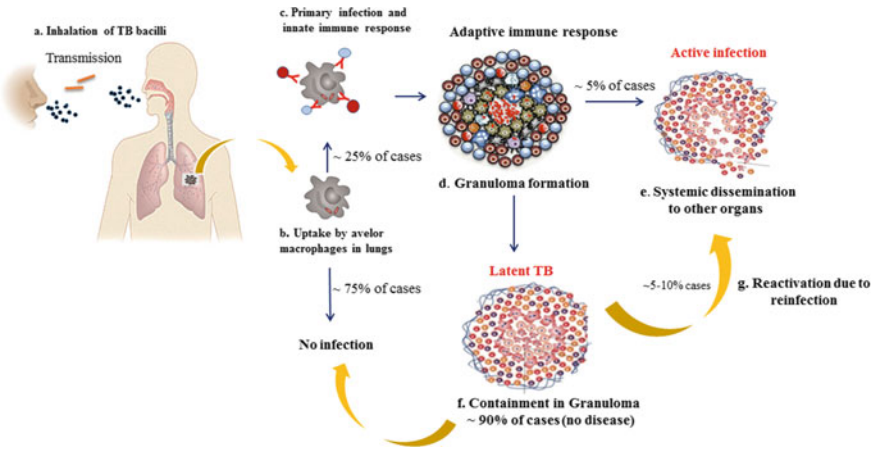

Fig. 4 Immune response against TB infection. Upon inhalation, TB bacilli are phagocytosed by alveolar macrophages. In around 25% of cases, systemic immune response leads to the containment of TB bacilli in granuloma, wherein it can either remain contained throughout a lifetime without any symptoms (90% cases) known as Latent TB or disseminate to other organs leading to active TB. Latently infected individuals carry a 5–10% risk of conversion into active infection due to reinfection an immunocompromised condition

to the lack of adequate and specific diagnostic tools for LTBI. These exposed cases carry a 10% lifetime risk for conversion to active infection thus serving as reservoirs for future TB infection (Kashyap et al. 2016). Moreover, the risk of conversion to active disease further increases in high-risk populations (occupationally exposed, malnourished and PHLHIV) living in endemic settings. The risk of developing an active disease is around five times higher (~50%) in PLHIV (Ahmad 2011; Saha et al. 2019). In countries like India, detection of active cases have remained a key priority for TB control programmes, rather than identification and treatment of LTBI, due to its high prevalence in Indian cohorts. However, it will be more meaning full to treat the target population (high-risk population) having reversible risk factors associated with the development of active TB infection. In India, limited epidemiological data on LTBI exists, especially in high-risk populations. Studies on LTBI in the malnourished tribal population, Melghat and those from TB-endemic settings in Nagpur, show high prevalence in the range of 48–75% (Kashyap et al. 2014, 2016). Lack of specific LTBI diagnosis in such high-risk settings constitutes a crucial gap in the current TB control programme which translates to higher TB incidences in India compared to other high burden countries on the global scenario.

7 Tuberculosis in Miners

7.1 Global Perspective

The mining industry represents one of the biggest industries worldwide. According to the International Labor Organization (ILO), each year around 23 billion tons of minerals are mined from the earth (Joyce 1998). Miners constitute 1% of the global workforce with one-third of them being coal miners (Stemn 2019). Although mining provides us with basic resources for sustaining civilization, it has been associated with a significant impact on human health. Worldwide mining has been regarded most dangerous occupation with an estimated 8% fatality rate reported in miners (Stemn 2019; Lang 2010). Mining occupation leads to the generation of large quantities of particulate matter, in the form of atmospheric dust and aerosols due to various anthropogenic activities. Long term occupational exposure of miners to these vast dust clouds often results in severe lung damage leading to various respiratory diseases. Among the various mining operations, exposure to coal and silica dust among miners have been associated with serious lung complication known as "pneumoconiosis" (Ross and Murray 2004). Pneumoconiosis is a chronic inflammatory lung condition characterized by granuloma formation and fibrosis in lung tissue leading to permanent damage to the lung (Fig. 5). Population-based studies indicate 10–30% of coal miners are associated with coal miners' pneumoconiosis (CWP) also known as Black lung (Joyce 1998). CWP is regarded as incurable and accounts for around 60% of mortality rates in coal miners. (Stewart 2020). Silicosis is another serious lung disease in stone mine workers resulting from inhalation of fine silica dust during mining operations and is regarded as a serious health hazard in both developed and developing countries (Joyce 1998; Ross and Murray 2004; Stewart 2020). Both CWP and silicosis have been linked as major risk factors for PTB in the mining population (Mohapatra et al. 2010).

TB has been regarded as a major health risk associated with mining. Various studies have established TB to be endemic in the mining population due to associated conditions like silicosis and HIV (Mohapatra et al. 2010; Stuckler et al. 2013, 2011). In Africa, the TB epidemic causes a US$570 million per year loss of productivity for the mining industry, with a salary loss of US$320 among the miners (Morgan 2014). While the association of silicosis with TB has been well established, some reports also suggest a high prevalence of PTB among miners with silica or dust exposure even in absence of silicosis (teWaternaude et al. 2006). Majority of mining population include migrant's workers which generally tend to have poor living and working condition. Miners working in an open cast and underground metalliferous and non-metalliferous mines are especially at high risk of acquiring TB disease due to high occupational exposure to silica and coal dust (Dhatrak and Nandi 2009; Roberts 2009). The presence of these associated conditions combined with lack of health surveillance in miners makes them one of the most vulnerable groups for the development of TB infection. According to reports, 40% of PTB infection remains undetected in miners (Stuckler et al. 2013). Despite being a disease of considerable

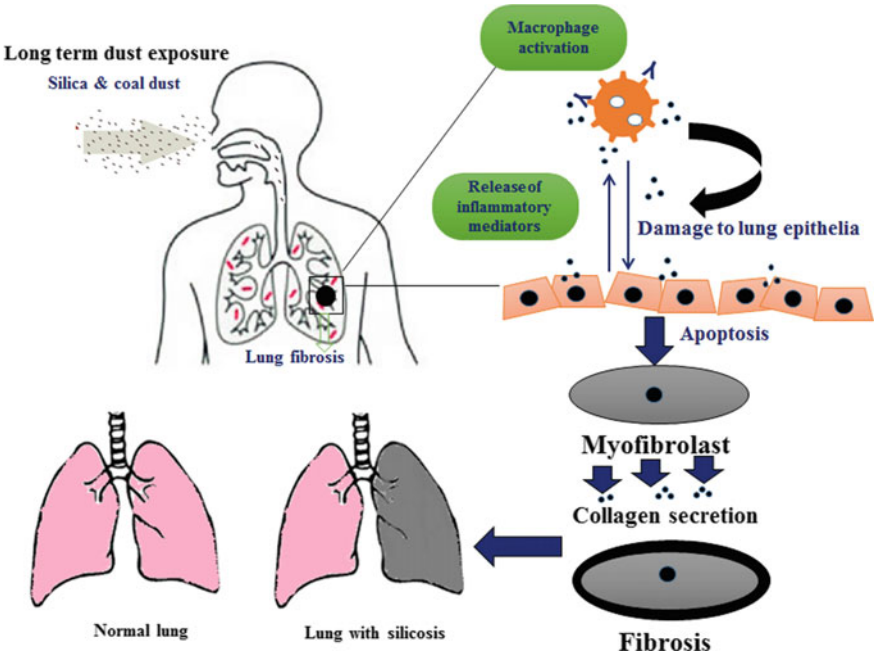

Fig. 5 Pathogenesis of silicosis among mine workers. Upon inhalation and ingestion of fine silica dust particles (quartz) in lungs, alveolar macrophages trigger a cascade of the inflammatory response which leads to damage of lung epithelium causing apoptosis and formation of the myofibroblast. Deposition of collagen secreted by these myofibroblast leads to fibrosis. Long term dust exposure to mine workers has chronic effects. Leading to progressive fibrosis and reduction of lung volumes

health importance in miners, limited epidemiological data exist from high burden countries regarding incidence and associated risk factors for TB among the mining population. Literature-based incidence and prevalence of TB in miners are mentioned in Table 1. The majority of data on TB in miners are from Sub Saharan Africa which shows a prevalence rate between 19–35% (Stuckler et al. 2011, 2013; Waternaude et al. 2006; Roberts 2009). South Africa's gold mining industry also contributes one of the highest annual incidences of TB in the world, which include 3000 and 7000 cases per 100,000 populations compared with a global incidence of 128 and a National incidence of 981 (per 100,00) (teWaternaude et al. 2006). Annually, around 760,000 cases of TB by mining industries in Sub Saharan Africa (Stuckler et al. 2011). Apart from occupational lung disease such as silicosis or CWP, the high prevalence of HIV in miners further increases their risk of acquiring TB infection. Population-based studies in China and Africa show mining industries to be significantly linked to the spread of HIV and other sexually transmitted diseases (STD) (Stuckler et al. 2013; Zhang et al. 2010). According to a report, the majority of miners contract HIV within 12–18 months of working in the mines (Deloitte. 2005). The most migratory population is illegally sub-contracted by mining industries and often works for an extended period away from their families. As a result, most workers often indulge in

Table 1 Incidence/prevalence of TB in miners as reported by different studies

Title	Type of study	Incidence/Prevalence	Reference	Year
Prevalence of tuberculosis in silicosis patients in southern part of Rajasthan	Original	Silico TB prevalence—44%	Atul Luhadia et al.	2021
Silico-tuberculosis, silicosis and other respiratory morbidities among sandstone mine workers in Rajasthan-a cross-sectional study	Original	Silicosis prevalence—37.3% Silico TB—7.4% TB without silicosis—10%	Saranaya Rajavel et al.	2020
HIV prevalence and TB in migrant miners communities of origin in Gaza Province, Mozambique: The need for increasing awareness and knowledge	Original	Active TB prevalence—0.3%	Cynthia sema Baltazar et al.	2020
Small contribution of gold mines to the ongoing tuberculosis epidemic in South Africa: a modelling-based study	Original	Active TB incidence in miners—63%	Stewart T. Chang	2018
Tuberculosis in the mines of Zambia: A case for intervention	Review	Prevalence rate of 0.6 (638/l00000) in miners aged 15 years and above	Pascalina Chanda-Kapata et al.	2016
Mining and Risk of Tuberculosis in Sub-Saharan Africa	Original	High incidence of TB in miners (33% high) compared to national data	David Stuckler et al.	2011
Prevalence of latent tuberculosis infection among gold miners in South Africa	Original	LTB prevalence in miners—89%	Yasmeen Hanifa et al.	2009
The epidemiology of tuberculosis in gold miners with silicosis	Original	Annual incidence rate of 2.2 in TB cases with silicosis compared to incidence of 0.9% without silicosis	R. L. Cowie	1994

unprotected sex which increases the risk for HIV and other STDs among them. Mine workers co-infected with HIV, have five times more risk of acquiring TB disease. Moreover, miners with HIV and silicosis have a 15folds more risk of developing TB than HIV negative miners free from silicosis (Churchyard et al. 1999). Apart from HIV, miners are also associated with high probabilities of development of DR. Migratory pattern among the miners are often leads to disruption in treatment leading to poor adherence and high default rates which is invariably linked to the acquisition of DR. As per reports, around 25% of DR-TB cases worked as miners in Africa (Stuckler et al. 2011).

7.2 TB Among Miners in India

Mining Industry in India contributes to a significant chunk of its economic growth. India has around 3,100 functioning mines in the country providing employment to around 1.5 million workers (Dhatrak and Nandi 2009). As per national data, India produces around 85 minerals and is ranked second in terms of the production of coal in the world (India's Mining Sector 2020). Figure 6 shows the statewide distribution of various coal mines across India. Similar to other high burden countries, like Africa, and China, the living and working conditions of miners in India are highly conducive to TB infection. The effects of migration, biosafety conditions within mines, crowded and poorly-ventilated mine shaft, combined with lack of adequate health services offered to miners has been invariably linked to high TB burden among Indian miners. In India, greater than 3 million mine workers are at risk of silicosis (Nandi et al. 2018). Studies among mine workers from Karoli district, Rajasthan showed that almost half of silicosis cases were co-infected with TB. Moreover, 99% of silicosis cases belonged to unprivileged and marginalized communities (Mohammad 2019). In India, there are fewer or no reported incidences of TB in the mining population possibly due to the lack of any epidemiological surveillance initiated by public or private organizations. Miners in India are also expected to contract STDs due to migratory patterns of work and are highly vulnerable to HIV (Living 2020). A significant proportion of the HIV population is associated with miners in India. Moreover considering the 40% Indian population harbouring LTBI (TB facts.org: TB India Statistics 2020), it is the general contention that large cohorts of miners must be latently infected. These Latent pools of miners under lack of health surveillance combined with poor nutritional status, living conditions and high HIV prevalence further translates into high active cases. Considering India, which accounts for a quarter of TB and drug-resistant TB cases along with the highest LTBI population and PLIV, it comes as no surprise that the mining population to be one of the major endemic groups contributing to the high TB incidence rate in the country.

From a clinical perspective, the first step in combating TB and preventing mortality is early identification of TB patients and initiating the correct treatment as close to the time of diagnosis as possible. This strategy has dual benefits. First, it allows

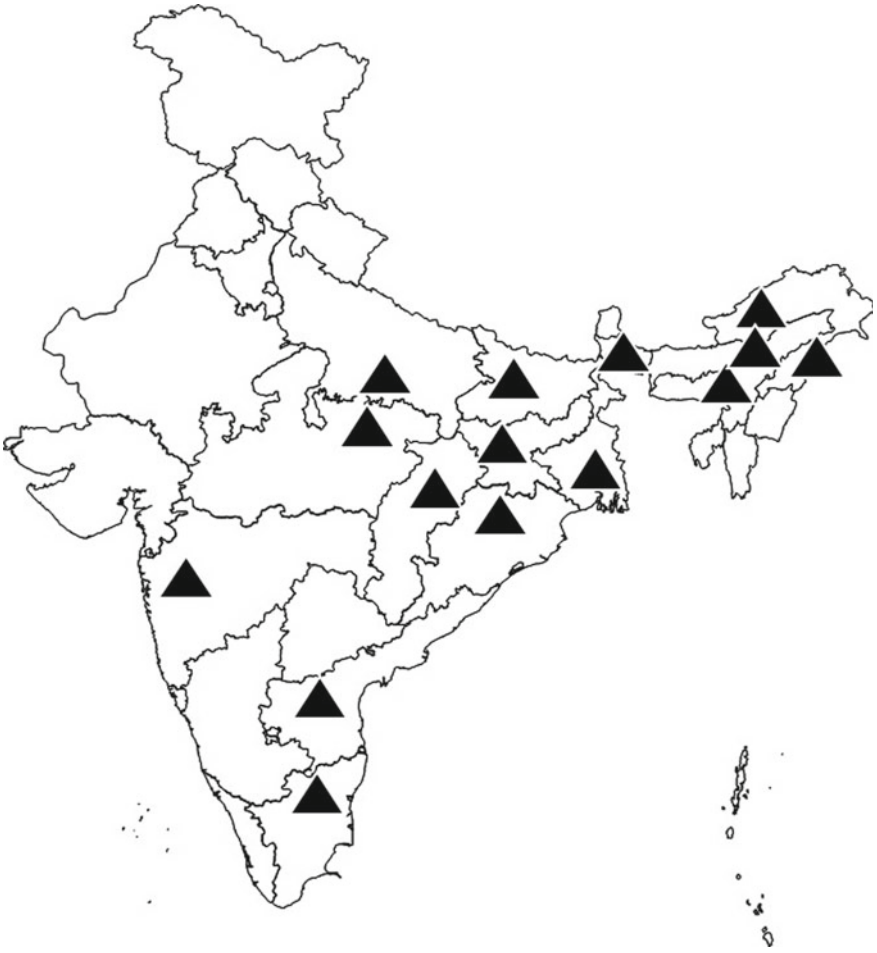

Fig. 6 State-wise distribution of coal mines in India

patients with TB to get early treatment and to experience lower risks of progressive lung destruction, morbidity, and mortality.

Lung function declines more rapidly in miners presenting with advanced TB and more significantly with each successive episode of TB making delayed diagnosis and its impact on the miner's endurance a mining workforce supply as well as health issues. Second, timely diagnosis and treatment initiation reduces the transmission chain and prevents the further spread of epidemics in high-risk endemic communities. From a public health perspective, timely diagnosis and management of TB constitutes in miners.

8 Diagnosis of Active TB Infection

Conventional diagnosis of TB is based on radiology and sputum (or site-specific sample) examination for TB bacilli through smear microscopy, liquid culture and Nucleic acid amplification test (NAATs). Despite significant advances in TB diagnostics, available tests have shown variable sensitivity and specificity with respect to the clinical outcome of TB (PTB or EPTB) and the sample used for investigation.

8.1 Chest Radiology

Chest radiology such as X-ray has been the oldest and primary tool for the diagnosis of PTB infection. In X-ray, the Posterior Anterior (PA) view of the chest is most commonly viewed for the presence of lesion, consolidation or cavities in the upper lobes of the lungs with or without mediastinal or hilar lymphadenopathy. Chest X-ray although a useful screening tool in presumptive TB individuals, lacks specificity (Kashyap et al. 2013a), and may often be negative even when the disease is present (Ryu 2015). As a result, chest X-ray often needs to be confirmed by smear microscopy. With the advancement in radiological tools, Chest computed tomography (CT) is regarded as a more sensitive and effective diagnostic tool than X-ray and may be generally used in cases with fine lesions or where X-ray films are inconclusive (Bomanji et al. 2015). CT scans are especially appropriate in cases of EPTB infection (especially the brain, spine). However, regardless of its advantages, radiological findings are not conclusive tools for patient management and need to be confirmed by bacteriological findings.

8.2 Smear Microscopy

Smear microscopy has remained the primary screening and most effective test for TB till date in resource-limited settings. The most widely used smear microscopy is Acid-Fast staining (also known as Ziehl–Neelsen (ZN staining) of TB bacilli from sputum or other body fluids. Although ZN staining is inexpensive and highly specific, it has poor sensitivity ranging from 34–80% (Yong et al. 2019). Smear microscopy often requires a high load of TB bacilli (10,000 bacilli/ml of sputum) to produce a positive result and often can be negative in samples with paucibacillary load especially in EPTB cases where sensitivity ranges between 0–40% (Rufai et al. 2017). Fluorescence microscopy has been regarded as an alternative to conventional ZN staining owing to its improved sensitivity and specificity but is expensive with infrastructure requirements (dark room). In 2008, WHO endorsed Light Emitting Diode (LED) technology for fluorescence microscopy, as an alternative to conventional fluorescence microscopy (Getachew et al. 2015). The LED fluorescence technology offers

several advantages without additional cost and infrastructure requirements to be used effectively in resource-limited settings.

8.3 TB Culture

Demonstration of MTB bacilli in solid and liquid culture media has been regarded as the gold standard for TB diagnosis (Kashyap et al. 2013a). Conventional culture techniques evolve inoculating clinical specimens on solid egg-based media known as Lowenstein Jenson (LJ) media. The culture technique is relatively more sensitive than smear microscopy, but is laborious and has a turnaround time of 3–4 weeks. The advent of automated liquid culture systems in past decades has been regarded as a major achievement in TB diagnostics combining benefits of automation with higher diagnostic accuracy and turnaround time compared to conventional techniques (Lee et al. 2015). The most widely used automated liquid culture system includes MB/BacT ALERT® 3D system [BioMerieux; France] and BACTEC™ MGIT™ 960 system [BD Worldwide; Franklin Lakes, NJ, USA]) (Lee et al. 2015; Zhao et al. 2016). The automated system consists of plastic tubing culture bottles with ready to use liquid media (Middlebrook 7H10) along with growth supplements and antibiotics for selective enrichment of TB bacilli in clinical samples. Despite the overall advantage and high specificity, MTB culturing methods has over all sensitivity of 30–80% (Kashyap et al. 2013b; Rufai et al. 2017) depending upon sample type and requires elaborate biosafety facilities which are beyond scope of most diagnostic capacities in resource-limited high TB endemic settings. In addition, liquid cultures are sometimes prone to contamination by NTMs and are not successful in recovering certain MTB strains which grow effectively in solid media (Yong et al. 2019).

8.4 Nucleic Acid Amplification Tests (NAATS)

In recent times, NAAT's have come across as the most promising tool in TB diagnosis. These assays rely on detecting both target MTB specific DNA and RNA, using polymerase chain reaction (PCR). WHO recommends NAAT as frontline tests for TB detection especially in EPTB cases and PLHIV due to higher diagnostic accuracy, and turnaround time compared with smear microscopy and culture methods (Nurwidya et al. 2018). Owing to its rapidity, NAATs are associated with improved patient management by facilitating diagnosis and treatment initiation in the same visit. The sensitivity of NAAT's is >90% in smear-positive and around 61–76% in smear-negative cases (Ryu 2015). Among various gene targets, IS6110, a multi-copy number, universal insertion sequence found in all MTBC has been widely used for the diagnosis of TB. IS6110 has higher sensitivity and specificity in the range of 82–85% and 88–100% respectively in respiratory specimens (Kashyap et al. 2013b; Nurwidya et al. 2018). In addition to IS6110, other gene targets such as devR, Rv0934

(38 kDa gene), Rv0355, mce3 operon, hupB, 23S rRNA have also been explored in various studies for diagnosis of TB in respiratory and EPTB specimens with variable sensitivities (62–90%) and specificities (72–100%) (Kashyap et al. 2013b). Despite advantages over conventional tools, NAAT's suffer from the limitation of differentiating live from dead bacilli and therefore needs to be correlated with clinical findings and supportive test. Besides, the requirement of infrastructure, high cost and skilled manpower vastly limit their applicability as an effective diagnostic tool in resource-poor settings.

8.5 Advance Molecular Diagnostics Tools for Detection of TB and Drug Resistance TB

In the last decade, there has been substantial development in NAAT technology replacing conventional tests with advanced automated cartridges based and rapid point of care systems, that have accelerated the diagnostic and treatment management for TB. A list of WHO-recommended molecular diagnostic assays for TB and drug resistance are enlisted in Table 2.

8.5.1 Cartridge Based Nucleic Acid Amplification (CBBAAT) Tests

In the last decade CBNAAT's have come across as significant advancement in molecular diagnosis of TB. GeneXpert (Cepheid, Sunnyvale, USA) is an automated real-time PCR (RT-PCR) system and offers the advantage of simultaneous detection of MTBC along with drug sensitivity to rifampicin (81 bp MTB *rpoB* gene) in less than 2 h (Steingart et al. 2014). The major advantage of this technique includes simplicity of operation due to automation which can be performed even by less experienced staff. The complete closed system along with ready to use sample cartridges further reduces the risk of contamination and false positivity making these assays superiors to liquid culture and conventional molecular-based assays. Hospital-based studies indicate good diagnostic accuracy of GeneXpert assays in smear-positive cases (sensitivity 99%) with variable accuracy in smear-negative and EPTB cases (28.2–80%) (Rufai et al. 2017; Nurwidya et al. 2018; Steingart et al. 2014). In 2014, GeneXpert was included as a mainstay test by WHO for diagnosis of TB in all suspected PTB cases and high-risk groups (EPTB, PLIV, pediatric population) replacing smear microscopy and phenotypic DST (Steingart et al. 2014; Eddabra and Ait 2018). In 2018, GeneXpert recommended as frontline test in the Universal Drug Susceptibility Testing (UDST) guidelines of the National TB program for appropriate management of TB patients (Prasad et al. 2018). In 2017, a WHO released an advisory, replacing conventional GeneXpert cartridges with next-generation Xpert®

Table 2 List of Molecular diagnostic assays recommended by WHO for TB and Drug Resistance TB

S. No	Diagnostic tests	Manufacturer	Platform/technology	Advantage	Limitation
1	*CBNAAT*				
a	Xpert MTB/RIF assay	Cepheid, Sunnyvale, USA	Automated-RT PCR	WHO recommended for diagnosis of TB and rifampicin drug resistance	Expensive Low sensitivity in smear negative and EPTB cases
b	GeneXpert Ultra	Cepheid, Sunnyvale, USA	Automated-RT PCR	WHO recommended with better sensitivity than Xpert MTB/RIF assay due to two additional gene targets	Expensive. Reduced specificity
c	Gene Xpert MTB/XDR	Cepheid, Sunnyvale, and FIND (USA)	Automated-RT PCR	Detection of MTB and drug resistance against multiple second line drugs	Under evaluation
2	*Line probe assay*				
a	GenotypeMTBDRplus V1	Hains Lifesciences, Germany	Hybridization assays	Detection of MDR compared to Xpert MTB/RIF assay	Requires positive culture/smear positive sputum sample
b	GenoType MTBDRsl v 1.0.0	Hains Lifesciences, Germany	Hybridization assays	Detection of resistance to first line and second line drugs	Requires positive culture/smear positive sputum sample
c	GenoType MTBDRsl V2.0	Hains Lifesciences, Germany	Hybridization assays	Detection of resistance to Second line drugs and injectable	Low sensitivity in smear negative samples

(continued)

Table 2 (continued)

S. No	Diagnostic tests	Manufacturer	Platform/technology	Advantage	Limitation
d	Genoscholar™ NTM + MDRTB II	NIPRO, Japan	Manual/Automated Hybridization assay	Differentiate MTB from NTM and detection of DR	Reduced sensitivity in smear negative samples
3	*TruenatTM*				
a	Truenat™ MTB	Molbio diagnostics/ Bigtec Labs, India	Microchip RT PCR	Low turnaround time. Battery operated for POC usage	Low sensitivity in smear negative specimen
b	Truenat™ MTB Plus	Molbio diagnostics/ Bigtec Labs, India	Microchip RT PCR	Low turnaround time. Battery operated for POC usage. Detection of MTBC along with DR to RIF	Low sensitivity in smear negative specimen
4	*Commercial LAMP assay*				
a	Loopamp MTBC Detection Kit	Eiken Chemical Company Ltd, Japan	Manual point of care PCR assay	WHO endorsed point of care PCR assay performed without thermal cycler. Result in less than one hour	Reduced sensitivity than conventional PCR assays

MTB/RIF Ultra cartridges to resolve sensitivity issues of an assay in smear-negative and EPTB cases (Dorman et al. 2018). The new cartridges are designed with a larger chamber to include higher volumes of sample along with targeting two MTB specific genes for higher diagnostic accuracy. Results evaluating the sensitivity of Ultra cartridges with conventional GeneXpert assay cartridges have shown higher sensitivity of ultra cartridges in sputum smear-negative cases with marginally reduced specificity (Eddabra and Ait 2018; Dorman et al. 2018). Despite being endorsed by WHO as a frontlines test, GeneXpert assays have been associated with several limitations. The biggest limitation includes the high cost of cartridges and the detection of mono-resistance. Additionally, GeneXpert assays are not able to detect resistance outside out 81 bp of the rpoB gene which can often lead to false-negative results when compared to genome sequencing methods (Eddabra and Ait 2018). Alternatively, being molecular-based assays, GeneXpert suffers from a lack of differentiation

between viable and dead TB bacilli in clinical specimens which sometimes leads to false positivity in patients with a previous history of treatment (due to circulating dead bacilli). To improve drug sensitivity coverage of CBBAAT for MDR diagnosis, Xpert MTB/XDR cartridges was launched in 2020 by Foundation for Innovative New Diagnostics (FIND) and Cepheid, Inc, which enables expanded drug resistance profiling against multiple drugs first-line and second-line TB drugs in around 60 min (Cao et al. 2021). Although it is significant development and will greatly accelerate MDR diagnosis, however, these cartridges are presently under validation at WHO testing sites.

8.5.2 Line Probe Assays (LPAs)

LPAs have been regarded as a robust technique that is recommended by WHO for the diagnosis and management of MDR-TB (WHO 2016). The first LPA endorsed by WHO was GenoType MTBDRplus (GenoType MTBDRplus V1), for the rapid detection of MDR (sensitivity to front line drug, INH and RIF) also known as front line (FL) LPA (Nurwidya et al. 2018; Eddabra and Ait 2018). In subsequent years, various upgrades to LPA become available for diagnosis of DR to second-line drugs. GenoType MTBDRsl version 1.0 (referred to as GenoType MTBDRsl V1) developed by Hain Lifesciences, Germany was the first commercial LPA introduced by WHO to detect resistance to second-line drugs (WHO 2016). In 2015, a slightly updated version of this LPA (GenoType MTBDRsl V2, Hains Lifesciences and Nipro detection kit 2, Tokyo, Japan) became available for diagnosis of DR to multiple second-line drugs in confirmed MDR/RR cases. Current WHO guidelines recommend the use of FL-LPA (GenoType MTBDRsl V1& 2, and Nipro) in place of phenotypic DST for detection of DR (WHO 2020). LPA's are associated with higher sensitivity for detection of mono resistance to RIF compared to GeneXpert assays (Rufai et al. 2014). The biggest shortcoming of LPA includes a requirement of smear-positive or culture-positive samples, which vastly precedes its advantage as an effective tool for MDR diagnosis. Secondly, there have been instances in which LPA tend to be negative even in a smear-positive specimen, making MDR diagnosis difficult to conclude.

8.5.3 Whole-Genome Sequencing

Conventional DST and WHO recommended molecular assays like GeneXpert and LPA's suffer from the limitation of detection of limited genetic mutation in DR cases often leading to false-negative results. With recent advancements in genetic tools, Whole-genome sequencing (WGS) methods have been regarded as reliable and accurate diagnostic methods for genome characterization and detection of multiple mutations associated with DR/MDR in clinical samples (Chawla et al. 2018). In contrast to CBNAAT and LPA, WGS methods generally provide in-depth sequence information for multiple genetic loci for detecting emerging mutations in population clusters (Walker et al. 2013). Data obtained from sequencing methods constitutes critical

information to National TB programmes to determine population-level risk factors for transmission and develop specific treatment guidelines to improve the outcome for DR-TB. Among the sequencing approaches, in recent times, Next-generation sequencing (NGS) assays, has surfaced as faster, affordable and widely used alternative for molecular epidemiological studies for mapping genetic heterogeneity and cataloguing mutation pattern associated with drug resistance in MTB strains (Al-Ghafli et al. 2018). Despite the high advancement and specificity of WGS methods, countries like India face substantial hurdles in the utilization of such tools due to the high cost of analysis, skilled manpower and limitation of data analysis and storage. NGS assays also require a high bacterial load for obtaining a bulk quantity of DNA for successful and accurate read outs which often might lead to diagnostic lags and delays in treatment initiation in programmatic management of MDR TB cases. Other limitations include the lack of Single nucleotide polymorphism prediction in non-epidemiologically linked pairs which makes this approaches problematic especially in high burden settings (Nurwidya et al. 2018).

8.6 Point of Care Molecular Diagnostics Assays for TB and Drug Resistance TB

8.6.1 Truenat™ Assay

Truenat™ is India's indigenous molecular diagnostic assay (micro-RT PCR) developed by Molbio diagnostics/Bigtec Labs, India for detection of TB and RR (Truenat™ MTB/ MTB-RIF Dx) (Nikam et al. 2014). Truenat™ owing to its compact size and battery operation can be used as a point of care (POC) for diagnosis and surveillance of DR TB in low resource healthcare settings and peripheral zones (Lee et al. 2019). Pilot studies in India; have shown high sensitivity and specificity of around 99% and 100% of Truenat™ devices in smear-positive specimens for diagnosis of TB and RIF resistance (Nikam et al. 2014). Studies have also shown high concordance between Truenat™ and GeneXpert assays (Nikam et al. 2014; Lee et al. 2019). In July 2020, the Indian Council of Medical Research (ICMR), Govt. of India, announced that WHO has recommended the Truenat platform as the mainstay test for diagnosis of TB and DR replacing smear microscopy (Press Release ICMR 2020). Point of care utility, cost-effectiveness and high concordance with CBNAAT makes Truenat™ an effective test for diagnosis of TB and DR with ease of scalability in resource-poor settings.

8.6.2 Loop-Mediated Isothermal Amplification (LAMP) PCR Assay

LAMP assay is a rapid point of care PCR developed by Notomi et al. (Eddabra and Ait 2018). LAMP involves, the isothermal amplification of the target gene at a constant

temperature using a set of specially designed primers and DNA polymerase through strand displacement activity. Since amplification is carried at a constant temperature, LAMP assays can be carried out using simpler instruments like water baths or heating blocks without needing a thermal cycler. Moreover, unlike conventional molecular assays, results of the LAMP can be visualized through the naked eye without the need of a gel-based system making it a simple, affordable point of care assay for TB diagnosis with wide-scale applicability in resource-limited settings. Various LAMP-based assays have been developed for molecular diagnosis of TB targeting different genes of MTB in PTB and EPTB samples. Although relatively simpler, LAMP assays have good sensitivity of 92.1–100% in smear-positive PTB samples (Ou et al. 2014). One of the major advantages of LAMP PCR includes its good sensitivity of around 95% in EPTB samples which is better than gold standards such as liquid culture and smear microscopy (Eddabra and Ait 2018; Nagdev et al. 2011). In 2016, LAMP was endorsed by WHO, over low sensitive smear microscopy for diagnosis of adult PTB.

9 Diagnosis of Latent TB Infection (LTBI)

Globally, no gold standard tests exist for the detection of LTBI (Carranza et al. 2020). However, LTBI can be established clinically among contacts of TB cases by demonstrating immune response against MTB antigen and ruling out active infection. The available tests for screening of LTBI infection include Tuberculin skin test (TST) and Interferon-gamma release assays (IGRA's) (Kashyap et al. 2014). TST has introduced almost a century ago and has been utilized in low resource settings for screening of LTBI. TST measures in vivo delayed-type hypersensitivity (DTH) skin reaction against MTB purified protein derivative (PPD) injected intradermally into the skin (Saha et al. 2019). The positive reaction is interpreted by measuring the zone of induration observed after 24–48 h. Positive TST results in healthy contacts of TB cases are taken as an indicator of LTBI. The main limitation of TST includes the high cross-reactivity of PPD antigens with other members of MTBC and NTM (Carranza et al. 2020). Due to this reason, TST is often associated with high false positivity rates in participants with previous BCG vaccination and exposure to NTMs which is usually profound in high endemic zones (Kashyap et al. 2013a). In addition, a requirement of follow up visits to measure results often limits their applicability in remote zones. IGRA's were designed to replace TST for the diagnosis of LTBI due to high their specificity for MTB and logistical advantages over TST (Pai et al. 2014). IGRA's are based on detection of cytokine interferon-gamma (IFN-γ) in blood after stimulation with MTB specific, region of difference1 (RD1) antigens (absent in BCG and NTMs). The two most commonly used IGRAs include Quantiferon TB in the tube (QFT-IT, Quantiferon TB gold) and T.SPOT. TB assay (Kashyap et al. 2014). Despite the advantage of high specificity over TST, IGRA's have suffered from limitation of high cost, lack of diagnostic ability to differentiate latent from active disease along with identification of LTBI cases that are likely to progress to active diseases (Zellweger et al. 2020). Additionally, although antigens coded by RD1 were

selected to avoid cross-reactivity with BCG and NTMs (as they lack RD1 region), it is unlikely that this cocktail of antigens may be expressed in all exposed cases and un-symptomatic healthy household contacts (HC) of TB due to heterogeneous immune response (Pai et al. 2014). As a result, a considerable number of the LTBI population may be missed by IGRA's. Studies evaluating the comparative diagnostic utility of both TST and IGRA's have found more or less similar accuracy rates for the prediction of LTBI (Kashyap et al. 2014; Bagheri Amiri et al. 2015; Pavić et al. 2015). As a result, both currently available tests are regarded as indirect predictors of TB infection rather than specific markers. Moreover, one of the crucial constraints of both the tests includes low precision for LTBI in immunocompromised individuals such as PLIV. This represents a critical gap in LTBI diagnosis as PLIV; especially in high TB endemic countries are associated with a 50% greater risk of conversion to active disease.

10 Diagnostic Landscape of TB Biomarkers

Despite significant advances in TB immunology and genome sequencing methods, efficient TB diagnostic tests aiding in monitoring disease progression, treatment response and identifying susceptible LTBI population for conversion to active disease are still lacking. In recent decades, increased interest has been invested in the identification of immune biomarkers that can act as surrogate endpoints of TB infection for monitoring its progression along with differentiating latent from active disease. The current WHO-end TB strategy calls for the identification of rapid, affordable, highly sensitive and minimally invasive diagnostic tests especially for High TB burden countries (Yong et al. 2019). In the past three decades, various immune markers have been investigated targeting the dynamic equilibrium that exists between host immunity and MTB to resist and establish infection. These markers include MTB components (antigens), host antibodies, T-cell markers, cytokines, and Transcriptional markers for diagnosis of active and LTBI (Fig. 7).

10.1 MTB Antigen Markers

Demonstration of immunogenic proteins of MTB in clinical samples has been long used as predictors of active infection and was a cornerstone of currently banned serodiagnostic tests (Kashyap et al. 2013a). Being associated with particular disease states, (active and latent), the expression of antigen markers in patient samples can be used as clinical end points to monitor disease progression and response to treatment. Various MTB antigens have been investigated till date for their diagnostic potential with variable sensitivity and specificity (Yong et al. 2019). The list of MTB antigens and their diagnostic accuracy for latent and active TB infection is mentioned in Table 3. The majority of antigen markers investigated include secretory and cellular proteins

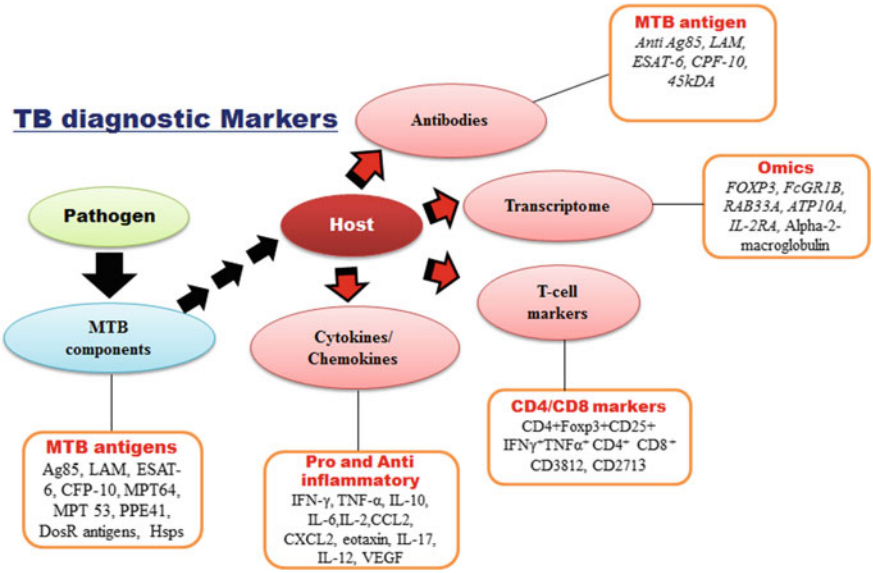

Fig. 7 Diagnostic landscape for TB biomarkers

associated with cell wall synthesis and MTB pathogenesis. Some of the major MTB antigens include 17.5kD lipoarabinomannan (LAM), 30kDA mycolyl-transferase (Ag85B), 6 kDa, early secretory antigen target -6 (ESAT-6), 10 kDa culture filtrate protein (CFP-10), MPT-64, 65kDA heat shock protein (Hsp-65), 45kDA glycoprotein, MPT53 and PPE41 which have been regarded as a major target of host immune response during infection (Yong et al. 2019; Gopinath et al. 2016). These antigen markers although immunogenic, have shown variable diagnostic sensitivity in the range 13–100% depending upon the study population and site-specific sample used (Table 2) (Kashyap et al. 2013a; Yong et al. 2019; Steingart et al. 2009; Turbawaty et al. 2017; Bekmurzayeva et al. 2013). Antigen detection tests are particularly useful in cases of EPTB and pediatric TB infection, where gold standards tests such as culture and ZN staining are often negative due to the paucibacillary load of clinical samples. Detection of antigens often depends on the stage of infection; as a result cases with chronic infections are often associated with variable antigen expression (low sensitivity). Secondly, since the immune response to MTB infection is heterogeneous, different hosts are likely associated with different antigen profiles. As a result, using single antigen readouts for diagnosis may lead to high false-negative rates due to inadequate sensitivity and specificity. Studies have shown that detecting multiple antigens using a cocktail of polyclonal antibodies considerably increase the diagnostic sensitivity of antigen test (Turbawaty et al. 2017). Such strategies can be used especially for high-risk groups such as PLIV in which antigen markers are seldom associated with low sensitivity.

Table 3 List of MTB antigens and their diagnostic accuracy for latent and active TB infection

Antigens	Clinical Sample	Sensitivity (%)	Specificity (%)	Reference
Active TB				
Ag85B (30 kDa mycolyl transferase)	Serum, CSF	80–84	90–96	*20,13, 83,86*
ESAT-6	Serum CSF, Pleural fluid, urine	67–100	51–94	*13,85,86,87*
CFP-10	Serum, CSF, Pleural fluid, urine	*48–63*	*70–71*	*13, 83,86,87*
LAM	Serum urine	*13–51*	*83–100*	*83,87*
MPT-64	Culture isolates, urine	*97.3–100*	*100*	*83,86*
PPE41, MPT53 and TB18.5	Serum	*88*	*88*	*84,87*
60 kDa antigen	Serum	*68–94*	*92–100*	*13*
Hsp71	Serum, CSF, Pleural fluid	*84–90*	*92–94*	*13, 94*
Hsp 65	CSF	*88*	*94*	*13, 94*
Rv2031c (HSP-X) alpha-crystaline	Serum CSF, Pleural fluid	*63–80*	*78–95*	*83,85,94*
38 kDa antigen	Serum	*61–89*	*73–100*	*13,83,85*
Rv3872 antigen	Serum	*90–92*	*92–95*	*13,83,87*
ESAT/CFP-10/MPT64	Urine	*68.2*	*33*	*83,86*
38 kDa, MTB48, CFP10/ESAT6	Serum/plasma	*73*	*77*	*13*
Latent TB				
Dos R protein Rv2623	CSF	*90.32*	*100*	*89*
other Dormancy regulon antigens (Rv1735c, Rv2006, Rv2625c, Rv1996, Rv2032, Rv2623, Rv2629, Rv3126c, Rv0081, Rv2631, Rv3130c, Rv2624c, Rv2007c, Rv2028c, and Rv3134R)	Serum/Plasma			*90,91*
Rv2626c and Rv3716c	Serum/Plasma	*88.5*	*100*	*94*
Rv2031c (HSP-X) alpha-crystaline	Serum/Plasma	*77.27*	*75%*	*94, 95*
Hsp65, Hsp71	Serum/Plasma	*31–59*	*67–82*	95
Hsp25, Hsp60, Hsp70	Serum/Plasma			94

In addition to active infection, considerable research has been directed to identify novel antigen markers for discriminating latent from active diseases. Antigen belonging to dormancy regulon of MTB (referred to as DosR) expressed during latent stage has been widely investigated as potential diagnostic markers of LTBI (Latorre and Domínguez 2015). A broad range of Dos R proteins (Rv1735c, Rv2006, Rv2625c, Rv1996, Rv2032, Rv2623, Rv2629, Rv3126c, Rv0081, Rv2631, Rv3130c, Rv2624c, Rv2007c, Rv2028c, and Rv3134R) have been investigated as either standalone markers (Latorre and Domínguez 2015; Jain et al. 2013; Shi et al. 2020) or used in conjugation with IGRA's to boost their diagnostic utility for differentiation of latent from the active disease (Serra-Vidal et al. 2014; Leyten et al. 2006; Prabhavathi et al. 2015). In addition to DosR proteins, the diagnostic potential of several heat shock proteins (HSP) associated with both host and MTB have been investigated in recent times for differential diagnosis of TB infection (Shekhawat et al. 2016; Rajpal et al. 2011). Among other proteins, Ras associated GTP binding protein (RAB33A) has been identified as potential markers expressed in patients of latent TB individuals (Jacobsen et al. 2005). Among host biomarkers, relevant to high-risk groups, antigens like Alpha-2 macroglobulin (A-2-M), sero-transferrin and Haptoglobin has been identified as clinically relevant markers for TB diagnosis and progression in high endemic malnourished population in India (Bapat et al. 2015).

10.2 Host Antibody Response to MTB Antigens

Detection of circulating antibodies against immunogenic MTB antigens has been regarded as potential indicator of MTB exposure and infection in clinical practice. Detection of IgG and IgM antibodies against MTB specific antigens (ESTA-6, Ag85B, CFP-10, LAM) has been widely used as diagnostic markers of TB infection in several studies available from India and other TB endemic countries (Yong et al. 2019; Steingart et al. 2009). Unlike antigens, MTB specific antibodies can be detected in later stages of infection wherein antigens are seldom not expressed (Kashyap et al. 2013a). Moreover, like antigen, antibody tests are also cost-effective and can be demonstrated using simpler techniques like ELISA and rapid later flow for both IgM and IgG for their implication in low resource settings. Demonstration of antibodies against latent specific antigens can be used convenient alternative to IGRA's and TST in epidemiological studies for mass screening LTBI cases from TB endemic settings. Despite being rapid and cost-effective, antibody assays shave shown variable diagnostic accuracy with sensitivity and specificity in the range of 14–85% and 53–98.7% respectively as observed in different population-based studies (Kashyap et al. 2013a; Yong et al. 2019; Steingart et al. 2009, 2007). It has been generally postulated that using antigen and antibodies in conjugation can significantly increase their diagnostic accuracy for TB infection and can even be used as an

alternative to conventional tools in the epidemiological screening of TB from high-risk endemic settings. Implementation of such approaches in epidemiological studies can bolster early diagnosis along with initiation of an appropriate drug regimen in a high-risk group, to curb the spread of the epidemic in such region.

10.3 Cytokine and Chemokine Markers

Cytokines are regarded as key inflammatory mediators in TB infection (Bapat et al. 2015). Development of antimycobacterial immunity and MTB re-infection in the host depends on the dynamic equilibrium of various pro and anti-inflammatory cytokines around granuloma (Ahmad 2011). As result, diagnosis of these key cytokines can provide vital information not only regarding the infection stage but also to monitor treatment response and progression of disease in TB cases. Although cytokines are non-specific and are expressed in a variety of infections, their diagnostic accuracy is significantly enhanced when used as surrogate markers for the diagnosis of PTB and EPTB infections. Detection of a panel of various inflammatory and anti-inflammatory cytokines such as IFN-γ, TNF-α, IL-8, IL-6, IL-17, IL-0, IP-10, IL-2, IL-2, IL-1α, MIP-1a, CCL22, CXCl2, eotaxin, VEGF has been used in several studies for the diagnosis of active TB and also to differentiate it from the latent disease (Clifford et al. 2019; Won et al. 2017; Tebruegge et al. 2015; Suzukawa et al. 2016; Boer et al. 2015). Among the various cytokine, IFN-γ, TNF-α, IL-10, IL-6 have been frequently used in TB diagnosis although, their diagnostic accuracy has been debatable in several studies (Yong et al. 2019; Clifford et al. 2019; Suzukawa et al. 2016). In recent times, measurement of various cytokines after in vitro stimulation with TB specific antigens has been used to enhance diagnostic specificity of IGRAs for latent and active infection. Population-based studies from different countries have shown higher diagnostic accuracy of IGRA's when additional cytokine panels (IL-6, IL-10, IL-2, IP-10, eotaxin, TNF-α, MCP-1) were investigated in antigen-stimulated plasma fraction for monitoring sputum conversion and diagnosis of LTBI infection (Clifford et al. 2019; Suzukawa et al. 2016; Boer et al. 2015).

10.4 T-cell Surface Markers to Differentiate Active and Latent Disease

T-cell mediated immunity has been regarded as paramount in the control of TB infection and the development of latency in the host (Ahmad 2011). Among various effector cells, CD4 + cells and CD8 + cells are central to host defence during TB infection and undergo various stages of differentiation in the immune-mediated killing of mycobacteria (Yong et al. 2019). However, some reports have suggested that mycobacteria can modulate these T-cells to their advantage during pathogenesis.

Reports have shown that most patients of TB and MDR-TB have increased amounts of T_{Reg} cells which suppress otherwise efficient CD4 response thereby delaying the development of adaptive immune response in the host (Semple et al. 2013). At present, the utility of flow cytometry-based approaches has gained momentum in TB immunology for understanding ell surface-based expression (immunophenotyping) and their correlation with TB disease (Pathakumari et al. 2018). Publish reports indicate the critical role of T-cell modulation by MTB during various clinical stages of infection. Studies suggest that higher expression of T-cell subsets such as CD4 + Foxp3 + CD25 + Tregs, IFNγ^+TNFα^+ CD4$^+$ and CD8$^+$ T-cells in active TB cases compared to those with LTBI (Marin et al. 2010; Cadena et al. 2016; Adekambi et al. 2015). Further, results from other studies have shown that central memory CD4 T-cell cells produced in response to MTB Dos R proteins can differentiate LTBI from EPTB and PTB compared to immunodominant antigens secreted during active TB (Portevin et al. 2014). In other studies, attempts have been made to increase the diagnostic specificity of IGRA'S, through the integration of CD3812, CD2713 as well as CD4 and CD8 levels with the IFN-γ readout. (Portevin et al. 2014; Yang et al. 2015). Despite reported studies, limited knowledge exists in regards to the functional composition of the T-cell response against the diverse antigen populations expressed by MTB during dormancy. Antigen-specific T-cell segregation by Dos R proteins could serve as important markers for differential and definitive diagnosis of LTBI infection. The studies focusing on Dos R protein-mediated T-cell surface markers expression in well-characterized cohorts such as TB; LTBI cases could potentially provide novel insights on modulation of immune response in various stages of TB infection. This could be potentially useful to screen LTBI cases in high-risk settings alone or in the conjugation of IGRAS to increase its diagnostic specificity.

10.5 Transcriptomic Markers

Transcriptomics studies have been a breakthrough in TB diagnostics in recent times. Transcriptomics focus on identification of host-specific genetic signatures associated with disease condition (Yong et al. 2019). Although the immune response to MTB is central to the lung and may be site-specific in EPTB cases, the pathological state associated with the disease condition may be often reflected in blood (Weiner et al. 2013). Numbers of studies have reported blood transcriptome signatures associated with development PTB, HIV TB and pediatric TB (Weiner et al. 2013; Sambarey et al. 2017). High throughput mRNA based expression signatures in blood allow us to acquire and quantify thousands of biomarkers associated with disease conditions in a single step. Identification of biomarkers through such an approach has implications not only in diagnostics but can also be used for understanding the pathogenesis of the disease. Among the transcriptomics approach, microarrays and RNA sequencing (RNA-Seq) platforms have been used widely in different studies (Yong et al. 2019;

Weiner et al. 2013; Sambarey et al. 2017; Esmail et al. 2020). RNA-Seq methods have come across as powerful tools in transcriptomics studies due to higher sensitivity and the advantage of providing rich insights into qualitative and quantitative information on gene expression compared to microarrays. Recently, whole blood signatures identified by RNA-seq methods have been used for risk of progression to active disease in LTBI cases (Esmail et al. 2020; Zak et al. 2016). Blood transcriptome studies in Indian cohorts using RNA-seq have identified several gene signatures for differential diagnosis of active TB from latent and healthy controls (Sambarey et al. 2017).

Despite being a robust tool in TB- biomarker research, transcriptomics has been associated with sensitivity and specificity limitations. Host immune response in TB is heterogeneous and varies according to the outcome of disease after infection. As a result, transcriptomics signatures may vary accordingly, reducing specificity (Yong et al. 2019). Reports also suggest reduced sensitivity of transcriptomics in people with incipient disease (Weiner et al. 2013). Also in some diseases especially in viral and other intracellular diseases, host gene signatures may often be cross-reactive to that in TB, limiting the specificity of transcriptomics approaches. Still, transcriptomics has been regarded as a powerful tool in TB biomarker research and should be inherently in clinical practice to monitor symptomatic progression and treatment response in TB cases. Biomarkers identification using transcriptomics can replace conventional proteomics tools and can increase the diagnostic accuracy of other commercial tests when used in conjugation.

11 Conclusion

Rapid and early diagnosis of TB infection in miners is paramount for the success of clinical treatment and reducing the risk of TB transmission in high-risk mining communities. Advances in recent molecular diagnostics such as CBNAATS, TrueNat, LPA and LAMP techniques can be used as rapid alternatives to conventional gold standards for surveillance of TB &DR-TB in mining communities. The current landscape of TB biomarkers such as antigen/antibodies along with T-cell and transcriptomic approaches can boost diagnostic surveillance which includes the development of tailored biomarkers assays to be used as a rapid point of care tools for TB diagnosis and monitor treatment response to reduce the burden of TB in miners in India. Increased advocacy and stronger political commitments are needed from TB stakeholders, health policy makers to support biomarker discovery, validation, and its further integration in the current national program.

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Goblet, Club and Alveolar Cells: Front-Line Defenders of the Airways in Chronic Obstructive Pulmonary Disease, a Most Common Lung Disease in Miners

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1 Introduction

India is poised with abundant mineral resources and has the root cause for industrial development. India stands with cutting edge global competition in the development of minerals, with the value addition, and development of resources. India has led on 95 mineral production, among them, 47 and 10 are non-metallic and metallic, 3 atomic and 23 are minor minerals. The minor minerals including building are the major part of the actual financial growth of India (Metallic and Non-Metallic Minerals Sector in India 2014). India is endowed with deposits of coal, lignite, bauxite, chromite, copper, iron, lead and zinc, manganese, silver, diamond, limestone, phosphorite etc.

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_4

The demand for coal was increased and India is the second-largest producer in 2015 and the importer of coal in the world. Amongst the various mining sectors in India, the coal sector is the most important for the economic growth of India. The demand for iron and steel are continuing overwhelming part of the growth of India. There are 3500 working mining leases includes 23 states of India. Out of these the operating mines are maximum in Madhya Pradesh, Tamil Nadu, Andhra Pradesh, Gujarat and Karnataka which covers 70% of the mine area of the total 316,290.55 hectors (Aggarwal 2020). The mining sector in India contributes approximately 2.1% to the GDP of the nation but its importance to the national financial system is considerable as it provides the essential raw material for the industrial, power and construction sectors of the country, which contributes 10–11% in the GDP (Recommendations of under 40 age group for Indian mining industry 2018). The value of minerals produced in other countries such as the USA, China, Russia, Saudi, Australia, etc. far exceeds that of India. The employment in the mining sector in India was quite high and stood second to China in this regard due to less mechanization of mining (Indian Minerals Yearbook 2013). These rich mineral deposits provided employment to 1.15 lakhs workers represented in 2013 which is being changed to around 7 lakhs individuals in former decades. Mining and mineral processing beneficiation is crucially associated with a modern society that will remain foreseeable for years together. However, it has a detrimental effect on the health of the miners which led to serious consequences which depend on many factors like the type of the mining and its geographical distribution (Younger 2007; Parry and Chiverrell 2019; Culshaw et al. 2000). The health of miners and the mining community will continue to be a challenge in view of the hazardous and arduous nature of working conditions in mines and the environment. The rapid expansion of the mining industry in India, the introduction of new technology, increased mechanization and globalization of Indian mining companies have added complexities in the prevention, control and elimination of occupational diseases.

Exposure to respiratory irritants and sensitizing agents like coal and silica dust is very common. Further, the apparent negative impact of the mining industry on the environment and society, and the role of contributors in sustainable development will continue to be an important issue.

1.1 Classification of Dust

The composition of dust generated in mines depends upon the mineral content, composition of the ore body, process of removal of overburden, extraction of ore and processing of ore. In mines, the composition of air is quite different from the composition of air on the surface. It is mainly due to the emission of gases from the seam, the exhaust of machinery. This type of mine air composition consists of methane, hydrogen, and other hydrocarbons. It also has dust particles, humidity, explosive particles, lubricated oil and acid vapour. The airborne respirable dust can be classified in the following manner:

i. **Fibrogenic Dust**

   a. Silica (quartz, cristobalite, tridymite, chert)
   b. Metal fumes
   c. Beryllium ores

ii. **Carcinogenic Dust**

   a. Asbestos
   b. Arsenic
   c. Diesel particulate matter (a suspended carcinogen)

iii. **Toxic aerosols (poisonous to body organs and tissues etc.)**

   a. Dust of ores of beryllium, lead, uranium, radium, thorium, chromium, vanadium, manganese, arsenic, mercury, cadmium, antimony, selenium, nickel, tungsten, silver.
   b. Mists and fumes of organic and other body-sensitizing chemicals.

iv. **Radioactive Dust**

   a. Ores of uranium, radium, thorium

v. **Explosive Dust**

   a. Metallic dust (Magnesium, Aluminium, zinc, tin, iron)
   b. Coal (bituminous, lignite)
   c. Sulphide ores
   d. Organic dust

vi. **Nuisance Dust (little adverse effects on humans)**

   a. Gypsum
   b. Kaolin
   c. Limestone.

However, when present in excess amounts, dust in any of the above forms can be harmful to human health causing permanent lung damage.

Working in a dust prone environment adds to the poor health condition of the miners. The release of toxicants, irritants, and dust below respirable size are the major players in increasing poor health conditions. These agents are equally harmful to the nearby residential population which is always passively exposed to the mining environment. Although there are numerous occupational and community health issues relating to mining that needs awareness.

Silicosis is the major issue faced by the miners. Long-term occupational exposure to silica is associated with an increased risk for respiratory diseases such as silicosis. Silicosis is an irreversible, autoimmune, respirable lung disease caused by prolonged exposure to silica dust. Silica is a well-documented workplace toxicant. Long-term occupational exposure to silica is associated with an increased risk of respiratory

diseases. The prevalence of the illness caused by silica exposure has peaked in the last half of the nineteenth century and the early part of the twentieth century when mechanized industries were developing and the relationship between dust exposure and diseases were not well understood (Aminian et al. 2008).

Coal workers' pneumoconiosis (CWP), is the most common lung disease caused in coal miners due to the accumulation of coal dust around respiratory bronchioles. Scaring in the lungs caused an inability to breathe and sometimes leads to complications of emphysema that may convert to fibrotic lesions (Guidelines for the use of the ILO International Classification of Radiographs of Pneumoconioses 2011; Kim and Lynch 2002).

Chronic obstructive pulmonary disease (COPD) is an age-old disease that needs global attention. In earlier settings of mines, pneumoconiosis was the only reported disease in the mining population. Eventually, after a few years, the British's faction led to COPD the major outcome of the mining's health consequences. Many countries accepted it as an occupation aided disease and stand it as a foremost in mining sectors. The vast data from all over the countries was studied to get into the understanding of COPD in the miners and other contributing factors add on to the worst prognosis of the disease (Devine 2008).

1.2 Global Scenario of Chronic Obstructive Pulmonary Disease (COPD) in Mining Occupation

According to World Health Organization (WHO) data published in the year 2005, the percentage of COPD was more in men as compared to women. Recent data is not in the agreement with this, rather the usage of tobacco in women has drastically increased. COPD is dependent on the economic status of the country. There are many causes of the spread of this respiratory disease in various groups i.e. the low, middle and high-income groups. In high-income countries, the incidence rate of COPD is highly increased in last few years, which has caused its equal distribution in both the gender. In addition to that, the increased exhaustive uses of biomass fuel in low and middle-income countries are the source for equal men and women exposure. The major cause of high mortality and morbidity in the high-income group of countries population is more prone to disease due to cigarette smoking and industrial exhaust. According to WHO (2005), the morbidity and mortality are assigned towards 65 million people for severe to moderate conditions and 3 million people died because of this worst inflammatory pulmonary disease. It was difficult to get the prevalence of COPD due to the complexities of the disease-associated data. Global strategy for the diagnosis, management and prevention of COPD have worked on COPD data of the 28 countries and carried out systematic review and meta-analysis. The Latin American project for the Investigation of Obstructive Lung Disease (PLATINO) studied the prevalence of COPD in Brazil, Chile, Mexico, Uruguay, and Venezuela. The data showed high prevalence in more than 40 aged group populations of the

men as compared to a lower age group of men and women. The reason for the increased prevalence of the disease with the age was the smokers and ex-smokers population of the country. The findings of the European cities Salzburg and Austria were not in agreement with the studies conducted by the PLATINO. Further, WHO stated that COPD will be the leading disease in 2020 in respiratory disorders and will be acquiring 5th position in all disabilities worldwide (Coggon and Taylor 1998; Melville et al. 2010; Lipworth et al. 2016; Masa et al. 2016).

1.3 Mechanism of Chronic Obstructive Pulmonary Disease (COPD)

COPD is a retort to inflammation, infection, smoking, hypoxia, altercates involving lungs causing airways dysfunction as depicted in Fig. 1. These encountered risk factors are reflected in irreversible airflow and abnormalities at the terminal bronchiolar level, where the exchange of the air gets impaired and airflow restricts. There are sequential episodes of the consequences of getting involved in systemic inflammation, muscle dysfunction with weakness and abnormalities. Although COPD is a chronic disease with a genetic predisposition, with early treatment, the disease can be cured at a certain level. COPD is a progressive pulmonary disease that involves the lungs to the most atrocious condition like emphysema and chronic bronchitis shown in Fig. 1. Lung function, mortality rate, emphysema, and bronchitis were studied

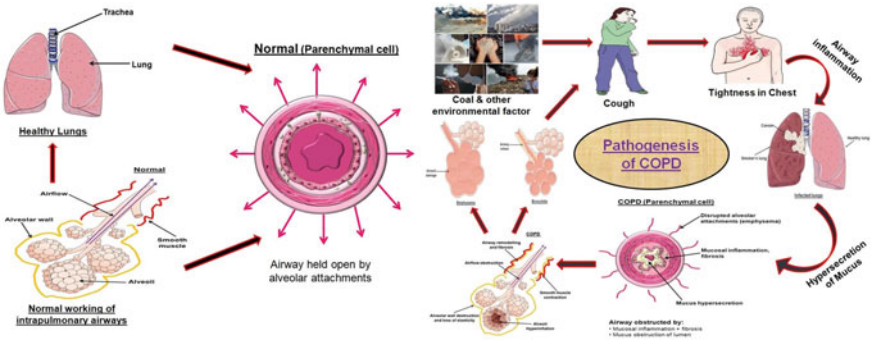

Fig. 1 Pathogenesis of COPD. The figure shows lung and trachea, occupied spaces of air passages with the thick cellular lining of the bronchus, and smooth muscles of the intrapulmonary air passage of the bronchiole. The heavy exposure of the environmental pollutants, expectorations, and tightness in the chest is shown. Irregularities in the lungs due to smoking and tumorigenic growth in the lungs revealed, the over secretion of mucus in the lumen hinder the airflow and clog the air spaces which disturb air pressure maintenance in the cells, the thick lining of the smooth muscles, with inflammation of columnar epithelial cells reduce the air spaces with the overload of the mucus and inflammatory cells inside the lumen give inflammatory signals and interrupt the gaseous exchange. Inflammation in the alveolar cells shows the interplay of the interleukins and cytokines reactions with the irritants and pollutants

extensively by scientists to reveal how the mining dust adds to COPD cases along with complications. Inflammation and narrowing of the peripheral airway are the physiological abnormalities observed in COPD. Decreased gas exchange and airflow limitations are the major outcomes of the emphysema caused by parenchymal destruction. The airflow limitation is also caused by the involvement of structural loss of small airways. The accelerated decline in the FEV1 is characteristic of COPD is highly correlated with the extent of inflammation, fibrosis, and luminal exudates in the small airways. Bronchitis has critical implications on the lungs and causes narrowing of the bronchial tubes, inflammation, and excess mucus formation leads to difficulty in breathing. As the disease progresses, the lungs get more deteriorated. There are difficulties in breathing with the progress of the disease; noisy breathing is a common feature along with tightness in the chest. Frequent respiratory infection with fever, chronic cough and lack of energy are also the common symptoms of the progressed COPD patients (Devine 2008; Coggon and Taylor 1998; Colak et al. 2019; Wells et al. 2012).

The mechanism of COPD is a complex event of the innate and adaptive immunogenic response of the lungs towards prolonged exposure to environmental irritants, dust and cigarette smoke. In disease conditions, the inflammation which is usually present in the small airways of cigarette smokers gets elicited, thus promotes tissue damage and blockage or impairment of normal repair mechanism. It also enhances the secretion of neutrophils, macrophages and T lymphocytes (CD8 andCD4) in the lung. This in turn activates fibroblast that initiates aberrant repair process by instigating unnecessary deposition of extracellular matrix thereby disrupting the normal tissue homeostasis leading to bronchiolar fibrosis (Fig. 2) (Sakai and Tager 2013).

Apart from inflammation; oxidative stress (OS) (imbalance between oxidants and antioxidants) and, protease-antiprotease imbalance are considered as significant events in COPD. OS stimulates mucous production or inactivates the antiprotease apart from activation of various transcription factors such as NFκB thus triggers the inflammatory reaction. An increase in the levels of TNF-α, IL-1β, IL-6 and Leucotriene B4 (a neutrophil) and T cell chemoattractant which is synthesized by neutrophils, macrophages and epithelial cells are observed in COPD patients as depicted in Fig. 2. The macrophages and epithelial cells also synthesize IL-8 which attracts cells in circulation and induces a pro-inflammatory response. As a consequence of cellular insults, OS and smoke; various protease and antiprotease are released by inflammatory cells. For instance, neutrophils produce proteases such the serine proteases, elastase, protease-3 and cathepsin G. Likewise proteases released by macrophages are cathepsins E, A, L, S and cysteine proteases. Apart from these, several matrix metalloproteases viz. MMP-8, MMP-9, and MMP-12 are also released by inflammatory cells. Secretory leucoprotease inhibitor, α1 antitrypsin, and tissue inhibitors of metalloproteases are few antiprotease released during COPD. Reduction in the level of Nuclear Factor Erythroid 2–related Factor 2 (Nrf2) transcription factor (which regulates the antioxidant gene) diminishes the production of antioxidants which is again involved in the generation of OS (Fig. 2) (Sakai and Tager 2013; MacNee 2006; Barnes 2013; Boardman et al. 2014).

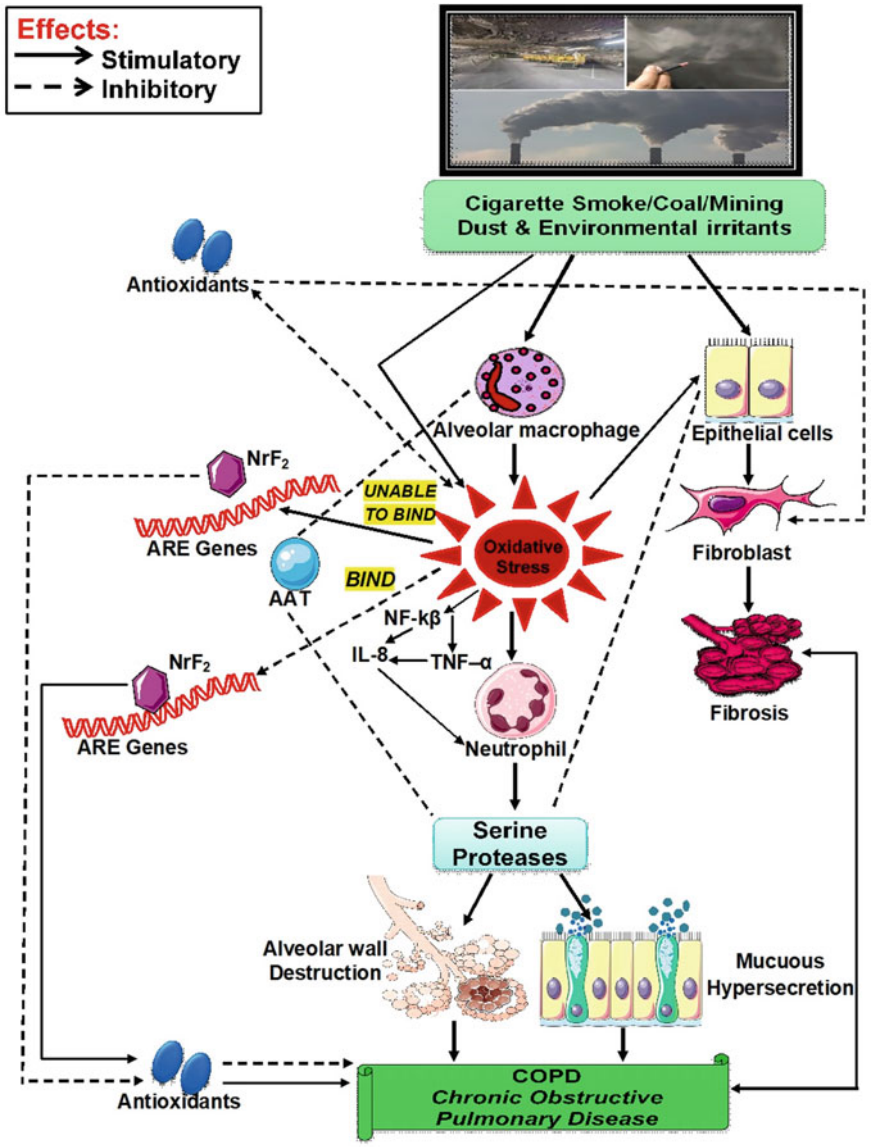

Fig. 2 Overview of COPD mechanism involving neutrophils, macrophages and T lymphocytes as a response to environmental irritants, dust and cigarette smoke. The cells release the chemotactic factors, cytokines, and inflammatory mediators and also activates fibroblast which causes fibrosis due to excessive deposition of the extracellular matrix. OS and protease-antiprotease imbalance are also considered major events in COPD. Mucous production increases due to the generation of OS. Release of the proteases from the neutrophils is involved in alveolar wall disruption, mucous hypersecretion and mucosal inflammation lead to COPD by break down the connective tissue of the lung parenchyma

1.4 Current Diagnostic Methods and Complications

The most effective and painless tests for the diagnosis of COPD are the chest X-ray, computerized tomography (CT) scan, blood gas analysis, trypsin gene predisposition, Lung Function Test(LFT)/Pulmonary Function Test (PFT) also called spirometry. Spirometry is the most reproducible, non-invasive and easy to perform a test to know the inhalation-exhalation capacity along with lung function. The total exhaled air is called Forced Vital Capacity (FVC) of the lungs (Colak et al. 2019; Jackson and Hubbard 2003). The maximum percentage of air exhaled in the first breath within a second is called FEV1(Forced Expiratory Volume). The peak of the expiratory volume is calculated by the speed of the lungs to get empty, which helps to understand the severity of the lung disease. The ratio of the FVC and FEV1 is calculated based on the reference value (Jackson and Hubbard 2003). Despite the good sensitivity and ease to perform in normal settings of the hospital, spirometry, can't be used reliably as the only source for diagnosis due to its low specificity (Miller et al. 2005; Pellegrino et al. 2005). The other tests are equally necessary to perform concurrently for further line of diagnosis. The extent of emphysema can be arbitrated by the X-ray and the CT scan. The diameter of the pulmonary artery can relate to history and risk of exacerbations, which helps in the interpretations of co-morbidities in COPD (Wells et al. 2012). The other important tests for the lung's capacity to bring oxygen in the blood can be analyzed by arterial blood gas analysis and oximetry, which can indicate the severity of COPD for further plan of action for the treatment. COPD is the spectrum of lung complications at different physiological levels starting from the trachea, bronchi to the terminal and respiratory bronchioles. The mortality rate of COPD increases due to the involvement of systemic complications (Amalakanti and Pentakota 2016; Kelly et al. 2001).

1.5 Markers of Chronic Obstructive Pulmonary Disease (COPD)

The biochemical markers of heart diseases in relation to COPD were studied to understand the complex physiological outcomes. Based on the fact studied by Mukherjee et al. (2017), a comprehensive report on the plasma homocysteine, serum C-Reactive Protein (CRP) and Lipoprotein were assessed. Homocysteine and CRP were equivalently sensitive to the progressing disease process rather lipoprotein is controversial. The definite relationship of these indicators of cardiac health with disease progression is used as a good prognostic marker in the management of the disease (Mukherjee et al. 2017). Sputum analysis is totalling to these tests to understand the etiology of the lung diseases as breathlessness can be caused by other ailments of lung diseases.

CRP is an acute-phase reactant protein that has the ability to bind to damage cellular membranes. CRP bears the burden of the elimination of pathogens by recruiting the complement system and phagocytic cells during the inflammatory process. The other

biochemical marker is the two major forms of the sialic acid, the glycoprotein products: N-acetylneuraminic acid (Neu5Ac) and N-glycolylneuraminic acid (Neu5Gc). Sialic acid (composed of alkylated derivatives of the neuraminic acid) is used as an acute phase response stimulated by proinflammatory cytokines such as interleukin-1 (IL-1), Interleukin-6 (IL-6), and Tumor Necrosis Factor-α (TNF-α). Sialic acid has a cell to cell communication and adhesion ability due to its determining sites present on the glycoprotein membrane. It has clinical importance owing to its property of condensation of aldol product from pyruvic acid. It has a major role in Mucolipidosis (are a group of genetic metabolic diseases) and in lung physiology, it is a major constituent of the mucoprotein (Pickup et al. 1997; Mehere et al. 2016). Sialic acid concentration increases in response to inflammation and can be used as one of the acute phase response markers (Nigam et al. 2006). Most of the immune response proteins are glycoproteins that have sialic acid as the terminal sugar on their oligosaccharide chain. Different workers have reported increased serum levels of sialic acid in tissue destruction and proliferation (Mackiewicz 1997; Sirsikar et al. 2016). Sialic acid plays a major role in global cell hyperplasia and submucosal gland hypertrophy due to altered glycosylation (Baos et al. 2012).

Ischemia and atherogenic heart diseases are very frequent findings in COPD patients. Pulmonary hypertension and hypoxic vasoconstrictions of small pulmonary arteries result in structural hyperplasia in COPD patients (Casanova et al. 2017). The inflammatory response and evidence of endothelial cell dysfunction relate to the loss of pulmonary capillaries lead to right ventricular hypertrophy causing a heart attack. CT scan revealed perturbations in pulmonary vasculature are major aspects that relate to COPD along with exacerbations (Dransfield et al. 2013). The reasons reported for these penalties are oxidative imbalance and disturbance of the antioxidant levels along with endothelial dysfunction. OS increases in exacerbations. The increased levels of the oxidants in COPD patients are an indicator of the amplifying mechanism of the systemic circulations (Bai et al. 2017; Calverley et al. 2018). Histoarchitecture of the COPD patients shows emphysema in air sacs where the connectivity between the sacs will end up and forms huge spaces between the alveolar communications (Fig. 2). Due to such conditions of alveolar sacs, the outward airflow gets interrupted. In the primary phase of the disease, these symptoms were mild but with the progress of the disease, it will be a physically powerful indication appears after a long time.

The complex interplay between environment and genetics is extensively studied by Silverman et al. (2001), to understand the role of the environment in COPD development (Silverman et al. 2001). However variable results were noted according to the genetic susceptibility of the individual. According to the studies of Larsson C and Crystal, RG. Alpha-1 Antitrypsin (AAT) is the most relatively established genetic risk factor among COPD patients (Larsson 1978; Janus et al. 1985; Crystal 1990).

The interesting genetic predisposition of lung development in childhood comes into view after the efforts of Laurell and Eriksson (1963). They observed the absence of alpha 1 protein in the serum protein electrophoresis studies characterized its association with pulmonary emphysema. Subsequently, the association with hepatic

cirrhosis, asthma, lung protection from inflammation, and the level of AAT was correlated (Sveger 1976; Eriksson et al. 1986; Eden et al. 1997). AAT is a 52 kDa glycoprotein that belongs to the SERPIN protein superfamily also called SERine Proteinase Inhibitor (McCarthy et al. 2016). This protein is synthesized by the bronchial epithelial cells, neutrophils, and alveolar macrophages and type II cells (Larsson 1978; McCarthy et al. 2016; Carrell and Travis 1985). The data studied on the deficiency of the AAT shows a high risk of the development of COPD in the earlier age group of the population. Heredity deficiency of AAT is a major circulating inhibitor of serine proteases, predisposes the group of population to COPD (Hunninghake et al. 2009). The other genes that are also susceptible to COPD codes for Matrix Metalloproteinase (MMP-12) and Glutathione S-Transferase (GST), which declines lung function and increases the chance of COPD when interacting with noxious environmental factors (Silverman et al. 1998; Tishler et al. 2002).

A major function of AAT proteins is the protection of the lung tissue from proteases by inhibition of human neutrophil elastase (McCarthy et al. 2016). While the absence of AAT, foster the dysfunction and the balance of protease–antiprotease affects directly the emphysema of the lungs (Hill et al. 2000; Kuhn 1986) The polymorphic nature of the gene was comprehensively studied in context to COPD. Till May 2005, 186 single nucleotide polymorphisms (SNPs) in the AAT gene were presented in the public database for the interest of researchers (Martin et al. 1987; Riva and Kohane 2002).

2 Cellular Defense Mechanism Against COPD

2.1 Primary Defense Mechanism, Goblet Cells (Epithelial Lining) and Secretion of Mucus

The respiratory system makes a functional distinction between the transportation of air as a conducting zone and gaseous exchange as a respiratory zone. The role of the conducting zone is to pass the air in and out of the lungs. The conducting zone includes the nose, pharynx, larynx, trachea, bronchi, and bronchioles and the respiratory zone includes respiratory bronchioles, alveolar duct, and pulmonary alveoli. The respiratory zone is at the lower side of the lung performs oxygen and carbon dioxide exchange through the blood capillaries (McDonagh et al. 1979). In the linings of the respiratory zones, epithelial cells are much thinner so the inspired air can be easily dissolved in the pulmonary capillaries. The respiratory tract's major patrol cells are epithelial cells mostly composed of cuboidal and non-ciliated cells. The tracheal lining of the conducting zone is made up of ciliated cuboidal epithelial cells and goblet cells. Apart from these cells, brush cells and basal cells are also hearkening biological protection of the respiratory tract. In the respiratory tract, the primary defender epithelial cells include ciliated epithelial cells present at the apical respiratory tract (Figs. 3, 4, 5 and 6) (Rokicki et al. 2016).

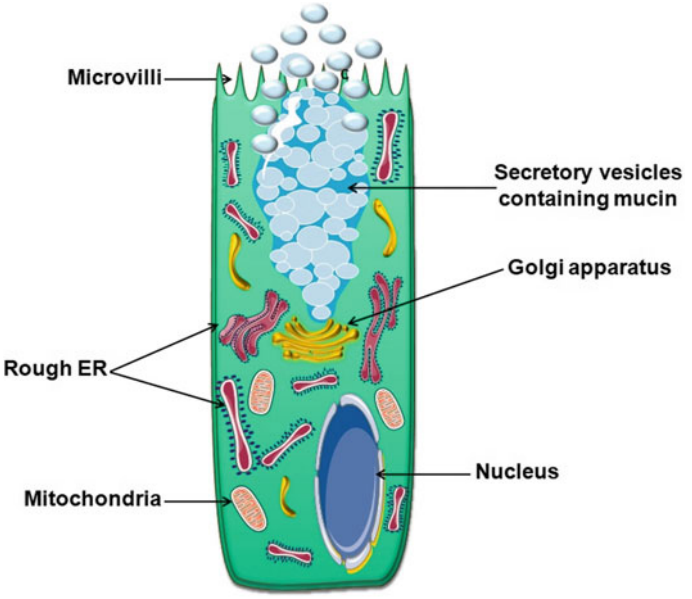

Fig. 3 The Goblet cell (beaker cells) possess a big nuclease at the bottom, densely packed mitochondria, Golgi bodies, and rough endoplasmic reticulum. Large secretory vesicles are present at the apical portion to form mucus

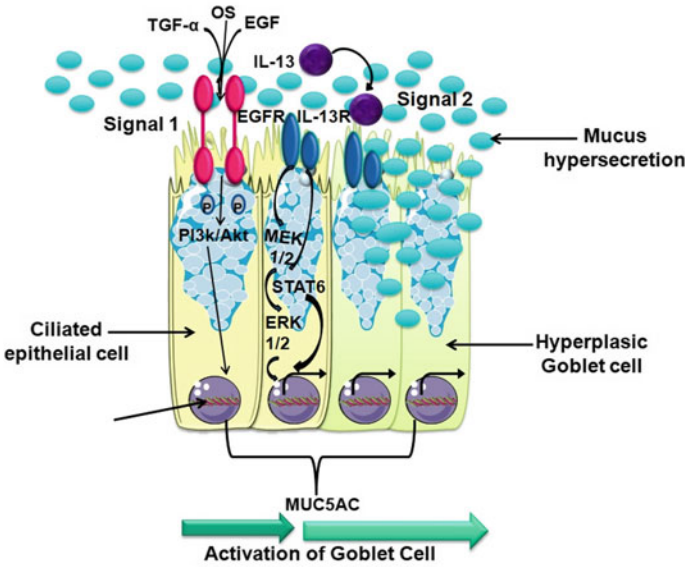

Fig. 4 The Goblet cell (beaker cells), Hyperplasia of goblet cells, and signals of inflammatory mediators to secrete mucus production as an effect of microbial products, and pollutants

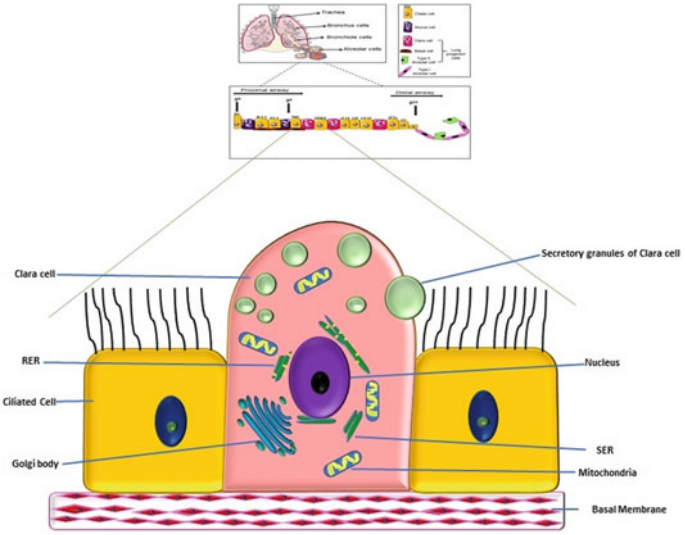

Fig. 5 The Clara cell, Club cells are morphologically columnar to cuboidal with a distinctive dome-shaped luminal surface cell found in the small airways (bronchioles) of the lungs also known as bronchiolar exocrine cells

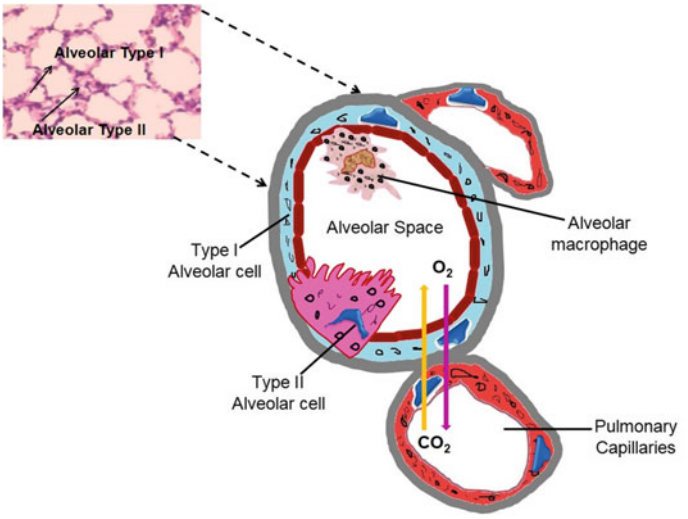

Fig. 6 The respiratory zone shows exchanges of gases in the blood capillaries ad alveoli of the lungs. The alveolar wall posses alveolar type I and II cells that maintain surfactants and cytoprotective molecules for the normal function of the lungs

The goblet cells are also called beaker cells, secrete mucin to form a mucus layer and plays an important function as an immune regulator. Mucus is an elastic and viscous compound formed by mucin, a large molecular weight glycoprotein that has a major role in defense mechanism against environmental pollutants and pathogens. Overexpression of membrane-bound (MUC1, MUC 4, and MUC 16) and gel-forming mucins (MUC2, MUC5AC, and MUC5B) in the airways have been evaluated in the COPD cited in Figs. 3 and 4. Overexpression of mucin is the key feature in COPD which clog the air spaces of the alveolar sacs and leads to the complications of breathing and exchange of gases. The signalling mechanisms of the mucus secretion and their role in mucus clearance may focus on the treatment part of COPD. Mucoactive agents like N-acetylcysteine, ambroxol, bromhexine, erdosteine and carbocysteine are being as therapeutic options as mucus alternators in upper and lower respiratory tract infections. The use of these mucoactive agents in COPD may help to lower the exacerbations frequency (Scaglione and Petrini 2019).

The mucus reported in COPD needs further scientific attention to reveal the mechanism of each mucin. Evidence poses on the MUC1 as a bacterial-adhesive, immunosuppressive, tumorigenic, and anti-inflammatory in other diseases. The prediction comes up as MUC1 in the airway is responsible for remodelling, mucus obstruction, immune suppression, bacterial integration, and disorder of epithelium layers in COPD. The role of each mucin is yet to understand rather the hypersecretion of mucus is well understood that it is a combination of microbial products, pollutants, and the interplay of inflammatory molecules.

2.2 Secondary Defense Mechanism, Clara Cells (Terminal Bronchiole), Secretion of Surfactant Proteins

These two zones of respiratory systems are being demarcated by margin-forming bronchiolar exocrine cells formerly called Clara cells [now known as Club Cells (CCs)]. CCs are columnar, cubical, epithelial cells having non-mucus, non-ciliated secretory dome shape luminal surface as represented in Fig. 6. These were discovered in early **1881** by **Rudolph Albert von Kolliker**. These studies get to pick up when **Max Clara**, an Australian Pathologist emphasized its specificity and distinguished function. The CCs are dynamic in nature and play a two-way role in the protection of the lungs. These cells secrete from the apical region as well as from the basal region which is known as apocrine and merocrine secretion (Reynolds and Malkinson 2010; Xing et al. 2010). Other names of this protein include Club Cell Secretory Protein (CCSP), Secretoglobin (SCGB), Club Cell Protein 16 (CC16), Club Cell Protein 10 (CC10), Urine Protein 1 and Human Protein-1 (Rokicki et al. 2016). Among the human lungs' airway epithelial cells, CCs constitute around 9% of the total cellular population in physiological conditions. Around 11–22% of these cells are found in terminal bronchioles. They are also found in the kidney, prostate and in the gravid uterus.

CCs are apically projected out and shading cell cytoplasm during secretion in the airway lumen. They formed secretory granules which are diffused predominantly from the basal region of the parenchyma. These cells are abundantly present in the terminal and respiratory bronchioles of the lungs. CCs are polarized and apically rich in secretory granules, mitochondria, smooth and rough endoplasmic reticulum for high metabolic activities. At the same time, the basal portion of the CCs is dense with proteins, lipids, and glycoproteins. One-third of the cell is covered with a densely packed centrally located nucleus. CCs play a major role in adapting to remodelling with a breathing environment. CCs are multifunctional and their major duty is to safeguard lungs from glitches of all external factors. It is a foremost metabolic site for xenobiotic metabolism through cytochrome P450 and oxidases (Singh and Katyal 2000; Aryal et al. 2003). Also, it plays a major role in the secretion of non-mucilaginous secretory surfactant proteins which cover the bronchiolar extracellular lining. During these functions epithelial cells get injured, to recover from the insulted episodes, club cells act as progenitor cells for ciliated and secretory cells to regenerate and maintain epithelial cells homeostasis. The major Secretory Proteins or Surfactant Protein (SP) are SP-A, B and D act as a bronchiolar surfactant, which limits lung collapse in diseased conditions (Haczku 2008). The non-ciliated CCs secrets principal small molecular size protein that is CC16 in large amounts to the airways. A readily diffusible CCs protein has two subunits of 10 and 6 kDa, which are present in bronchioles. The CC-10 kDa protein was identified in the urine of the renal failure patient called uteroglobin, which is similar to the Urinary protein 1 (Mukherjee et al. 2007). The protein is reported to control the inflammation and OS in the lungs. The CCs has the same location as other genes i.e. chromosome 11 which is responsible to control allergy and inflammation. Also, it is being studied that the Clara cell has the ability to modulate the response to inflammatory mediators like interferon-gamma (IFN γ) and (TNF-α). Clara cell has the ability to arrest the migration of the cancer cells. CCs CC16 marker was studied according to disease standpoint. In the case of silicosis, scientists opined to use it as a prognostic marker. In sarcoidosis, this protein was studied extensively as a permeable molecule that passes through the glomerular filtration from the kidney in the urine. The role of the ascribed CCs in the lungs was studied in many lung diseases which are yet to clear even scientists have studied morphology and histopathology of these elusive cells. The mitochondrial and smooth endoplasmic reticulum rich CCs granular secretions were the key attraction as a diagnostic molecule among researchers. This protein is confined to associate with inflammatory and infectious pulmonary diseases. This was extensively studied in the Bronchoalveolar Lavage (BAL) fluid as a potential diagnostic marker in silicosis, pneumonia. In the line of the inflammatory marker CC-10 was demonstrated in Bronchial asthma and Chronic Eosinophilic Pneumonia (CEP) with decreased levels while Idiopathic Interstitial Pneumonia (IIP) showed increased concentration in the serum samples along with BAL fluid (Wang et al. 2007; Wutzler et al. 2012).

2.3 The Third Line of Defense: Alveolar Cell I and II in Chronic Obstructive Pulmonary Disease (COPD)

The third vital pulmonary alveolar layer is comprised of type I and II pneumocytes. The SP-A and SP-D are the collagenous surfactants associated with carbohydrate-binding protein playing a role by agglutinating the microorganisms which enter from the upper respiratory tract to the lower portion. SP-A and SP-D help to reduce the surface tension at the air lipid interface which is possible to reduce the collapse of the alveolar cells. SP-A and SP-D, secrets in airspaces belong to the collectins group of the C-type lectin superfamily which is sourced by the CCs and alveolar II epithelial cells (Haczku 2008; Han and Mallampalli 2015). These lectin proteins have the property of defense and elimination of microorganisms by binding to oligosaccharides present on microorganisms. The selectins have the ability to anchor the specific surface receptors of the bacteria. It facilitates inactivation and arrest of the functional ability of the bacteria. They kill the microorganisms by binding to receptors by aggregation. It has the property to generate innate immunity, complement activation, and triggering phagocytosis (Watson et al. 2019). The determining points of the collectins are the allergic response, clearance of apoptotic cells that serve in COPD patients.

3 Conclusion

COPD affecting severity includes progressive airway obstruction, accounts for pulmonary and extrapulmonary involvement. The loss of parenchyma and elasticity of the lungs restrict airflow indicating the intensity of chronic inflammation in COPD. The inflammatory exudates and neutrophil deposits in the lumen of the airways correlate best with the severity of airflow obstruction causing the decline in lung function. Diagnosis of COPD is being performed by biochemical markers by introducing various diagnostic methods at different phases based on the severity of disease, nevertheless, large scale better characterization and validation of the diagnostic, prognostic and pathologic role of the markers produced by the Goblet cell, CC and Alveolar I and II cells is warranted.

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Skin Diseases in Miners

Minal Trivedi and Sushanth Somayaji

1 Statement of the Problem

The occupation of mining has a great risk of injury as well as a disease (McIvor and Johnston 2016). Miners are exposed to various factors like heat, noise, dust, and certain chemicals that over the period of time exposure to such substances can lead to a disease (Prüss-Ustün et al. 2011). One such disease is the skin infection that may disrupt the skin which plays a very important role as a barrier to chemicals and other contaminants entering the body (McIvor and Johnston 2016; Prüss-Ustün et al. 2011). Skin diseases are the 4th leading cause of non-fatal diseases globally (Seth et al. 2017). This article discusses the various causative factors which lead to a skin infection in the mining population & their treatment.

2 Introduction

Skin is the largest organ in the body and is exposed, on a daily basis, to various chemicals and harmful agents (English et al. 2003). With rapid industrialization, there is accompanying growth in the need for metals, coals and other minerals. The rapid growth in mining to fulfil the needs of the industrialized community has caused a growth in the incidence of occupational skin diseases. Mining, more than any other industry exposes the skin to fuels, reagents, solvents, detergents, chemicals, coal dust, silica dust, diesel particulate matter, asbestos, welding fumes, poisonous plants and metal dust (Prüss-Ustün et al. 2011; Scott et al. 2004). In addition to being absorbed

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_5

from the skin, these can also be inhaled, ingested, or be absorbed from the mucous membrane, eye or ears. It however takes decades of exposure for miners to show any adverse effects (Scott et al. 2004).

2.1 The First Line of Defense

The skin is the first line of defense against a wide variety of biological, chemical and physical harm to the body (English et al. 2003). The majority of the workforce manages to remain free of disabling occupational skin disorders. Partly due to the inherent protection the skin provides as a function of the skin's design. The daily use of personal protective measures directed towards minimizing skin contact with known skin hazards at the worksite also helps in the prevention of diseases (Ringen et al. 1995).

The skin is divided into majorly two parts: (a) the Epidermis and (b) the Dermis. The parts are further subdivided into subparts (Fig. 1). Various parts and the subparts of skin play different parts in the defense to mechanical, chemical or biological trauma (Kolarsick et al. 2011).

a. **Epidermis**

i. Stratum Basale (Kolarsick et al. 2011; McGrath et al. 2004):

This is the lowermost layer of the epidermis consisting of epithelium. This layer attaches to the dermis via the basement membrane of the numerous dermal papillae

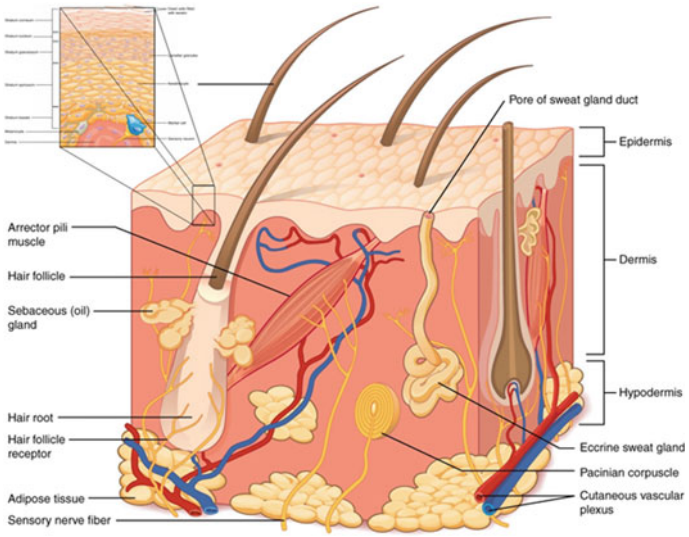

Fig. 1 Structure of the skin (Betts et al. 2013)

which are the projections of the epidermis into the dermis. Various cells in the layer are:

- Basal cell: a precursor to keratinocyte they are constantly undergoing mitosis, and pushed superficially to form keratinocytes. They also provide the replication and repair system against physical damage.
- Merkel's cell: it is the sensory receptor cell for the touch sensation
- Melanocyte: it produces the pigment melanin which acts to prevent the damage from ultraviolet radiation

ii. **Stratum spinosum** (McGrath et al. 2004; Gilaberte et al. 2016)

The layer, on staining, appears as spiny due to the desmosomes. These desmosomes interlock with each other and strengthen the bond between the cells. They are comprised of 8–10 layers of keratinocytes formed from the basal cells. Interspersed amongst them are Langerhans' cells which function as macrophages by engulfing bacteria, foreign particles, and damaged cells that occur in this layer. The cells form keratin and a water repellant glycolipid which makes the skin relatively waterproof.

iii. **Stratum Granulosum** (McGrath et al. 2004; Gilaberte et al. 2016)

This cell forms keratin and keratohyalin which appears as granules giving it the grainy appearance. Slowly as the cell moves superficially the nucleus and the cell organelle disintegrate leaving the protein and the cell membrane. These form the stratum corneum, stratum lucidum, and the accessory structures of hair and nail.

iv. **Stratum Lucidum** (McGrath et al. 2004; Gilaberte et al. 2016)

This thin layer of seemingly translucent cells is mainly present in the thick skin of sole, palm, and the digits. These cells are densely packed with eleiden, a clear protein rich in lipids, derived from keratohyalin. This lipoprotein gives the layer its translucent appearance and provides a barrier to water.

v. **Stratum Corneum** (McGrath et al. 2004; Gilaberte et al. 2016)

This is the most superficial layer of the skin most exposed to the external atmosphere. It comprises 15–20 layers of flattened, dead keratinocytes. This dry, dead layer helps prevent the penetration of microbes and the dehydration of underlying tissues. It also provides mechanical protection against abrasion for the more delicate, underlying layers. The cells are frequently shed and replaced by the cells of underlying layers with the entire layer being replaced in 4 weeks.

b. **Dermis** (Kolarsick et al. 2011; Arda et al. 2014)

i. **Papillary layer**

This is the superficial layer of the dermis interspersing the dermal papillae binding with the epidermis. It consists of loose areolar connective tissue, formed from the loose mesh of collagen and elastin fibres. Along with the connective tissue it contains fat cells, an abundance of small blood vessels, phagocytes, nerve fibres, touch receptors called the Meissner corpuscles. Vascular dilation and constriction under nervous

control are vital to regulating body heat. Phagocytes are defensive cells that help fight bacteria or other infections that have breached the skin.

ii. **Reticular layer**

This layer is composed of a dense articulated irregular mesh of connective tissue, blood vessels, sensory and sympathetic nerve fibres. The appendages of the skin such as the sweat and sebaceous gland, hair follicles are also present in this layer.

2.2 Mechanism of Skin Disorders

The irritants are known to interact with certain enzymes and block their activity, for example, few blister gases target certain enzymes involved in carbohydrate-protein & fat metabolism (Diepgen 2012). Skin is rich in keratin, upon reaction with alkali or acid, the structure of keratin is dehydrated& disturbed. It is a well know fact that oils & fats can be dissolved in organic & inorganic solvents; the same effect can be seen of irritants on the cutaneous lipids (Birmingham and Key 1964). Prolonged exposure to such irritants leads to inflammatory reactions resulting in contact dermatitis (Slodownik et al. 2008).

Various chemicals like calcium oxide, calcium chloride combine with the water within the skin or on the surface of the skin and cause a chemical reaction. Other compounds cause stimulation of pigment-producing cells to over function upon exposure to sunlight like crude petroleum, coal tar pitch, aromatic compounds resulting in hyperpigmentation & abnormal cell growth leading to skin cancer (Rice and Mauro 2008). Hypopigmentation can be seen upon exposure to burns, contact dermatitis with phenols &hydroquinone. The T-cell activation causes allergic sensitization because of alteration in its reactivity (Rim and Lim 2014).

2.3 Causative Agents for Occupational Skin Diseases

The causative agents for skin diseases can be classified into biological, chemical, mechanical & physical agents.

2.3.1 Biological Agents

A few species belonging to various microbial categories like bacteria, fungi, parasites or viruses cause primary & secondary skin infections. Bacterial infections are seen more in people working as fishermen, farmers, poultry workers & animal breeders (Dutkiewicz et al. 1988). Agricultural workers are also known to suffer parasitic infections more commonly people working in the bakery or confectionery industry, child care workers, bartenders,cannery workers, house helpers are prone

to yeast infections (Steele 1968). Skin infections caused by viruses are very few some to include are Herpes simplex Virus common in medical personnel's, milker's nodules in the workers in the dairy industry and sheep pox in livestock handlers (Williamson 1981). Skin disease due to biological agents is less common as compared to other agents. Bacterial skin infections when there is a break in the continuity of the skin giving them an entry. Fungal infection is commoner due to hot & humid conditions of the mine, bulky & thick clothes used by miners for protection & stale conditions of mine like waterlogged tunnels, infrequent exposure to fresh air. These conditions promote the growth of fungal infections like Athletes' foot, Ringworm, Paronychiae (Chauhan et al. 2008).

Chemical Agents

Chemicals from ages are known to be harmful to humans. Both organic as well as inorganic chemicals can act as allergic sensitizers or skin irritants. Approximately 75% of occupation dermatitis are caused by chemicals. Chemicals like a few concentrated acids, salts & alkalis on exposure can injure a person's skin and destruct it completely within few minutes of exposure (Rozas-Muñoz et al. 2012). There are few weak irritants too that require repeated exposure up to several days or weeks to display toxic effects, such chemicals include cutting fluids, dilute acids, alkaline dust etc. (Chauhan et al. 2008; Rozas-Muñoz et al. 2012). Many chemicals found in plants also does serve as a source of skin irritation. The polyhydric phenols found in the species belonging to the family *Anacardiaceae* cause allergic contact dermatitis. Other allergic plants in crop harvesters include garlic, onions, asparagus, chicory, primrose, tulips, castor beans, pineapple (Hermans and Treadwell 2010). Many chemicals are used as pesticides &preservatives like DDT, naphthalene, fluorites, arsenic compounds, mercury compounds & tar for wood, increasing the chances of skin infections in carpenters & craftsmen working with wood (Birmingham and Key 1964).

2.3.2 Mechanical Agents

The use of vibration producing instruments can cause spasms in fingers. Pressure or friction can lead to the formation of blisters & callus leading to myositis, laceration, tissue abrasion and even can damage the nerve. Those who use hammers, riveters & chippers can injure the soft tissue & cause bone injury too (Cormina and Kuykendall 1955).

2.3.3 Physical Agents

Humidity & High temperature can cause sweat retention syndrome. Mild heat exposure leads to chafing, bacterial or fungal infection & skin maceration (Gubernot et al. 2014). The people working in furnaces, labourers working for road construction, pipeline workers can be prone to burns. Not just the high temperature but even cold

temperature can be hazardous, leading to blistering, ulceration, gangrene (Gubernot et al. 2014; Lushniak 2004). Cold injuries in form of frostbite can affect the nose, ears & throat, hands & legs of construction, miners & military workers. Prolonged exposure to sun rays or artificial ultraviolet lamps can damage the skin, commonly seen in metal welding workers, glass, laser beam operators. High-intensity electromagnetic energy associated with laser beams is well able to injure human tissue, notably the eye though skin damage is less of a risk but can occur (Lushniak 2004).

Skin diseases can be not just because of occupational exposure but also due to some non-occupational factors. A pre-existing condition can worsen the occupational influences. Several non-occupational diseases affecting the skin can be worsened by various occupational influences. Overweight workers can suffer from prickly heat. People who tend to sweat a lot can be also prone to skin irritation caused by chemicals formed due to the hydrolysis of sweat (Gubernot et al. 2014). Dark-skinned people have a good tolerance to sunlight but display quick response to inflammatory pigmentation as wells as develop keloids. Young employees suffering from acne can have the worse condition when exposed to grease, coal tar, oils etc. while mining (Birmingham and Key 1964).

2.4 Types of Occupational Skin Diseases

Acute Contact Dermatitis (Chew and Maibach 2006)

The symptoms of acute contact dermatitis include itching, burning, redness, swelling and oozing. It can occur anywhere on the skin mostly seen on the inner wrists, back of hand & forearms of the workers. It can occur on the forehead, face, eyelids, neck, ears if a worker is exposed more to the dust or vapour. It is usually caused by wearing contaminated clothing, exposure to an irritant, photoreactive agents. Severe blistering can occur if exposed to the strong irritant. Subacute contact dermatitis occurs due to repetitive exposure to weak irritants and can be seen in form of dry & red plaques.

Chronic Eczematous Contact Dermatitis (Luelmo-Aguilar and Santandreu 2004)

Chronic eczematous contact dermatitis occurs when dermatitis recurs over an extended period of time. The symptoms seen on hands, wrists, fingers & forearms include dry, scaly & thickened skin, cracking & fissuring of fingers & chronic nail dystrophy. Frequent, repeated exposure to the causative agent can lead to oozing from the lesions.

Folliculitis and Acne (Pigatto and Bigardi 2000)

Follicular openings develop lesions in the workers involved in dirty jobs and having poor personal hygiene. These are caused due to exposure to aromatic compounds, chlorinated hydrocarbons & tar products. These occur on the forearm, thighs &

buttocks. Another serious issue is chloracne caused by chloronaphthalene, chlorobiphenyls, tetrachlorobenzene leading to hyperpigmentation & scarring.

Granulomas (Peate 2002**)**

Granulomas can be caused by occupational exposures to microbes like bacteria, fungi, viruses or parasites. Granulomas are also caused after skin embedment of gravel, wood splinters, silica, bone fragments or zirconium.

Photosensitivity Dermatitis (Nag et al. 2010**)**

Light either in natural or artificial form can cause phototoxic effects on the skin. Common photoreactive chemicals are anthracene & coal tar. Plants belonging to *Umbelliferae* like celery, fennel and dill are also photoreactors.

Pigment Change (Harries and Lear 2004**)**

Occupational exposure to heavy metals, dyes, chlorinated compounds, petroleum oil & sunlight can lead to change in skin pigment. It leads to permanent skin discolouration along with argyria. Petroleum products are known to cause the overproduction of melanin. A previous burn or contact dermatitis can lead to hypopigmentation or depigmentation.

Sweat-Induced Reactions (Harries and Lear 2004**)**

Sweat is one of the factors which can lead to skin infections. Too much sweating can lead to prickly heat & chafing. Sweat in the underarm area & groin area can cause microbial infection of the skin appendages like hair follicles, sebaceous glands, sweat glands.

Ulcerative Changes (Harries and Lear 2004**)**

Chemicals like arsenic trioxide, calcium oxide, calcium nitrate, chromic acid & calcium carbide are ulcerogenic chemicals that affect the hands, palms & fingers. Burns caused by chemicals or heat may give rise to infections by bacteria or fungi.

2.5 Diagnosing Occupational Skin Diseases (2012)

For the diagnosis of occupational skin disease, it is very necessary to consider the family history especially related to allergy. The next parameter to be considered is the occupation, nature of the work, location & duration of the work. These factors should be critically noted as they can help in diagnosing for example if a rash is seen, it's important to know when,where it appeared, any first aid or medicines taken and whether other workers have been also affected or not.

The following points play a vital role in the clinical diagnosis of skin infections.

Site affected: Finding the site affected is an important point to be considered first, usually hands, wrists forearms are commonly affected. Exposure to fumes or dust can affect sites like the face & neck.

2.5.1 Appearance

The lesions that appear need to be carefully examined. Acneform, Follicular, neoplastic, ulcerative granulomatous lesions, pigmentary, amongst all chronic eczematous contact dermatosis are most common.

2.5.2 Diagnostic Tests

Laboratory culture from the ulcer or wound is done to recognize the offending microbes. Their quantification can be done with the help of Real-Time PCR (Chew and Maibach 2006; Harries and Lear 2004). Allergic reactions are diagnosed with the help of a Patch Test of different commonly exposed chemicals. An analytical examination of other body fluids like urine, blood andof tissue should be done. These are required to rule out systemic causes of the skin disease and also to rule out complications.

2.5.3 Treatment and Course (Lushniak 2000)

The frequency of skin infections should be monitored. Some improve on cessation of contact. Ulcerations too improve post removal of source. For example, if a patient suffering from dermatosis doesn't improve within two months after ceasing the contact with the suspected agent then other causative agents should be looked upon including the non-occupational sources also. Further proper medications should be taken with the proper completion of antibiotic courses. Application of creams & sunscreen lotions as prescribed by the medical practitioner. Proper dressing of any open wound and keeping it dry.

2.5.4 Prevention (Nag et al. 2010; Lushniak 2004)

The occupation skin disease can be prevented taking into following considerations.

- Elimination of the hazard or by substituting a less hazardous chemical process
- Minimizing the direct exposure to dust, fogs, gases & their vapors
- Maintaining the hygienic conditions at the workplace
- Wearing proper protective clothing like protective suits, aprons, gloves, eyewear & headgear. Also applying sunscreen if work demands exposure to the sunlight
- Quick access to first aid kit & medical facility should be available
- Proper health assessment of the personnel should be carried at regular intervals
- The personnel working should be educated about the hazard and how to tackle them.

3 Conclusion

Skin being the barrier to the external environment that can enter the body, should be very well taken care of. This skin can be damaged due to unavoidable factors at the workplace like dust, fog, gases & vapors, sunlight etc. If a skin infection occurs should be properly treated under the guidance of a medical practitioner. Also, the precautionary measures at the workplace should be strictly followed. With the advent of technology, there is a need to search for a better alternative for existing hazards so that the global burden of occupational skin diseases can be reduced.

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Determination of Arsenic Extraction by an Indian Ecotype *Pteris vittata*; Arsenate Reductase Activity Assay and *arsC* as a Molecular Marker

Sarita Tiwari and Bijaya Ketan Sarangi

1 Introduction

Arsenic is a hazardous metalloid known for toxic effect on living organisms and the environment (Smedley and Kinniburgh 2013; Upadhyay et al. 2019). Arsenic pollution has aggravated insidiously in soil, water and air due to uncontrolled industrial activity, natural and geogenic processes (Mandal and Suzuki 2002; Chung et al. 2014). This metalloid exists in different organic & inorganic forms in the environment, but under natural conditions, it exists predominantly in arsenate (AsV) and arsenite (AsIII) (Butcher 2007) both of which are proved to be perilous to biological organisms having different modes of action (Sharma and Sohn 2009). Chronic arsenic exposure to human beings causes severe health effects and also prolonged exposure results in a disease named arsenicosis. Further, arsenicosis sufferers develop issues related to heart, renal, gastrointestinal, infertility and also develop cancerous tumours (Khan et al. 2009). So far, apart from preventive measures for less exposure to the toxic metal, there is no effective drug for the treatment of arsenicosis (Ahmad et al. 2018). Mitigation of As pollution is of great priority. Although technologies for mitigation of As pollution are available, and have been implemented for cleanup of As from water and soil (Choong et al. 2007; Yuan and Chiang 2007), these technologies have limitations of high energy input, operation cost, environmental footprint, non-sustainable approach and not feasible for applying in large areas with contamination.

Phytoremediation is epitomized as one of the promising "green technologies" for the containment of pollutants in comparison to other physio-chemical methods,' coupled with public acceptance and its environmentally benign nature (Suresh and Ravishankar 2004; Ali et al. 2013; Yan et al. 2019). However, employment of this

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_6

technique for mitigation of different toxic metal contaminants has met with limited success due to limited choice of potential plant species with essential characteristics for such application based on phytoremediation principles (Zhao and McGrath 2009). Plants laced a unique property for accumulating a high amount of metals inside their biomass are identified as hyperaccumulator plants, which provides wider scope in the optimization of the phytoextraction process. Till date, the proven As hyperaccumulators are mostly fern species within *Pteridaceae* family (Zhao et al. 2009). However, *P. vittata* is the first discovered and established As hyperaccumulator having the exceptional ability of As uptake and accumulation in its biomass (Zhao et al. 2009; Ma et al. 2001), its classification details are given in Fig. 1.

Pteris vittata (Indian ecotype)

Arsenic accumulation by plant species depends on their ability to tolerate the metal stress, and sequester it in its biomass, which is a function of genetic and biochemical organization of the plant system (Sarangi et al. 2009; Sheoran et al. 2011). Stress tolerant prokaryotes and eukaryotes have evolved specific physiological and biochemical mechanisms to cope with the adverse condition by virtue of specific molecular determinants in their genome. The primary step approach for reduction of As toxicity is by reduction of As(V) to As(III) which is reported in bacteria, fungi and hyperaccumulator plants (Shi et al. 1999; Mukhopadhyay et al. 2000; Xu et al. 2007; Zhu and Rosen 2009). Arsenate reductase is the transcript of *arsC* gene, one of the exons of the *ars* operon identified in the plasmids of *E. coli* and *Staphylococcus,* as well as in the *E. coli* genome (Diorio et al. 1995). The presence of *arsC* ortholog has also been reported in prokaryotes (Rosen 2002), eukaryotes (Mukhopadhyay and Rosen 1998) and also in the As hyperaccumulator *P. vittata* plant. The corresponding gene is designated as *PvACR2* (Liu et al. 2009a). This scientific evidence support reason to utilize *arsC* gene as a genomic marker to identify As hyperaccumulator candidate plants.

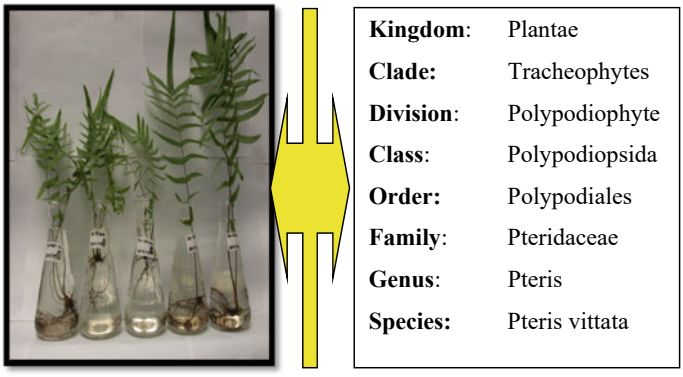

Fig. 1 Pictorial representation of arsenic treatment concentration and its classification

Identification of potential plant species for better performance of phytoremediation system is an important issue. Although many other plants were reported as As accumulators before *Pteris vittata* was reported, many of them were found not true (Meharg and Hartley-Whitaker 2002). The reason being, although deposition of As inside the plant was determined, no molecular marker was used to ascertain the occurrence of specific active mechanism(s) in the plant conferring such behaviour. In view of this, molecular biological tools have been applied to identify potential plant species using biomarkers and understand the molecular mechanism underneath detoxification. Several studies have been carried out to relate probable mechanism acting in As tolerance and detoxification in different ecotypes of *P. vittata* (Mathews et al. 2010; Lei et al. 2012). It has been established that; *P. vittata* uptake As with the help of root and translocate it into frond where As gets converted into less toxic form, and finally get stored inside the cell vacuole (Chen et al. 2005; Wang et al. 2010). The present investigation was carried out to determine As tolerance and accumulation ability by an Indian ecotype *P. vittata* plant at different As levels, as well as to find out the occurrence of a molecular marker involved in As detoxification and hyperaccumulation mechanism.

2 Review of Literature

Uncontrolled trade, anthropogenic activities, and geogenic constitution to a certain extent have polluted the cleaner environment with contaminants of different nature and intensity amongst which heavy metal marks a noteworthy position due to its non-destructible nature (Yang et al. 2018; Vareda et al. 2019). Arsenic (As) listed among the top 10 toxic heavy metals exist in the earth's crust, averaging about 3 mg As kg^{-1} (Mandal and Suzuki 2002; Zhao et al. 2010), but in many localities it is aggravated due to various anthropogenic activities (Mandal and Suzuki 2002; Benner and Fendorf 2010). Arsenic is not an essential nutrient for plants, their entry into plant biomass has deleterious effects at multiple levels. As a chemical analogue of phosphate, As(V) interferes with oxidative phosphorylation, while As(III) exerts inhibitory effects on enzyme activity by binding to thiol groups (Zhao et al. 2010; Dixon 1996; Hughes 2002). By virtue of its chemical and biological reactivity potential, these heavy metal imparts toxicity to exposed biota depending on its type and chemical form. Proven cytotoxicity, mutagenicity and carcinogenic character of As is a big threat to animals and plants, especially to human health that warrants immediate implementation of appropriate technology for abatement, and prevention of its entry into the natural environment (Hadjiliadis 2012). In some parts of India such as, West Bengal, Gangetic plains, Central provinces and Coastal parts of south India, As toxicity induced human diseases is alarming which needs urgent attention. Mitigation of As pollution in large areas using the conventional engineering techniques is of limited success due to feasibility issues, high cost, generation of secondary wastes and its non-sustainable nature. Research and Development for As pollution mitigation is a priority area; researchers are persistently involved in the exploration

of a tenable and sustainable eco-friendly approach for remediation application. A plant driven method called phytoremediation; employ plants to extract metal from soil/water matrix, found to be a sustainable methodology in many counts (Saxena et al. 2019; Thijs et al. 2017). Phytoremediation classified into four subtypes on the basis of its way of approach for remediation of the pollutant and/or toxicant, such as; I) **Phytotransformation** in which plant metabolites transform, neutralize or diminish the pollutant II) The second type employ root dwell microbes for remediation called **Rhizodegradation**, (III) **Phytoextraction** is the third type in which pollutant is compartmentalized inside plant biomass and can be further reused (IV) The fourth type i.e. **Phytostabilization** involves root assisted immobilization of toxicant on their site, as in the case of mine tailings (Awa and Hadibarata 2020; Ashraf et al. 2019). Of the four types, Phytoextraction is mostly preferred due to entrapment of the contaminant reducing the risk of its re-escape into the environment. The up-gradation of the phytoremediation method demands the employment of a hyper-accumulator plant bestowed with unique characteristics of accumulating a high concentration of heavy metal inside its biomass efficiently and in lesser time (Yu et al. 2010). The hyperaccumulators are the elite candidate of the phytoextractions technique with the advantage of intaking several folds of metal inside the plant in comparison with other plants (Yan et al. 2019; Yadav et al. 2018). However, the practicality of phytoremediation method has limitations due to tame growth of the plant, hinderance in metal availability in the root zone and scarce biomass. Extensive researches are in progress to surpass these limitations, and improvise the parameter for optimization of the present method aiming at heavy metal remediation (Luo et al. 2016).

The initial response in plants under As stress is enzymatic synthesis of phytochelatins (PC_n), the polymers of Glutathione (GSH), by the enzyme phytochelatin synthase (PCS). The synthesized PC_n travel from root to shoot and *vice versa*, which along with GSH form different complexes with As(III) rendering its detoxification. The complexes so formed, can be sequestered in the vacuole by *ABC*-type transporter many aspects of which are still uncovered. Apart from the complexed As form, the presence of a free form of As(III) are also reported in vacuoles, but the form in which it is translocated to the vacuole is unknown in eukaryotes. The probable onset of inorganic As inside humans is through phosphate (exact types not known) and aquaglyceroporins transporter (Rosen 2002). The mechanism known underlying the primary detoxification of As is by conversion of As(V) to As(III) in presence of arsenate reductase (AR). The existence of AR gene has been reported in some plants like *Arabidopsis (AtAsr/AtACR2), Holcus (HlAsr)* and *Pteris (PvACR2).* The gene *Acr2p* is homologous to AR gene,which is reported to having similar activity of As detoxification in yeast (*S. cerevisiae*), as well as was also found in the Chinese brake fern (*P. vittata*) (Duan et al. 2005). Enhanced AR activity up to sevenfold was prominent in As tolerant plant in comparison to non-tolerant plant species. This signifies the pivotal role of AR in detoxification of As in As hyperaccumulating fern.

3 Material and Methods

3.1 Experimental Setup

The studied *P. vittata* ecotype was collected from the Kerala state of India and the plants were maintained in the glasshouse at CSIR-NEERI, Nagpur under controlled conditions. The acclimatization and treatment of plants under different As concentrations was done as per our previous work (Tiwari et al. 2016). The concentration of As selected for treatment were 25, 50, 75, 100 and 150 mg L^{-1} in the form of sodium arsenate ($Na_2HAsO_4.7H_2O$), and treatment was carried out for 14 days.

3.2 Arsenic Estimation in the Plant Biomass

Biomass from control & treated plants were harvested after the growth period, and As content inside plant biomass was estimated as per the protocol of Tiwari et al. (2016).

3.3 Arsenic Speciation in the Plant Biomass

For As speciation assessment, plant samples were ultrasonically extracted in 10 ml of methanol (HPLC grade)/water mixture (1:1 v/v) two times for 4 h at 60 °C (Zhang et al. 2002). Extracts from both steps were pooled and volume adjusted to 100 ml with MilliQ water. The extracts were passed through the disposable As speciation cartridge which is packed with 2.5 g of selective aluminosilicate adsorbent obtained from Metal Soft Centre, Highland Park (NJ08904), USA, which binds to As(V) and does not adsorb As(III). The difference between total As concentrations in the digested plant extract to that of the As(III) concentration in the filtrate sample passed through the cartridges, is equal to the concentration of As(V) in the plant extract. The cartridges were used for the separation of inorganic As species only. The As content was estimated using the instrument as carried out in our previous work (Tiwari et al. 2016).

3.4 Determination of as Bioaccumulation and Growth Performance

The BF of As concentration in plant biomass was determined as the ratio of the concentration of metal accumulated in the biomass to that in the treated nutrient solution (Rascio and Navari 2011). The translocation factor and Relative Growth

Rates (RGR) of the plants were estimated as per the formula used in our previous work (Tiwari et al. 2016).

3.5 Molecular Analysis

3.5.1 PCR Amplification and Analysis of *arsC* Gene

The DNA sequences of *ACR2* and *ACR3* genes of *arsC* exon of *Saccharomyces pombe*; which are parts of *ars* operon (Mukhopadhyay et al. 2000), and also coding for AR in *P. vittata* (Ellis et al. 2006) and *Arabidopsis thaliana* (Dhankher et al. 2006), were retrieved from GenBank. The PCR primers were designed using PRIMER3PLUS software (www.pubmed.de/cgibin/primer3/primer3plus.cgi) as listed in Table 1. The primers were custom synthesized (Sigma) and used for PCR amplification using genomic DNA of the studied *P. vittata* genotype as a template.

Genomic DNA was extracted from fresh leaves of *P. vittata* plant by the CTAB method (Reichardt et al. 1993) and stored at −20 °C for PCR reaction. All PCR reactions were carried out in a mini MJ thermal cycler (BioRad). The thermocycling profile for each primer is given in Table 2. The PCR products were resolved on 2.5% agarose gel and purified using the Zymoclean GE Gel DNA recovery kit (Prolab D4001). Purified amplicons of 18S rRNA were further sequenced through a service provider. The query sequence was analyzed through the BLASTn tool (NCBI Gene Bank database).

3.6 Protein Extraction and Arsenate Reductase Enzyme Assay

For the enzymatic assay, plants grown in different As concentrations in nutrient solution were taken out after 9 days, washed thrice with tap water followed by deionized water and wiped with a paper pad. The roots and shoots were separated and used for protein extraction. Known amount of each material was homogenized with liquid nitrogen and extracted with buffer containing 50 mM MOPS and 50 mM MES (pH 6.5). The tissue extract was filtered through four layers of cheesecloth, centrifuged for 30 min (10,000 × *g*) at 4 °C and passed through Sephadex PD-10 desalting columns (Amersham Biosciences), pre-equilibrated with the extraction buffer to remove interfering low M_r compounds. All the above steps were carried out at 4 °C. Protein concentration in the extract was determined by Bradford's method (Bradford 1976) using albumin (Bovine V, Sigma) as standard. The protocol followed for the assay of arsenate reductase enzyme in plant biomass was according to Tiwari et al. (Tiwari et al. 2016).

Table 1 List of primers used for amplification of 18S rRNA, *ACR2* and *arsC* genes

Gene	Primer name/ specific to	Direction	Sequence (5'–3')	Expected amplicon size	Source
18S rRNA	18SCOMF/ Universal eukaryotic system	F	TGCATGGCCGTTCTTAGTTGGTGG	500 bp	Senjie and Zhang (2001)
	18SCOMR Universal/ eukaryotic system	R	CACCTACGGAAACCTTGTTACGAC		
ACR2 (designated in *Saccahromyces pombe)*	*Arsenate reductase*	F	TGTTGGGCACATTGCGGG	137 bp	This study
		R	GTCAGCATAGTGGACCAGCGT		This study
ACR3 *(*designated in *Saccahromyces pombe;* part of *ars* operon of *E. coli* also found in *Pteris vittata)*	*Arsenate reductase*	F	CATAACGTCTAGGCAACTCAAGG	246 bp	This study
		R	ACTTTTGGTCCCCTATTCTTGG		This study
Pteris vittata **NCBI Ac. No. EU884387 gi|197,210,519**	**1A and 1B**	F	AAACGTCGAACCGTATGAGG	216 bp	This study
		R	ACGACTTTCTCGCCATCTTCC		
Arabidopsis thaliana **NCBI: NC_003076.5**	**2A and 2B**	F	TAGCTGGATCGCTACACTATGC	215 bp	This study
		R	TCTACGAATAGCCAATTGATGC		
Saccharomyces cerevisiae **NCBI: NC_001148 > gi|50,593,503**	**3A and 3B**	F	CATAACGTCTAGGCAACTCAAGG	246 bp	This study
		R	ACTTTTGGTCCCCTATTCTTGG		

Table 2 Primers with PCR condition

Primer name	PCR condition
18 s rRNA	94 °C 4 min, followed by 35 cycles of 95 °C 1 min, 58 °C 30 s, 72 °C 1 s min and 4 min final extension at 74 °C
ACR2	94 °C 4 min, followed by 35 cycles of 94 °C 45 s, 58 °C 30 s, 72 °C 45 s min and 5 min final extension at 74 °C
ACR3	94 °C 4 min, followed by 35 cycles of 95 °C 1 min 56 °C 30 s, 72 °C 45 s min and 4 min final extension at 72 °C
1A & 1B/2A & 2B/3A & 3B	94 °C 4 min, followed by 35 cycles of 95 °C 1 min 50–55 °C 30 s, 72 °C 45 s min and 4 min final extension at 72 °C

4 Results and Discussion

4.1 Arsenic Tolerance and Concentration in Treated Plant

Total As concentration in the plant biomass showed linear increment with an increase in treatment concentration. Arsenic concentration was predominantly higher in the aerial biomass as compared to underground biomass (Fig. 2). The trend of more As translocation to the upper part observed in the present research are in agreement with findings reported in other As hyperaccumulating ecotypes of *P. vittata* (Cong et al. 2002; Xie et al. 2009). Arsenic accumulation potential of the studied ecotype

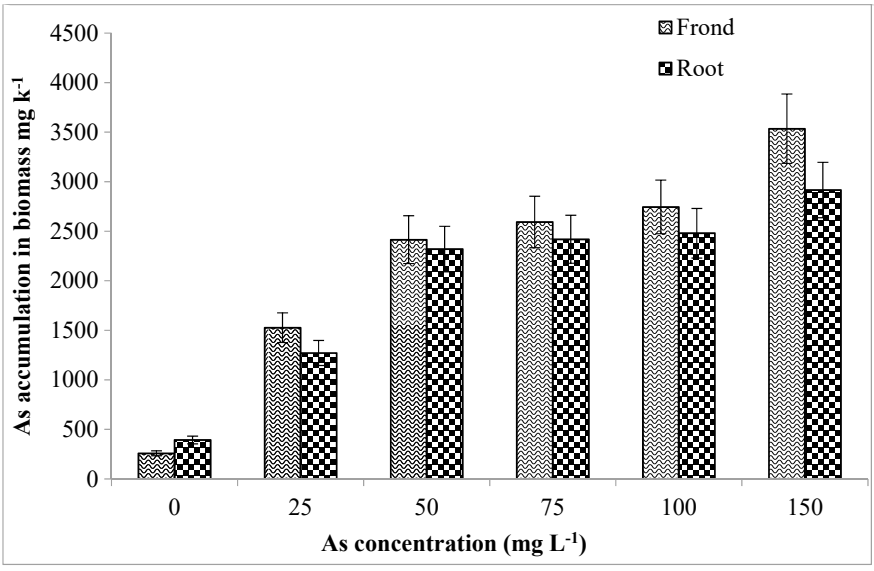

Fig. 2 Arsenic concentration in root and frond of *Pteris vittata* grown with a different arsenic concentrations in the nutrient solution. (mean ± standard deviation(SD))

varied significantly ranging from 1526 to 3535 mg kg^{-1} shoot biomass, and 1271 to 2916 mg kg^{-1} root biomass. Lampis et al. (2015) had observed As uptake of about 1,200 mg kg^{-1} dry wt. in frond, and 80 mg kg^{-1} dry wt. in the root of *P. vittata* after 4 months treatment in contaminated soil having 180 mg As kg^{-1} soil. Which is substantially less than As accumulation in our experiment with the studied ecotype. A study by Singh et al. (2010) elucidated a As hyperaccumulator with As concentration of more than 1000 mg kg^{-1} of its above-ground biomass which is similar to our findings in the Indian ecotype studied by us. Higher As concentration in the frond of this Indian ecotype indicates that a major portion of the absorbed As get transported to the above-ground biomass for accumulation. Arsenic is toxic to plants even at low concentrations but, in the studies *P. vittata* ecotype there were no toxicity symptoms up to the end of treatment; all appeared green and healthy similar to control, except treatment at 150 mg As L^{-1} which showed slight necrosis. The RGR of the studied plants treated with all concentrations of arsenic was determined with reference to controls (Table 3). The results clearly indicate that in all As treatment concentrations *Pteris* showed positive RGR and high RGR in treated plants in comparison to control. The As BF in this ecotype varied from 43 to 111, with the highest BF at 25 mg L^{-1} (Table 3). The Translocation factor (TF) value for all treated plants was greater than 1. On the basis of BF & TF, this Indian ecotype of *P. vittata* is categorized as As hyperaccumulator in line with other *P. vitiata* plants (Ma et al. 2001; Rascio and Navari 2011; Verbruggen et al. 2009) those exhibited high metal uptake, and BF & TF > 1 (Salt et al. 2000). The TF is an indicator to differentiate between excluders and accumulators. Tolerance is an adoptive mechanism (Hall 2002) that allows plants to accumulate metal in their biomass higher than the concentration in the growth medium and the plant species still carrying out metabolic processes (Pollard et al. 2002). Based on these backgrounds and in the light of present experimental findings it is confirmed that this Indian ecotype of *P. vittata* studied by us is also a As hyperaccumulator and has potential for As phytoremediation application.

As(V) structurally resemble phosphate and may replace phosphate in several reactions, while As(III) may react with critical thiols in proteins and inhibit their activity (Hughes 2002). Due to differential mode of action, As speciation is required

Table 3 BF and TF of *Pteris vittata* at different concentration

Arsenic concentration (mg L^{-1})	Bioaccumulation factor	Translocation factor	RGR
0	–	–	0.011
25	111	1.20	0.014
50	94	1.04	0.016
75	66	1.07	0.019
100	52	1.10	0.022
150	43	1.21	0.003

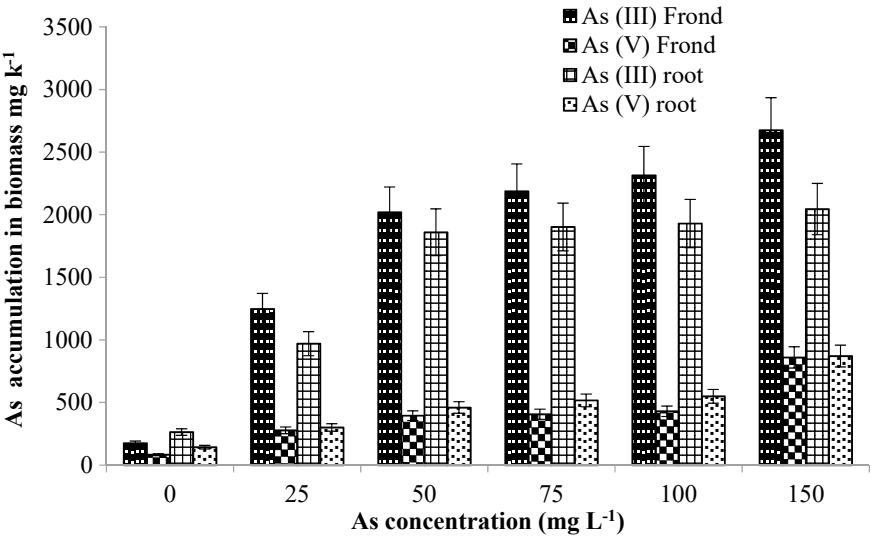

Fig. 3 Speciation of arsenic in root and shoot of *Pteris vittata* at different As concentration (mean ± standard deviation(SD))

for understanding As metabolism in plants. In our study, it was found that As(III) was predominant in both root and shoot of the Indian ecotype *P. vittata* compared to As(V) (Fig. 3). Of the total As accumulated in the biomass, As(III) ranges from 39 to 57% in frond, and 43 to 61% in root respectively. According to Zhao et al. (Zhao et al. 2010), many plant species revealed the predominant presence of As(III) in their biomass including *P. vittata* which showed As(III) more in its frond. In the contrary, Su et al. (Su et al. 2008) found that As(III) was highest in the xylem sap of *P. vittata,* regardless of As species supplied. Further, he hypothesized that As(V) reduction mainly occurs in the roots, and the reduced As(III) is then rapidly translocated to the fronds. However, in our experiment, rhizomes were attached to the roots. Therefore, it is unclear whether As(V) reduction occurs in the roots and/or rhizomes. In another study, Mathews et al. (2010) reported elevated As(V) reduction in rhizome comparable to other parts of *P. vittata.* In our study, it was observed that As(V) to As(III) conversion takes place in fronds as proven by other investigators (Bondada et al. 2004; Tu et al. 2004). Non-removal of rhizome from the root may be the cause of high As(III) in the root. These differences in the chemical speciation and distribution of arsenic in *P. vittata* and other angiosperms suggest that *P. vittata* and its relatives have evolved a mechanism for tolerating, transporting, and accumulating arsenic that is unique in plants.

4.2 *Detection of* arsC *Gene*

PCR was carried out with genomic DNA of the Indian ecotype *P. vittata* as template using arsenate reductase gene specific primers designed from *arsC* cistron to determine the presence of AR gene conferring reduction of As(V) to As(III) in relation with As hyperaccumulation and detoxification. It is proven that AR enzyme mediates reduction of As(V) to As(III) to prevent an increase in intracellular As(V) which hinders ATP synthesis as a competitor of phosphate and therefore, it plays a very important role in As detoxification (Tripathi et al. 2007).

Based on the available information with relation to As detoxification & hyperaccumulation, genome of the studied Indian ecotype of *P. vittata* was analyzed to determine the presence of *arsC* as the molecular signature for As detoxification. Amplification of *P. vittata* genomic DNA with the *arsC* gene-specific primers resulted in amplicon except for 2A & 2B primer sets (Fig. 4). This confirms that the gene responsible for the conversion of As(V) to As(III) is present in this ecotype of *P. vittata.* To ascertain the genotype of the studied Indian *P. vittata* species, genomic DNA was amplified using 18S rRNA based universal primers which resulted in a 500 bp amplicon. The amplicon was sequenced and blasted in GenBank (NCBI) database. The query sequence returned hit with homology with *P. vittata*, and the sequence was deposited in NCBI database with new accession no *JF491437* as 18 s RNA *P. vittata* of Indian ecotype. Our study indicates, these biomarkers could be used to screen and assess prevalence of As stress tolerance in plants.

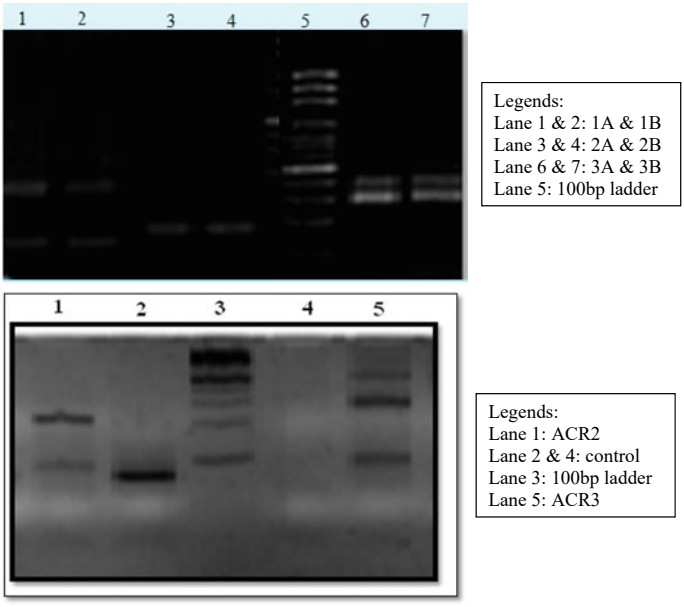

Fig. 4 Amplification of arsenate reductase gene-specific primer using *Pteris vittata* genomic DNA

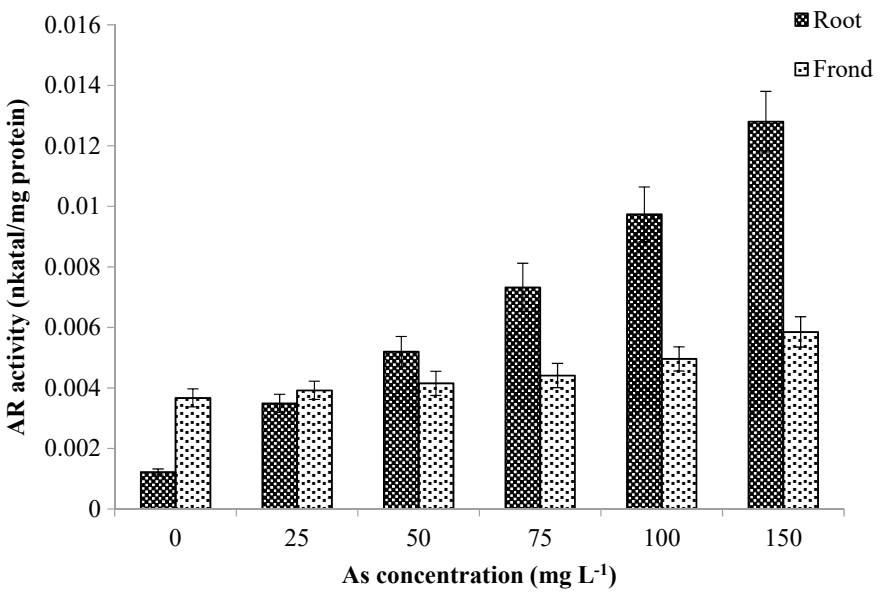

Fig. 5 Arsenate reductase enzyme activities in frond and root of *Pteris vittata*

4.3 Arsenate Reductase Enzyme Assay

Arsenate reductase activity in the protein extract of the *P. vittata* plant was assayed as per the protocol described in materials and methods. The enzyme activity was found to be high in root in comparison to frond (Fig. 5). The pattern of enzyme activity showed linearity with the increase in treatment concentration. Enzyme activity showed up to the three-fold increase in treated plant parts in comparison to control. The present finding supports the finding of other investigators who also observed more activity in the root, but not in the fronds (Duan et al. 2005; Liu et al. 2009b).

5 Conclusion

Arsenic accumulation in the plant biomass of the studied Indian ecotype *P. vittata* has been determined through treatment with 25 -150 mg As L^{-1} nutrient solution. This plant accumulates up to 6451 mg As kg^{-1} plant biomass under treatment with 150 mg As L^{-1} nutrient solution. The *arsC* gene of the *ars* operon was used as a molecular marker to ascertain the genetic potentiality of the As accumulating Indian ecotype. It was found that the activity of the arsenate reductase enzyme, which is the transcript of *ars*C, was also enhanced 2–3 times under As treatment. The *arsC* and AR activity could be used as molecular markers to identify potential plant species

suitable for As phytoextraction. This Indian ecotype could be used for remediation of As pollution through an appropriately designed phytoremediation treatment system.

Acknowledgements The authors are thankful to Director, NEERI for providing a research facility to carry out the work.

Funding This study was carried out under financial support from the Department of Biotechnology (Grant number BT/PR7453/BCE/8/980/2013), Ministry of Science and Technology, Govt. of India.

Conflict of Interest The authors declare that they have no conflict of interest.

Compliance with Ethical Standards This article does not contain any studies with humans or animals performed by any of the authors.

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Metal Toxicity in Humans Associated with Their Occupational Exposures Due to Mining

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1 Introduction

Humans are very well aware of the metal from prehistoric times and perform metal extraction from different ores. In the present time, it has been assessed that more than 1.15 billion tons of heavy metals like copper, cobalt, lead, cadmium, zinc, mercury, nickel, and chromium, and some other metals mineral has been mined by humans. But it was observed that only a tiny portion (<2%) comes as an end product, i.e., the wanted metal, whereas the rest, 98% of end product wastes, are cleared from the processing areas to the nearby dumping site either of land or water (Sheoran and Sheoran 2006). The earth's natural and different anthropogenic activity introduces various heavy metals from the inner earth to the upper earth crust, and the soil accumulates many of them. But the leading causes of heavy metal contamination in the ground and nearby environment are human activities, including heavy metal mining and smelting, fuel production for energy, industrial activities for human needs, solid waste, wastewater, and sludge disposal after different applications, automobile exhaust discharge, etc. The pollution level of the soil is assessed by the determination of its entire metals contents but, by this, it cannot envisage the mobility, bioavailability, and toxicity of these metals (Wieczorek et al. 2018). In many areas of the world where metal ores are mined and processed, heavy metal like arsenic, lead, cadmium, mercury, nickel, manganese, zinc, thallium, and iron is released into the environment as directly or through the end product waste. These heavy metals produce adverse effects in that particular geographical area and enter the food chain in the plants by the soil and ultimately into the animals and humans. Most humans

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_7

are come into contact with these heavy metals by contaminated groundwater, air, and soils of that occupational area (Agnieszka et al. 2014). There is highly progressive industrialization going on in the developing and developed countries, which leads to an increase in the global demand for the production and the consumption of heavy metals; thus, it also increases metal pollution (Bernhoft 2013). Some of these heavy metals are mandatory for the living being in some specific quantity for the well-functioning of specific metabolic processes, and amounts of these metals depend on the organism's metabolic requirements. But these required metal species converted toxic to most living organisms after the specific level in the body; that is why environmental metal pollution has developed into a significant global problem. Most of the heavy metal compounds (sulfide, chloride, and oxides forms) effortlessly form their aqueous solution so that they have higher mobility and tend to gather in high amounts in the living organisms (Vasile and Vlădescu 2010). Some of the health hazards triggered due to heavy metals are man-made as only a selected group of people with occupational exposure to these heavy metals are the primary victims of these toxicities. Moreover, these toxic effects are restricted to a relatively small group of individuals who are exposed to toxic metals in their workplace (Järup 2003). In the past few decades, heavy metal toxicity linked to health problems is dramatically increased, which also raises our understanding of occupational disorders of professionally exposed individuals. Many occupations modify the air, water, and soil through urbanization, industrialization, transportation, and the overutilization of chemicals in agriculture-related industries (Das et al. 2018; Chang et al. 2019).

The clinical effects of heavy metal toxicity are prominently dependent on specific features like the exposure route, the concentration of the toxicant, and the time duration of exposure. In occupational settings, exposure is mainly via inhalation, while domestic exposure is due to the ingestion of heavy metals by contaminated drinking water or food. Heavy metal poisoning has been documented to affect almost every part of the body. Acute and chronic health hazards of heavy metal toxicity include respiratory, cardiovascular, gastrointestinal, renal, hemopoietic, and central nervous, moreover it causes allergies mainly to the skin and upper respiratory tract of the individual (Tchounwou et al. 2012; Jaishankar et al. 2014). Metal poisoning is either acute or chronic, resulting in death or reversible to the usual health condition. The defects of metal poisoning may be diagnosed by biochemical or physical tests or identified by abnormal clinical symptoms. The clinical effects of metal poisoning entail that defective biological alternations have been produced in the organism and impairment in cellular functions (Sharma et al. 2014; Egorova and Valentine 2017).

Acute gastrointestinal metal poisoning is mainly caused due to the consumption of contaminated food, commonly marked as 'food poisoning,' including symptoms like vomiting and diarrhea. Chronic gastrointestinal effects can be induced due to the ingestion or inhalation of metal-like lead over a longer time, resulting in anorexia, nausea, vomiting, and diarrhea followed by constipation (Sharma et al. 2014; Begovic et al. 2008). Inhalation of metal fumes, dust, or metal salts may induce clinical respiratory effects like acute chemical pneumonitis, pulmonary edema, and asthma. Metal toxicity occurs because the fumes of metal oxides have been reported to cause

chronic pulmonary effects like dyspnoea associated with emphysema. The cardiovascular effect of metal toxicity includes disorders like arrhythmias, as metallic ions alter the normal function of myocardial cells. Metal poisoning is reported to the dysfunctional central nervous system, giving rise to defects like psychosis and renal damage to cause tubular necrosis, leading to oliguria or anuria. Overall, heavy metal toxicity is one of the major health concerns worldwide. It can cause abnormalities in almost every vital organ system, leading to life-threatening disorders (Gerhardsson and Kazantzis 2015).

In detecting metal toxicity, the history of exposure very crucial role in the metal exposed person. Maximum heavy metal exposed diseases show specific medical symptoms and affect different organs and metabolism in humans, which the clinician needs to be diagnostic by the clinician. Correct diagnosis help in stopping the exposure and also prevent disease in others by avoiding that specific exposure. The analysis is done by physical examination, biochemical and analytical tests. Different spectroscopic methods help for the qualitative and quantitative detection of heavy metals. The biomarker-based assay also helps in the detection of heavy metal exposure (Barbosa et al. 2005; ATSDR (Agency for Toxic Substances and Disease Registry) 2007).

There are several types of therapeutics approaches that were applied for many years to prevent metal toxicity. The removal of heavy metal should be necessary from infected victims without any delay. There are several preliminary steps applied for the removal of contamination from the subjects. The heavy metal was absorbed in different ways like inhaled or administrate through the skin, gastrointestinal tract, respiratory organ. The absorbed heavy metals will be inactivated by different means like the use of charcoal, metal antagonists, or chelating agents. Chelation therapy is the most successful therapy for removing or reducing the harmful effect of heavy metals. Different types of synthetic chelators and their combinations are used like ethylene diamine tetraethyl acetate (EDTA) dimercaprol, sodium 2,3-dimercaptopropane-1-Sulfonate, meso-2,3-dimercaptosuccinic acid, etc. Antidot therapy through natural antioxidants is also used significantly (Gerhardsson and Kazantzis 2015; Andersen and Aaseth 2002; Christophersen et al. 2002; Amadi et al. 2019a).

2 Metals Associated with Mining

2.1 Environmental Occurrence, Source, and Distribution of Metals

2.1.1 Arsenic

Arsenic (As; atomic number–33; MW–74.92 u) is extensively dispersed and is exists in the Earth's crust at a range from 1–40 mg/kg. Arsenic pollution of mine and

metallurgic waters has broadly been known as a global problem. The International Agency for Research on Cancer (IARC) of WHO classified and notify arsenic as one of the ten most dangerous chemicals and Group-1 carcinogens in 1987, as a Group-1 carcinogen for the presence in drinking water in 2004. Modified arsenic compounds mono-methyl arsinic acid (MMA) and dimethyl arsinic acid (DMA) are notified as Group-2B carcinogens, which are probably carcinogenic for living beings, in 2012 (Chang et al. 2019; Tchounwou et al. 2003). Naturally, arsenic is found in about 200 mineral forms, in which arsenates (approximately 60%), sulfides and sulfosalts (20%), arsenides, arsenites, oxides, silicates, and elemental arsenic main. Arsenic is exposed to the atmosphere by anthropogenic sources, in which metal mining (especially in gold mining) and smelting are of the utmost importance.

In contrast, in some areas, coal mining and burning of arsenic-rich coals are the other sources of arsenic contamination (Garelick et al. 2008). It is estimated that the mining and metallurgical industry released about 3.5×10^7 kg/yr of arsenic into the environment, which is approximately 22% of the total arsenic-free into the atmosphere by different sources or activity (Zhao et al. 2019). Arsenic pollution of the soils, deposits, shallow waters, and underground water is described from mining regions worldwide. In natural water bodies, arsenic can present in numerous oxidation states, in which trivalent arsenite (As(III)) and pentavalent arsenate (As(V)) are the prevalent ones. The H_2AsO^{4-} and $HAsO^{4-}$ are the utmost thermodynamically species in the pH range 4–7 and groundwater redox conditions. While in acid rock drainage waters (pH below 5) H_2AsO^{4-} found, which is more stable. Whether in highly reduced water, $As(OH)_3$ is the prevalent species. Oxidation of sulfide form of arsenic ore and reduction of iron oxyhydroxides of arsenic is mainly uncovered to earth crust by its movement and through the water. These activities are the primary factor involved in arsenic mobilization (Chakraborti et al. 2013; Baker et al. 2018).

2.1.2 Lead

Lead (Pb; atomic number–82; MW–207.2 u) is one of the primogenital recognized and most extensively studied industrial and environmental toxins. The battery industry is the most prominent occupation affected by lead toxicity. Industrial workers who work in smelters, storage batteries production, and paint factories are at significant risk for lead exposure (Gupta and Gupta 2016). It is a highly poisonous, non-disintegrative bluish-gray colored heavy metal that exists in organic (mainly exist in the dust, soil, old paint, and other different user products) and inorganic form (leaded gasoline) in the environment. Although organic and inorganic forms are toxic for humans, the organic Pb-complexes are incredibly harmful compared to inorganic lead (Kumar et al. 2020). Lead is seldom present in its elemental form. In the Earth's crust, Pb is mainly found as the galena (PbS) ore, and to a minor level as sulfate ore (anglesite; $PbSO_4$) and as carbonate (cerussite; $PbCO_3$) form. Lead is easily found in its ore form but not in elemental form, and lead deposits are broadly distributed and readily available globally (ATSDR 2019a).

2.1.3 Mercury

Mercury (Hg; atomic number–80; MW–200.59 u) is familiar to humans for the past 3000 years. It is a heavy, silvery-white liquid metal at room temperature. Nowadays, it is widely used in thermometers, barometers, manometers, whitening cosmetics, and dental amalgam. In mining, Hg is extensively used to extract gold from its ore which is present as a stable amalgam. Afterward, mining, this ore is heated at high temperature to remove the Hg as Hg vapor and isolate the remaining gold. Mercury-dependent artisanal and small-scale gold mining (ASGM) is the prime source of mercury pollution on Earth (Esdaile and Chalker 2018; Ţincu et al. 2020). Most studies suggested that approximately 2000 Mg/year of mercury has been estimated by anthropogenic activity. The first record of worldwide freshwater Hg contamination assessed that ASGM releases around 880 Mg/year, the highest compared to industrial and wastewater discharges (220 Mg/year) and terrestrial mobilization (170–300 Mg/year). It is also estimated that worldwide, China and India release aquatic mercury around 50% in the West Pacific and North Indian Oceans. In the environment, mercury exists in three forms (elemental, organic, and inorganic), and each state shows its specific chemical and physical properties and toxicity. Globally, due to unfitting mining activity, about 400 tons of airborne elemental mercury are released into the environment. Organic mercury (methyl, ethyl, or phenyl mercury) is build up by the biomethylation process performed by the aquatic microorganisms, and at the end, it is released into the environment (Obrist et al. 2018; Afrifa et al. 2019).

2.1.4 Cadmium

Cadmium (Cd; atomic number–48; MW–112.41 u) is a soft, silver-white toxic metal and presents a concentration of 0.1 part per million in the earth's crust. Cadmium is present in the Earth's crust in small quantity as an impurity in the sulfide ore of zinc (Zn), copper (Cu), or lead (Pb). Cadmium commonly presents as a divalent complexed form in association with other elements (e.g., $CdCl_2$ and $CdSO_4$, both are soluble in water) (Bernhoft 2013; Genchi et al. 2020). Cadmium has existed in food, air, water, and other media. Globally, about 13 million tons of Cd is formed and emitted every year primarily from the smelting process of Zn, Pb, Cu, and Cd, and during the manufacturing of products like nickel–cadmium batteries, dyes, chemical stabilizers, metal coverings, metal blends, phosphate compost, and municipal and sewage sludge incinerators. In the mining and milling process, mainly during the exploitation concentration and disposal of ores, vast quantities of Cd are released to the Earth's surface. Post mining processes like metal smelting yields large amounts of waste gases, wastewater, untreated slags, and other tailings products, which are the principal sources of Cd release to the environment. Phosphate fertilizers are also a key source of Cd involvement in agricultural soil. Naturally, tobacco leaves gather vast quantities of Cd, so it also presents in tobacco smoke, which exposes to humans actively and passively (Rani et al. 2014; Du et al. 2020).

2.1.5 Chromium

Chromium (Cr; atomic number–24; MW–51.99 u) comes under the element which is found most abundantly on Earth's surface, with a typical concentration of 125 mg/kg. Chromium is found in seven oxidation states, Cr(0) (elemental chromium) to Cr(VI) (hexavalent chromium form), but the maximum stable and common form is the trivalent form, Cr(III). Chromite ore is the natural source of trivalent chromium. After that, hexavalent chromium, which rarely occurs in nature, is the second most stable form of Cr (Sun et al. 2015). Occupational are exposed to chromium in >80 diverse manufacturing sectors. The cement manufacturing sector and cement-related construction sites are the most contributing industrial fields that expose Cr into the environment. Worldwide, chromium also releases as chromium sulfate from ~90% tanned leather. Rest all other occupational source includes chrome plating, metal finishing, metal welding, wood preservatives products, production for textiles like dyes and pigments (Pavesi and Moreira 2020). For nonoccupational human populations, the primary source of oral chromium exposure is food and drinking water. In food, the Cr contamination ranges from <10 to 1300 μg/kg, where the most excessive amount reported in meat, fish, fruits, and vegetables. In natural sources, chromium is reported in the range of 1–10 μg/l in rivers and lakes, 0.2–1 μg/l for rainwater, and about 0.3 μg/l for the ocean (Sun et al. 2015).

2.1.6 Copper

Copper (Cu; atomic number–29; MW–63.546 u) is exposed to the environment by copper mining, copper-related material manufacturing sector, waste landfills, burning of copper-containing fossil fuels, and phosphate manure manufacturing industries. It is present in the soil at 5–70 mg/kg concentration, and the high copper contamination was reported in the area where copper-related smelting and mining operations occur regularly (Tsuji et al. 2016). The total releases of copper into the environment in 2001 were approximately 5,050 Mt, of which around 373 Mt (7.4% of the total) were free to air, about 21 Mt (0.4% of the total) were accessible into the water, 24 Mt (0.5%) was injected underground, and about 91.9% (4,360 Mt) was released to land (ATSDR (Agency for Toxic Substances and Disease Registry) 2004). In reference to United States Geological Survey (USGS), globally, about 720 Mt running copper reserves are present. At the same time, USGS also states that approximately 3,500 Mt undiscovered and 2,100 Mt unmined identified copper reserves are present. Pure copper or natural copper seldom occurs in nature (1% of total copper compounds). Copper is mainly found in the sulfide form (about 90%) and oxide (about 9%). Copper ore is extracted by open-pit, underground, and leaching mining methods where open-pit is the dominant worldwide (Pietrzyk and Tora 2018).

2.1.7 Manganese

Manganese (Mn; atomic number–25; MW–54.94 u) is the 12th most rich element and broadly dispersed throughout the Earth's crust and soil concentrations in earth crust ranging from 40–900 mg/kg. It has numerous significant industrial metal alloy uses, like in steel production, steel, batteries, animal feed, pigments, and ceramics. At the industrial level, manganese ions are used in dyes and as oxidation chemicals (Tsuji et al. 2016; Erikson and Aschner 2019). According to the United Nations Framework Classification for Resources (UNFC) system, the complete resource of manganese ore is estimated at 430 Mt globally in 2010. From these total deposits, 142 Mt (about 33%) are categorized as a reserve, and the remaining 288 Mt (67%) fall under other resource categories (IBM 2014).

2.1.8 Nickel

Nickel (Ni; atomic number–28; MW–58.69 u) is a hard, silvery-white transition metal, found in multiple oxidative states (from -1 to $+4$), in which divalent nickel is the most ubiquitous in the natural and biological systems (Das et al. 2018; Genchi et al. 2020). By weight percentage, after the iron, oxygen, magnesium, and silicon, nickel stands as the 5th most occurring element. Naturally, in the Earth's crust (about 3% of the composition of the earth), it exists mainly as oxides and sulfides. Naturally, it also presents in the dust generated from the weathering of rocks and soils, volcanic releases, forest fires, and vegetation. In the air, it releases by the burning of coal, diesel oil, fuel oil, waste, and sewage (Cempel and Nikel 2006). In modern metallurgies, nickel is extensively used in different metallurgical processes, like alloy preparation, nickel electroplating, nickel–cadmium battery industries, and catalysts in the chemical and food industry. The other environmental sources which produce nickel contamination include tobacco, dental or orthopedic grafts, stainless steel kitchen apparatuses production, and cheap jewelry formation (Das et al. 2018; Genchi et al. 2020).

2.2 Quantitative Requirement and Limitation of Metal to Humans

2.2.1 Arsenic

There are no studies reported which provide any information regarding the nutritional importance of arsenic for humans. Although the role of arsenic in different metabolic functions is not very well understood in humans, in rats, it was found that arsenic may play a role in methionine metabolism. Arsenic presence is also seen in numerous foods at concentrations ranging from 20 to 140 ng/kg due to arsenic-based

pesticide or waste disposal in agricultural land (Tchounwou et al. 2003; Trumbo et al. 2001). The US EPA, the WHO, and the European Pharmacopoeias recommended the maximum contaminant level (MCL) for arsenic in drinkable water is 10 mg/l or 10 ppb for household water supplies. According to the Occupational Safety and Health Administration (OSHA) regulations, the permissible exposure level (PEL) for inorganic arsenic is 10 mg/m^3 in air, be around 8 h without the use of a respirator in mines (Baker et al. 2018; Palma-Lara et al. 2020). Because of lacking relevant studies of minimum risk levels (MRLs), no inhalation MRLs were calculated for inorganic arsenic. An MRL of 5×10^{-3} mg As/kg/day has been observed for oral introduction to inorganic arsenic in acute-duration (14 days or less). An MRL of 3×10^{-4} mg arsenic/kg/day has been found for chronic-duration (365 days or more) oral exposure to inorganic arsenic. No breathable MRLs were derived for organic arsenic due to the accessibility of limited human data of occupational exposure. A reported study of exposed workers finds the MRL is 0.065 mg/m^3 ansanilic acid. It is also reported that arsenic found in passive individuals is <1 μg/l in blood, <100 μg/l in urine, ≤1 ppm in nails and hair (ATSDR (Agency for Toxic Substances and Disease Registry) 2007).

2.2.2 Lead

Lead is not proven to be crucial to human nourishment. Still, the WHO and Food and Agriculture Organization suggested an acceptable level of Pb consumption for adults is 490 μg of lead per day or 7 μg/kg body weight per day (FAO/WHO Expert Committee on Food Additives 1978). The national code of practice decides the inorganic lead concentration for the nonoccupational working area for the control and harmless use limit is 0.73 μmol/l and for occupational area 2.41 μmol/l, which is equivalent to 1.5 μg/ml and 5 μg/ml respectively, set by the American National Institute for Occupational Health and Safety (ANIOHS) (Cunningham 2007). The US Centres for Disease Control and Prevention (CDC) and the WHO defines the minimum danger level of lead in the blood as 1 μg/ml or above. There is no specific value below which its contact can be considered safe in the case of lead. Epidemiological studies define that adverse effects at the lowest blood Pb levels studied are ≤ 0.5 μg/ml since these levels are related to significant adverse effects (e.g., decreasing intellectual activities in children), MRLs for Pb have not been defined. Urinary lead over 120 μg in a day also indicates recent exposure (Gupta and Gupta 2016; Wani et al. 2015; ATSDR 2019b).

2.2.3 Mercury

It was reported that an average human accumulated about 13 mg of mercury, and physiological it did not produces any known beneficial health effect. The International Union of Pure and Applied Chemistry (IUPAC), and the International Commission on

Occupational Health (ICOH), set the highest tolerable value of blood Hg concentration at 2 μg/l for non-fish-eaters (Afrifa et al. 2019). The usual range of Hg present in hair set between 1 and 2 μg/g, but for fish-eater, it is >10 μg/g which is the lowermost detected concentration that shows adverse neurotoxic effects (paresthesia) in adults (Ye et al. 2016; Branco et al. 2017). ATSRD reported the MRL for mercuric chloride ($HgCl_2$) for oral ingestion for the acute duration (<14 days) has 0.007 mg/kg/day and for intermediate exposure 0.002 mg/kg/day. In the case of elemental mercury exposure through inhalation, the MRL of 0.002 mg/kg/day has been calculated for a chronic period (≥1 year) (ATSDR (Agency for Toxic Substances and Disease Registry) 2020).

2.2.4 Cadmium

For cadmium which is exposed through inhalation, the MRL of 3×10^{-5} mg Cd/m^3 has been reported for acute-duration inhalation exposure to Cd (≤14 days), while chronic-duration inhalation exposure to Cd (≥1 year) is 1×10^{-5} mg Cd/m^3. No intermediate-duration inhalation MRL was reported for Cd. For orally exposed Cd, no acute-duration oral MRL was noted for cadmium. The MRL for intermediate-duration oral exposure to Cd (15–364 days) is reported at 5×10^{-4} mg Cd/kg/day concentration. In contrast, for chronic-duration oral exposure to Cd (≥1 year), the MRL found 1×10^{-4} mg Cd/kg/day. The EPA set the exposure to Cd in drinking water at 0.04 mg/l cadmium concentration for up to 10 days, and lifetime exposure is 0.005 mg/l Cd, not predictable to cause any adverse effects. OSHA established a permitted limit of Cd exposure in air averaged over an 8-h workday is 5 μg/m^3 Cd (ATSDR (Agency for Toxic Substances and Disease Registry) 2012). The WHO set a threshold urine-cadmium level of 5.24 μg/g creatinine, while the European Food Safety Authority (EFSA) set it 1 μg/g of creatinine (Wu et al. 2016).

2.2.5 Chromium

The principal form of chromium Cr(III) is the major part of multi-vitamins and nutritional supplements. Predominantly Cr(III) is present in its picolinate, histidine, dinicocysteinate, and niacin-bound chromium compound. It is proposed that Cr(III) may be essential for glucose and lipid metabolism, curing diabetics, and in the progression of weight loss and muscle build-up. While Cr(VI) is very toxic to humans, and by cell DNA damage, cell chromosomal aberrations, variations in the cell epigenome, and microsatellite volatility, it damages the cell. Food and Nutrition Board of the National Academies of Sciences, Engineering, and Medicine established the optimal dietary intake of Cr(III) is 25 mg/day for women and 35 mg/day for men. The US EPA and IARC have categorized chromium as a group-1 human carcinogen when the exposure route is inhalation. In 2000, OSHA set the PEL for soluble hexavalent chromium (as CrO_3) in workplace air was 100 μg/m^3; later, this limit has been lowered to 50 μg CrO_3/m^3, and the National Institute for Occupational Safety and Health (NIOSH;

recommended exposure limit) is even lower, 1 μg/m^3 (as Cr). But in 2006, OSHA further reduces the PEL of soluble hexavalent chromium in the occupational work area to 5 μg/m^3 per day. For drinking water, the current standard fixed by US-EPA and OSHA for total chromium is 0.1 mg/l (100 ppb), 8 μg/l for Cr(III), and 1 μg/l for Cr(VI). In the wastes discharged from chromium industries, chromium was found in the range of 2–5 g/l (Sun et al. 2015; Pavesi and Moreira 2020; Tsuji et al. 2016; Costa and Klein 2006; Proctor et al. 2014; DesMarias and Costa 2019).

2.2.6 Copper

Copper is a crucial trace element in the human diet but toxic in large amounts like other metals. Copper work as a co-factor of several essential enzymes involved in iron metabolism, RBC development, blood coagulation process, oxidation–reduction reactions, and scavenging of reactive free radicals. The principal amount of copper is present as divalent Cu in the human body and can shift from the cupric (Cu^{2+}) to cuprous (Cu^{+}) valence states. The United States and different European countries set the average dietary copper consumption for men and women as 1.2–1.6 mg/day and 1.0–1.1 mg/day, respectively. It is predicted that the typical adult may take roughly about 1.85 mg Cu/day, or equivalent to 0.026 mg Cu/kg/day, and for infants, it is about 40–80 μg Cu/kg body weight/day (Tsuji et al. 2016; Margaritis et al. 2017; Taylor et al. 2020). The US-EPA set a maximum contaminant level goal (MCLG) and drinking water tolerance level for copper at 1.3 mg Cu/l. A controlled human study suggested that the gastrointestinal symptoms show at about ~3 mg Cu/l in drinking water while 2 mg Cu/l is safe. WHO stated that in 104 countries, there is a recommendation regarding copper concentration in drinking water, with an average value of 1.5 mg/l with a permissible range of 0.05–3 mg/l (Taylor et al. 2020; WHO 2018). The acute-duration (14 days) oral MRL is 0.01 mg copper/kg/day while an intermediate-duration (60 days) oral MRL of 0.01 mg copper/kg/day was calculated for copper. These data are created on the incidence of gastrointestinal instabilities in women ingesting 0.0731 mg Cu/kg/day and 0.091 mg Cu/kg/day in drinking water for acute and intermediate duration, respectively (ATSDR (Agency for Toxic Substances and Disease Registry) 2004).

2.2.7 Manganese

Manganese is also one of the trace metals crucial for the normal biology of humans and mammals. Manganese is the essential cofactor of three enzymes, including the primary antioxidative enzyme in mitochondria, manganese superoxide dismutase, and activator of other enzymes of the host. Although frequently it is considered an ultra-trace element, Mn displays very high importance to human health and possesses an essential role in many biological functions, including bone strength and fitness, another macronutrient metabolism, and defense against reactive free radical species. While maintaining the ammonia level in the body, manganese plays a vital role via

arginase activity. The daily dietary requirement for manganese is 2.3 mg for adult men and 1.8 mg for adult women. Adult Mn intake ranges from 2 to 9 mg/day, mainly depend on the diet, where vegetarians are consuming a higher intake. The Institute of Medicine's Dietary Reference Intakes (DRI) found the Tolerable Upper Limits (TUL) for manganese as 2 mg/day for infants, 6 mg/day for older children, and 9–11 mg/day for adults (Tsuji et al. 2016; Erikson and Aschner 2019). The Food and Nutrition Board of the National Research Council (NRC) also assessed the tolerable and safe consumption of manganese for adults at 2–5 mg/day. EPA has suggested that Mn concentrations in drinking water, not more than 50 μg/l and have a definite lifetime health recommended value of 300 μg/l. An occupation like manganese mines, metal-producing plants, steel-manufacturing facilities, dry-cell battery facilities, OSHA decides the exposure levels should not surpass the time-weighted average PEL of 1 mg total Mn/m^3 (ATSDR (Agency for Toxic Substances and Disease Registry), 2012; Livingstone 2018).

2.2.8 Nickel

Even though not any report shows the nutritional value of nickel in humans, but it has been documented as a crucial nutrient for some microorganisms, plants, and animals. The daily humans' nickel requirements have been estimated between 5 and 50 μg, but nickel deficiency was never observed because the intake of nickel by food is always surpassed from the above limits. Nickel is suggested as a standard component of the food, and its compounds are usually predicted as harmless when used as a natural constituent in human food at a certain level. Scattered studies suggested that in most countries, the typical daily intake of nickel from food ranges from 100–300 μg/day. Nickel levels in foodstuffs generally range from <0.1 mg/kg to 0.5 mg/kg. But in 1990, IARC placed soluble and insoluble nickel compounds (except for metallic nickel) in Group-1 (carcinogen for humans), while nickel and its alloys in Group-2B (possible humans carcinogen) (Genchi et al. 2020; Cempel and Nikel 2006; Denkhaus and Salnikow 2002). Generally, average airborne levels of nickel are 0.00001–0.003 μg/m^3 in isolated areas, 0.003–0.03 μg/m^3 in municipal areas having no metallurgical industry, while in nickel processing areas, it is 0.07–0.77 μg/m^3. In drinking water generally, its concentration found >10 μg/l. The day-to-day consumption of nickel in adults is set between 7.5 and 15.0 μg through drinking water, while in nickel ore mining, these values were recorded at the range from 75–200 μg/l (Cempel and Nikel 2006). There is no acute-duration inhalation MRL was fixed for nickel (≤14 days). For intermediate duration inhalation exposure (15–364 days), the MRL was found to be 0.2 μg Ni/m^3. And for chronic-duration inhalation exposure (≥1 year), the MRL is 0.09 μg Ni/m^3 has been derived. For the oral ingestion of nickel, no MRLs were derived for nickel (ATSDR (Agency for Toxic Substances and Disease Registry) 2005).

2.3 *Routes of Exposure, Uptake, and Bioaccumulation of Metal*

2.3.1 Arsenic

Polluted water is the primary source of human contact with arsenic, while it is a minor amount by breath and skin contact. Arsenic can be easily take up by ingestion (oral route), inhalation (cigarette smoking, mine dust, smelters, and chemical factories), dermal contact (insert through the skin cut), and interaction with mucous membrane. From total ingested inorganic arsenic (iAs^{3+} and iAs^{5+}), about 70–90%, it is without any difficulty taken up by the GI system. Afterwards, absorbed arsenic is circulated by the blood to different organs, principally to the liver, kidneys, lungs, and bladder, and later on to muscles and nerve tissues. Aquaglyceroporins membrane proteins, predominantly found in the liver, spleen, lung, adipose tissues, and kidneys, are engaged in the absorption of arsenic (Tchounwou et al. 2003; Palma-Lara et al. 2020; Khairul et al. 2017). In the human body, the distribution of the various arsenic species is governed by different factors, which includes the type of arsenic administered, plant or animal species, types of cells, the presence of biomolecules like glutathione (GSH) and biomolecule contain thiol (-SH) groups, methylating arsenic enzymes, and the pH of the matrix. It was also seen that the cytosol of testes performs the maximum quantity of arsenic methylating activity, then after by the kidney, liver, and lungs. The highest build-up of inorganic arsenic is seen in the liver (Palma-Lara et al. 2020; Khairul et al. 2017).

2.3.2 Lead

In the present time, almost every living being is exposed to environmental lead. Lead and lead-containing chemicals exposure can happen via inhalation, ingestion, dermal absorption, absorption from reserved or implanted external lead material, and transplacental (endogenous) way, in which inhalation and ingestion are the most common route. It is assessed that around 35–40% of inhaled lead dust is transferred into the blood and then binds with the erythrocytes. Within a week, it is circulated predominantly to the liver, kidney, brain, bone, and bone marrow. It was also found that the inclusion bodies (aspartic and glutamic amino acids rich) may serve to sequester lead, through which it can also be translocated into the cell nuclei and alter gene expression (Cunningham 2007; Lockitch 1993). Large particles (>2.5 μm) of lead-containing compounds are dropped in the ciliated airways (in the nasopharyngeal and tracheobronchial regions) can be relocated by the mucociliary transport system into the esophagus and swallowed. Like other "bone-seeking" elements, lead on chronic exposure, merged into calcified tissues such as bone and teeth at the highest concentrations, can persist for much long time (half-life of bone-Pb ranges from 10 to 30 years) it also accrues in the kidney. Organic lead-containing compounds are also absorbed by the skin (Barbosa et al. 2005; Wani et al. 2015; ATSDR 2019b).

2.3.3 Mercury

Because of the electrophilic nature of mercury, after absorption, it may react with electron-rich groups, like thiols (-SH), selenols (-SeH), cysteine (-Cys), and selenocysteine (-Sec) present in peptides and proteins. In blood, about 90% of methylmercury (Me-Hg) is bound to the hemoglobin of RBCs, whereas inorganic mercury (Hg^0 and Hg^{2+}) is equally dispersed between RBCs and plasma. Me-Hg also binds with sulfhydryl (SH-) groups of keratin and is integrated into hair follicles, where it is transported to the brain. It also reported that the hair mercury amount is linked with the amount present in the brain and whole blood in the ratio of 250:5:1, respectively (Branco et al. 2017). WHO reports say that the vital route of mercury exposure is breathing up the mercury vapor, which is mainly forms in the gold amalgam smelting process. The skin poorly absorbs mercury as an elemental form (3–4%) and gastrointestinal tract (2–10%) and is less toxic for humans. It can't cross the blood–brain barrier and is ultimately collected by the kidney. Upon inhalation, mercury vapor quickly enters the blood system through pulmonary alveolar membranes and attacks into the CNS, blood cells, and kidneys. It can be moderately transformed into $HgCl_2$ and engaged for many years. In the non-occupational mercury are primarily introduced through dietary consumption of polluted fishes and seafood and the dental amalgam. In various forms of mercury, methylmercury is the most toxic, having extensive bioaccumulation properties in the aquatic food chain and sequentially in human beings (Afrifa et al. 2019; Ye et al. 2016; Godfrey et al. 2003).

2.3.4 Cadmium

The key route of cadmium exposure to the human body is inhalation (via contaminated dust or vapors produced from high-temperature processes, contaminated tobacco smoke), ingestion (direct assimilation of water and unintentionally the soil, eating the food items which are grown in polluted fields), and dermal contact (through contact of soil and water). About 10–50% of inhaled cadmium dust and 5–10% of ingested cadmium is absorbed from the comprehensive cadmium source, mainly depends on particle size. Intestinal absorption (3–5%) was found greater (about double) in persons who are deficient in iron, calcium, or zinc. Skin absorption of cadmium is usually poor (0.2–0.8%). In smokers, blood and kidney cadmium levels are steadily higher than nonsmokers. Cadmium accumulates in terrestrial plants, vegetables, aquatic organisms, and crops, so it bioaccumulates at all levels of the food chain. After cadmium absorption, it is circulating all over the body and typically attaches with the protein having sulfhydryl group like metallothionein. Soluble cadmium salts can accumulate in various organs (about 30% store in the liver and kidneys each, with the rest 40% circulated all over the body) and tissues and create toxicity to the kidney, liver, lungs, brain, testes, heart, and central nervous system. The kidney (tubule region) is the most sensitive target organ for cadmium effects (Wieczorek et al. 2018; Bernhoft 2013; Rani et al. 2014; ATSDR (Agency for Toxic Substances and Disease Registry) 2012; Wu et al. 2016). The most hazardous property

of the cadmium is its long clearance half-life which is measured at about 25 years. While it was seen that the half-life of cadmium in the blood is 75–128 days, but this half-life mainly characterizes deposition in organs, not clearance from the body (Bernhoft 2013; Rani et al. 2014).

2.3.5 Chromium

Due to its ubiquitous nature, the general population may be exposed to Cr(VI) via air (includes industrial and automobile discharge, cigarette smoke, etc.), industrial released Cr contaminated water, and leaching of Cr in wastewater (due to the improper dumping of industrial waste) (Pavesi and Moreira 2020). There is almost a thousand-fold difference in Cr(VI) and Cr(III) toxicities based on the ability to enter inside the cell. Structurally, Cr(VI) (tetrahedral divalent (CrO_4^{2-}) anion, shows similarity with sulfate oxyanion (SO_4^-) and phosphate anions; therefore, it is simply absorbed by cells through non-specific anion transporters. After entering into the cell, Cr(VI) is converted to Cr(III) by rapid metabolic reduction, while Cr(III) compounds are not able to transport inside the cells by transport mechanism (Sun et al. 2015; DesMarias and Costa 2019). In several biological fluids like saliva, gastric juice, and epithelial-lining fluids, Cr(VI) reduces into Cr(III) and which other forms in binary [Cr(III)-ligand] and ternary [ligand-Cr(III)-ligand] complexes [e.g., GSH-Cr(III)-GSH]. Ascorbate and small thiols are the principal biological reducer (up to 80% of total) of Cr(VI). Intermediates such as Cr(V), Cr(IV), and thiol radicals can also be formed by the reduction of Cr(VI), which are less stable. Cr(VI) uptake is also done by erythrocytes, which is size-dependent on Cr(VI). Welding fume contains smaller particles (<0.5 μm) which is more competently reduced in the lungs, rather than the larger particle such as chromate dust (>10 μm). As compared to the stomach, the lung provides a large surface area for easy deposition and absorption. Inhaled Cr(VI) may be gathered in lung bronchi, and subsequent deposition can overcome the local reductive capacity for chromium (Proctor et al. 2014; Denkhaus-Sall et al. 2020). Still, chromium contains deficient bioavailability human body accumulates about 4–6 mg of chromium, and it was also found that the GI tract takes up only 0.4–2.5% of the consumed chromium. The majority of chromium (up to 0.4 mg/day) is eliminated in the urine and feces, and those that contain simple carbohydrates in their diets have increased chromium excretion (Tsuji et al. 2016).

2.3.6 Copper

Copper can be introduced into the human body by taking up the copper contaminated water or through soil containing copper contact with humans or by inhaling Cu-containing dust. Rather than diet and supplements, a predominant source of copper exposure is tap water, where copper is mixed in it by leached through supply pipes. Copper is mainly absorbed (55–75% absorption) by the small intestine through energy-independent, carrier-mediated diffusion, and divalent cations, such as iron

and zinc, can prevent the absorption of copper (Tsuji et al. 2016; Taylor et al. 2020). The absorption of copper mainly occurs in the upper part of the small intestine, after which it is transferred to the liver. The copper absorption rate diverges from 12–71% and mainly depending on age, gender, food type, dietary copper quantity, and the use of oral birth control drugs. After the intestinal absorption, about 75% of copper is engaged up by the liver, and the rest stream into the peripheral circulation, mainly as abounded with albumin. The liver re-excreted back about 20% copper into the gastrointestinal tract, and the rest 80% is bound to ceruloplasmin and exported to the periphery (Margaritis et al. 2017).

2.3.7 Manganese

On average, only about 1 to 5% of dietary manganese (containing 3–4 mg/day) is absorbed in the gut. Manganese is believed to be taken up in its ion form (Mn^{2+}) in all parts of the small intestine by the divalent mineral transport system. Homeostatic controlling mechanisms typically control the absorption of manganese to stabilize its concentration in the required range. So that, the competency of manganese taken up is inversely connected with dietary intake. Several factors affect manganese absorption, including the pH of the intestine, divalent metal transporter (DMT1) occurrence, and divalent metals (e.g., Fe, Cu, Zn, or Ca) chelating compounds like phytic acid. Manganese is then exported to tissues from the liver in portal blood. The main portion of manganese (60–80%) is absorbed by the RBCs and blood plasma in different means, where it complex with albumin (84%), hydrated (6.4%), or bind with bicarbonate and citrate ions. Upon reaching the blood circulation, manganese is speedily separated from their respective complexes and transported into the cells. The half-life of manganese in the blood is about 10–42 days, and it is eliminated, mainly by the bile (about 90%) in feces, with the remainder being excreted in the urine. A minimal amount of Mn can be done by dermal absorption was seen when the skin comes into contact with liquids containing manganese (Tsuji et al. 2016; Erikson and Aschner 2019; Livingstone 2018).

2.3.8 Nickel

The assessed body load of a fit non-exposed mature human is around 7.3 μg Ni/kg body weight. The entry route of nickel in the human body is inhalation, ingestion with food, and dermal absorption. The assimilation of nickel is mainly relaid on its physicochemical nature and water-soluble forms (chloride, nitrate, sulfate), where it is more eagerly taken up by the body. The insoluble, particulate nickel-metal enters the cell by phagocytosis process, while nickel carbonyl complex (a lipid-soluble complex) can effortlessly cross the cell membrane (Cempel and Nikel 2006; Denkhaus and Salnikow 2002). The nickel exposure is predominantly done by oral ingestion of contaminated drinking water (about 27 ± 17% of the dose) and food (about 0.7 ± 0.4% of the ingested dose). The skin absorbs a minor portion of divalent

Ni ions and nickel particles through sweat ducts and hair follicles. Nickel can also be entered into the body by inhalation, where nickel-containing particles are overthrown in the alveolar, tracheobronchial, and nasopharyngeal sections of the respiratory system. The absorption is based on various factors, like the diameter of the inhaled particles (4–100 μm), the solubility, the amount deposited, aeration, and holding rates (Genchi et al. 2020; Cempel and Nikel 2006). For non-occupational subjects, soft drinking-water and acid beverages are sources to expose nickel because they may mix nickel from pipes and storage containers. Leaching or corrosion prominently contribute to oral nickel consumption, seldom up to 1 mg/day (Das et al. 2018). Tobacco smoke is the additional source of non-occupational contact of nickel. In each cigarette, about 1.1–3.1 μg of nickel is found, from which 10–20% of nickel is inhaled in gaseous form. The water-soluble nickel compounds are also take-up by the lungs and excreted by the kidney (Genchi et al. 2020). Nickel tends to be effortlessly gathered in the living organism, especially in the phytoplankton or other aquatic plants (Cempel and Nikel 2006). The kidney, along with the lungs, brain, pancreas, and other tissues, are the end-organ for nickel accumulation subsequent to the high levels of nickel exposure (Denkhaus and Salnikow 2002).

3 Toxicology Associated with Metals

3.1 Global Burden of Metal Toxicity

The contamination of heavy metals is a global problem, where the predominant contaminants are arsenic, chromium, cadmium, mercury, and lead. More often, they are termed as "most problematic heavy metals" and "toxic heavy metals" (THMs) (Denkhaus-Sall et al. 2020). Metal poisoning can result from the exposure of ions of essential metals like copper and iron and non-essential metals like lead, cadmium, and mercury (Tchounwou et al. 2012). There are around twenty-five elements that have been reported to play a vital role in many biological mechanisms. Most of them are function as a cofactor of many enzymes and are essential for the catalytic activity of enzymes (Cooper 2000; Crichton 2016). The metals with a specific density of over 5 gm/cm^3 are considered heavy metals, which adversely affect both environment and human health (Järup 2003).

3.2 Pathophysiology and Mechanism of Metal Toxicity

3.2.1 Oxidative Stress

Most of the heavy metal produces reactive species which affect human metabolism by altering the oxidative-reduction system. Arsenic is one of the poisonous metalloid elements present in both inorganic and organic forms. The inorganic arsenic is found highly lethal than its organic form. The common denominator of arsenic toxicity-induced pathogenicity is Reactive Oxygen Species (ROS)-mediated oxidative damage. Besides this, toxicity due to arsenic causes morphological alternations in mitochondria's integrity, which disrupt the mitochondrial membrane potential. In humans, the construction of ROS, including superoxide radicals, peroxyl radicals (ROO*), hydroxyl radical (OH*), singlet oxygen, and hydrogen peroxide, is increased upon exposure to arsenic which will cause DNA damage. Numerous bioactive molecules like peroxides, ROS, and isoprostanes along with aldehydes like malondialdehyde (MDA) and 4-hydroxy-nonenal (HNE) are generated via the formation of arsenic-induced toxicity. Besides ROS, exposure to arsenic triggers the formation of reactive nitrogen species (RNS) (Jomova et al. 2011).

The lead-induced toxicity causes damage to the cellular membranes, DNA, and proteins resulted due to the unbalance between the production and elimination of ROS in tissues and cell organelles (Yiin and Lin 1995). The mechanism of lead-induced oxidative stress comprises deviations in the fatty acid composition of cellular membranes. The unsaturation and span of fatty acid determine the susceptibility of the membrane for the peroxidation, while the enhanced lipid peroxidation of the membrane occurs as a result of lead-induced arachidonic acid elongation (Lawton and Donaldson 1991). Lead toxicity produces disturbances in the different antioxidant defenses, both enzymatic and non-enzymatic which are essential to prevent peroxidase tissue damage and thus contribute to damage to the renal, liver, and nervous system (Kumar et al. 2010).

Mercury is a ubiquitous environmental toxicant mainly generated by occupational activities like coal combustion, mining, and relevant industrial activities that emit mercury in the atmosphere (Farina et al. 2011; Dos-Santos et al. 2018). Aquatic sulfate-reducing bacteria transform mercury into Me-Hg via bio methylation, which enters the food chain. The food containing Me-Hg is absorbed by the gastrointestinal system (Dos-Santos et al. 2018; Compeau and Bartha 1985). The absorbed Me-Hg induces overproduction of ROS and also disrupts glutamate and calcium (Ca^{2+}) homeostasis along with a reduction in antioxidant defenses and thus damage cells (Farina et al. 2011; Aschner et al. 2007; Ceccatelli et al. 2010). The Me-Hg damages astrocytic glutamate transport, which overproduces ROS (Dos-Santos et al. 2018; Lafon-Cazal et al. 1993). The activities of an antioxidant enzyme such as glutathione peroxidase (Gpx), thioredoxin reductase (TrxR), and thioredoxin (Trx) have been reduced by the exposure of Me-Hg, which increases the production of ROS (Dos-Santos et al. 2018; Farina et al. 2009; Wagner et al. 2010). Me-Hg can also cause

dysfunctions mitochondrial system via the loss of mitochondrial membrane potential by targeting specific thiol-containing proteins in the mitochondria, which include respiratory chain complexes (Glaser et al. 2010; Yin et al. 2007). Mercury interferes with the function of selenocysteine antioxidant enzymes and other sulfhydryl-containing proteins, which leads to alterations in the cellular redox equilibrium. This leads to a prooxidative state which inhibits pro-inflammatory cytokine release and intercellular communication isolating cells from their tissue-specific homeostasis, thus inhibits the immune system's defense (Chen et al. 2018).

As per the WHO, Cadmium is considered one of the significant threats to public health. Cadmium can quickly enter the food chain via its absorption by plants due to its high water solubility (Jomova and Valko 2011; Satarug 2012). The cellular route of cadmium accumulation is uncertain. Still, it is hypothesized that cadmium uses the transport mechanism of essential elements like Fe and Zn for its uptake by competing with them (Zhang et al. 2003; Abouhamed et al. 2007; Johri et al. 2010). Besides, it is considered as deregulation of transition metal homeostasis is associated with the cellular uptake of cadmium (Moulis 2010; Vesey 2010). In the liver, cadmium binds to metallothioneins (MTs), glutathione (GSH), which are cysteine-rich, low molecular weight proteins that bind and neutralize cadmium, thereby detoxifying and removing it from the cells; moreover, MTs scavenges cadmium-induced ROS due to its thiol groups (Hart et al. 2001). As a result of decreased metal-binding stability, cadmium dissociates from MTs, resulting in cell lysis by interfering with mitochondrial oxidative phosphorylation and reducing basal respiration (Zhang et al. 2003; Cannino et al. 2009; Thévenod 2009).

In chromium, previous in vitro studies show that chromium, notably Cr^{4+} induces the generation of free radicals from H_2O_2. The toxicity caused by the free radical generation due to chromium is mainly associated with the reduction of chromium [Cr(VI)] into its trivalent form in the cellular system, which decreases the detoxifying ability of the cell and generates free radicals (Engwa et al. 2019; Husain and Mahmood 2017).

There is two mechanism via which copper induces oxidative stress, first ROS generation via a Fenton-like reaction and second by decreasing glutathione levels due to high exposure to copper (Liochev and Fridovich 2002; Prousek 2007). Cupric ion (Cu^{2+}) is reduced to cuprous ion (Cu^{+}) in the presence of ascorbic acid or GSH, which catalyzes the formation of reactive hydroxyl radicals by decomposing H_2O_2 via the Fenton reaction. The OH* radical is tremendously reactive, reacting with biological molecules like unsaturated fatty acids forming lipid radical. Copper can also denature DNA by oxidation of nitrogen bases via ROS (Jomova and Valko 2011).

Manganese dysfunctions the cellular defensive mechanism like glutathione and elevates the generation of free radicals that damage the mitochondrial DNA. Both the trivalent (Mn^{3+}) and divalent (Mn^{2+}) forms have been considered neurotoxic because both of them can cross the blood–brain barrier (Li and Yang 2018).

Nickel induces neurotoxicity via the formation of ROS and mitochondrial dysfunction. Nickel can impair the mitochondrial membrane potential, reduce mitochondrial ATP production, and break the mitochondrial DNA. It also interferes with the electron respiratory chain (Genchi et al. 2020).

3.2.2 Inflammation

Inflammation is one of the vital phenomena in the pathogenesis of heavy metal-induced abnormalities in different organ systems. Metal toxicity has resulted in the production of ROS/RONS, which triggers the inflammatory pathways. Heavy metals like mercury disturb cellular redox equilibrium by altering the activity of selenocysteine antioxidant enzymes and other sulfhydryl-containing proteins, giving rise to a peroxidative state which is followed by the generation of proinflammatory cytokines. This inflammatory condition isolates cells from their tissue-specific homeostasis weakens the immune system defense (Chen et al. 2018). In vitro studies on cadmium have shown that pro-inflammatory cytokines and chemokines (IL-8, IL-6, IL-18) are up-regulated in the epithelial cells after cadmium intake. It is demonstrated that a nontoxic concentration of cadmium can induce IL-6 and IL-8 production through MAPK phosphorylation and NF-jB activation, without changing cell morphology and viability from astrocytes the large neuroglial cells (Hossein-Khannazer et al. 2020). Very limited studies were done in contrast with the heavy metals that produce inflammation, but the main pathway of inflammation by heavy metals in the human body is the alteration of ROS balance.

3.2.3 Carcinogenicity

A lot of heavy metals produce a harmful effect on the human in which the alteration of cellular metabolism is one of them, and these changes ultimately lead to cancer generation in the body. Arsenic is among the potent environmental carcinogen which causes several types of skin and internal cancers such as bladder, prostate, liver, kidney, and lung cancers. Skin cancer is the most frequent form of neoplasm induced due to arsenic exposure, while lung cancer is considered the most lethal. The methylated form of arsenic is considered more carcinogenic, altering the epigenetic mediated mechanism in the cellular system (Hubaux et al. 2013; Wei et al. 2019). It is evidenced that occupational exposure to lead causes a variety of cancers among workers. At the molecular level, lead interferes with DNA repair and acts synergistically with other mutagenic agents. Animal studies have shown that in rodents, lead acetate induces brain cancer (gliomas), renal cancer, and lung cancer (Steenland and Boffetta 2000; Kim et al. 2015). Mercury is another potent carcinogen that causes cancers via several specific mechanisms such as free radical generations, impairment of DNA repair, reducing glutathione concentration, and elevating lipid peroxidation (Yuan et al. 2016). Cadmium exposure has a causal association with carcinogenesis in multiple tissues and organs, including the stomach, breast, lungs, esophagus, prostate, intestines, and testes (Bertin and Averbeck 2006; Bishak et al. 2015; Larsson and Wolk 2016). Epidemiological studies have evidenced that nickel toxicity is associated with various types of cancer, including lung, nasal, and sinus tissue cancer (Chen et al. 2018; Pavela et al. 2017).

3.2.4 Neurotoxicity

The elevated levels of environmental exposure to heavy metals produce cognitive and neurological deficits in adults and children. Heavy metal, especially arsenic, lead, cadmium, mercury, manganese, etc., produces neurotoxicity in human beings. The heavy metal generates neurotoxicity mainly by damaging the different regions of the central nervous system (CNS), and brain-like cerebral microvessels thought generating oxidative stress by ROS. The distinct neurological effects will be produced according to different targets and modes of action. In the case of lead, its lower concentration (10 μg/dl) while the elevated manganese levels (water range 0.1–2700 μg/l, geometric mean 20 μg/l) can affect the intelligence quotient (IQ) of children. It is believed that lead affects the learning ability and recall processes of the brain by suppressing the N-methyl-D-aspartate receptor (NMDAR) and neuronal voltage-gated calcium channels (VGCCs), which is necessary for hippocampus-mediated learning and memory. By inhibiting either VGCCs or NMDARs by lead would result in a significant deprivation of Ca^{2+} entry into the cell and affect the neurotransmission.

The elevated level of manganese produces extrapyramidal effects within the globus pallidus and other basal ganglia structures of the human brain. Manganese accumulates in neurons, globus pallidus (GP), astrocytes, and oligodendrocytes of the substantia nigra (SN), and striatum (STR) and also intracellular within the mitochondria, where it interrupts ATP synthesis. The interruption of ATP synthesis decreases intracellular ATP levels and increases oxidative stress. Manganese generated intracellular oxidative stress oxidizes dopamine (DA) into reactive quinone species, and this reactive DA species (reactive quinone species) is taken up by the dopamine transporter (DAT1), which results in dopaminergic neurotoxicity (Garza et al. 2006; Neal and Guilarte 2012). Cadmium also produces oxidative stress in the human body and induced injury in the cerebral micro-vessels. The elevated level of cadmium decrease microvessel enzymes that are mainly involved in the proper functioning of the cellular redox reactions, such as glutathione peroxidase, superoxide dismutase, and catalase. Hence, the reduction of micro-vessel antioxidant defense systems increases lipid peroxidation (LPO), which provokes micro-vessel damage (Wang and Du 2013). The neurotoxicity of mercury is through elevated levels of Me-Hg is well recognized both in humans and laboratory animals. The immature central nervous system (CNS) of the fetal brain is susceptible to Me-Hg neurotoxicity even if the mother has no symptoms of poisoning. The elevated level of mercury (Me-Hg) produces neuronal degeneration either by necrosis or apoptosis. The relatively high (5–10 mM) exposure level of Me-Hg causes the rapid damage of mitochondrial activity, plasma membrane lysis, and de-energization of mitochondria resulting in extensive necrotic death. In comparison, in low Me-Hg ($\leq$1 mM) concentrations, exposure causes the death of cerebellar granule cells mainly by apoptosis. At a low exposer level, the Me-Hg interrupts calcium homeostasis, causes an increase in intracellular calcium in cerebellar neurons, and ultimately causes neuronal cell death (Castoldi et al. 2001). The other heavy metals also produce an almost similar mode of action to produce neurotoxicity, which is discussed above section.

3.3 Health Hazards Due to Metal Toxicity

3.3.1 Gastrointestinal

Arsenic

Agency for Toxic Substances and Disease Registry and the Environmental Protection has kept arsenic at the top position in the priority list of hazardous substances. Arsenic toxicity causes multiple gastrointestinal abnormalities in humans upon its ingestion. Short-term high-dose and prolong lower-dose exposures to inorganic arsenic show symptoms like gastrointestinal irritation, diarrhea, vomiting, including nausea, and abdominal pain; moreover, previous animal studies have reported hemorrhagic gastrointestinal lesions. Organic arsenic has also been toxic to the human and animal gut causing vomiting, hyperactive bowel, abdominal pain, and diarrhea. Arsenic-induced gastrointestinal toxicity led to thickening of the large intestine wall and caused edema and hemorrhagic, necrotic, ulcerated, or perforated mucosa of the large intestine along with squamous metaplasia of the epithelial columnar absorptive cells in the colon and rectum (Genchi et al. 2020; Jomova et al. 2011; Li and Yang 2018).

Lead

Lead toxicity induces dysfunction in many organ systems, including the gastrointestinal tract of animals and humans. Gastrointestinal organs can easily absorb lead, while its absorption depends upon the factors like nutritional status and age of an individual. Lead causes acute symptoms of gastrointestinal diseases like abdominal pain, vomiting, nausea, and diarrhea; however, in few cases, extreme gastric dilation and chronic erosive gastritis have also been reported in gastroscopy (Begovic et al. 2008). Some microbiome studies revealed that lead exposure alters the composition of gut microflora which is also referred to as our second genome. The lead-induced dysbiosis of the gut microflora is associated with allergies, gastric cancer, anorexia, Crohn's disease, inflammatory bowel diseases, and other diseases (Gao et al. 2017).

Mercury

Occupational exposure to mercury vapor is one of the major routes of mercury-induced toxicity in humans. Mercury is toxic in its organic and organic form because it can bring alternations in the tertiary and quaternary structure of proteins. Acute mercury poisoning can lead to severe gastrointestinal abnormalities, whereas chronic poisoning causes coarse peripheral neuropathy, tremor, irritability, and acrodynia,

also known as "Pink Disease." Occupational exposure and ingestion of contaminated fish, grain, or pork cause peripheral neuropathy, choreoathetosis, and ataxia (Dasgupta and Wahed 2014; Tekulve et al. 2017).

Cadmium

Cadmium is one of the prime environmental toxicants which has widely been reported for its toxicity all around the globe. The gastrointestinal tract absorbs cadmium, while its solubility and absorption are affected by gut and intestinal pH. It reacts with hydrochloric acid to form cadmium chloride, which causes inflammation in the gastrointestinal tract (Rahimzadeh et al. 2017). Some studies revealed that cadmium reduces the intestinal absorption of calcium, leading to calcium deficit in the body (Asagba 2013).

Chromium

Chromium is considered a primary heavy metal toxicant to human health and broadly exists in the environment. Previous studies show that Cr^{6+} exposure increased the risk of gastric cancer. The contamination of chromium in the topsoil correlates with the mortality due to the upper gastrointestinal (GI) tract carcinogenicity in females. Prolong exposure to chromium contaminated topsoil could potentially increase gastrointestinal cancers (Yuan et al. 2016).

Copper

Copper is an essential element that has many vital functions in body physiology and enzyme catalysis. Copper exists in its divalent form in drinking water and is primarily not responsible for the biological effect; however, excessive intake of copper via contaminated water or food leads to the development of various gastric disorders in humans such as gastric pain, nausea, vomiting, and diarrhea (Pizarro et al. 2001).

Manganese

Manganese is one of the essential trace elements in humans, but overexposure to manganese leads to toxicity. It has been reported that manganese-induced poisoning alters the gut microbiota involved in many necessary physiological and metabolic activities. The dysbiosis of gut microflora negatively Impacts host immunity and metabolism. Previous studies mentioned that manganese-induced dysbiosis could also lead to depression and anxiety and negatively impact CNS (Chi et al. 2017).

Nickel

Ingestion of nickel may lead to Irritable bowel syndrome (IBS), which is also termed systemic nickel allergy syndrome. Previous studies explore that nickel has been prevalent in the diet of females with irritable bowel syndrome (Rizzi et al. 2017).

3.3.2 Respiratory

Arsenic

Arsenic is one of the prime environmental toxicants, and its overexposure is associated with obstructive lung diseases, respiratory symptoms, and mortality from respiratory diseases. Acute exposure to arsenic via drinking water harms the respiratory system. The inhalation of arsenic dust produce during the mining activities creates respiratory complications such as laryngitis, chronic cough, bronchitis, and rhinitis. The common symptoms of arsenic toxicity to the respiratory tract are chronic cough, laryngitis, bronchitis, and rhinitis (Mohammed Abdul et al. 2015). Low and moderate exposure to arsenic induces emphysema, airflow obstruction, lower lung function, shortening of breath, and several other lung complications (Powers et al. 2019).

Lead

It was observed that lead has a role in the progression and development of asthma; the studies on animals revealed that lead exposure induces morphologic changes and increased tracheal responsiveness, which supports the involvement of lead in the pathogenesis of asthma. Organic lead compounds can cross the skin and respiratory tract. Lead has several routes of exposure like drinking water, food along with occupational activities like mining. In workers with exposure to the lead, an impaired respiratory function was reported with an elevated Pb level in blood which demonstrates the role of leads in the development of occupational chronic obstructive pulmonary diseases (Powers et al. 2019).

Mercury

Mercury is considered lethal to the environment due to its chronic toxicities to the different organ systems; despite the restrictions in the use of mercury, it continues to impact health. Mercury has always been a health concern due to its ability to deposit in most organ systems. Previous case studies on workers reported that occupational exposure to mercury vapors leads to several life-threatening respiratory failure, pneumomediastinum, and quadriparesis and showed symptoms like fever, chest pain, dyspnea, cough, and chills. Prolonged mercury exposure can cause lethal respiratory diseases like pneumonia, fibrosis, chemical pneumonitis, respiratory distress

syndrome (ARDS), bronchiolitis, and pneumothorax, resulting in death (Cooper 2000; Lim et al. 1998).

Cadmium

Cadmium is one of the xenobiotics which is associated with inflammation and is also a potent carcinogen. Cadmium is absorbed in the body in various ways, most probably via inhalation; after absorption, it up-regulates the pro-inflammatory cytokines and cell cycle regulatory molecules and induces lung inflammation and cell proliferation. Acute poisoning due to cadmium can also develop cough and respiratory distress symptoms, which may progress to pneumonitis and ARDS (Koons and Rajasurya 2021).

Chromium

Hexavalent chromium [Cr(VI)] compounds are reported in the involvement of the development of respiratory deformities and disorders. Workers with occupational exposure like the chromate industry have always prone to respiratory diseases, including fibrosis, lung fibro-sarcomas, adenocarcinomas, and hyperplasia of the bronchial epithelium, and squamous cell carcinomas. Cr(VI) exposure triggers peri-bronchiolar inflammation along with alveolar and interstitial inflammation, which induces pneumonitis. Cr(VI) has also been reported to cause nasal mucosa injury, ulcerated septum, inflamed mucosa, and perforated septum in workers (Beaver et al. 2009; Wilbur et al. 2012).

Copper

Copper has been used in several applications like electronics, catalysts, wood protection, solar cells, and antimicrobial products, which raised the concern about their health hazards. Some previous research revealed that prolong exposure to copper, which is present in various forms and along with other compounds, produces bronchiolitis, alveolitis, and vacuolation of the respiratory epithelium. In vitro studies showed that copper nanoparticles (CuO NPs) are associated with the development of oxidative stress, cytotoxicity, and genetic toxicity in cultivated human lung cells, while in some animal studies, it has been found that CuO NPs toxicity induces neoplastic lesions, inflammation, and intra-tracheal installation of CuO NPs induced oxidative stress (Ahamed et al. 2015; Gosens et al. 2016).

Nickel

Nickel absorption and deposition in the body, particularly in pulmonary, nasopharyngeal, or bronchial regions of the respiratory tract, depending on the particle size. Nickel can be characterized as respirable and non-respirable based on its size. The immunotoxicity of nickel causes lung fibrosis and respiratory tract cancer are some of the conditions/diseases related to the respiratory system; moreover, nickel has been considered a potent carcinogen to the respiratory organs (O'Neal and Zheng 2015).

3.3.3 Cardiovascular

Only a few Heavy metals are also involved in the development of cardiovascular disease, which is as follows:

Arsenic

Previous epidemiological studies show that arsenic exposure will also develop peripheral vascular disease and hypertension, leading to cardiovascular diseases (CVD). It is reported that chronic exposure to arsenic has been involved with the sub-clinical CVD markers and CVD risk factors (Tchounwou et al. 2003; Ratnaike 2003; Moon et al. 2012).

Lead

Population studies conducted previously demonstrated that lead exposure is linked with the subsequent development of cardiovascular diseases and hypertension via oxidative stress generation. Lead toxicity induces hypertension by limiting the nitric oxide availability, affecting nitric oxide signaling, increasing adrenergic activity, enhancing endothelin production, modifying the renin-angiotensin system, augmenting, vasoconstrictor prostaglandins, diminishing vasodilator prostaglandins, elevating inflammation, decreasing endothelium-dependent vasorelaxation, and altering and modifying the vascular response to vasoactive agonists. It has also been documented that atherosclerosis, thrombosis, and cardiovascular diseases have a causal association with lead exposure (Vaziri 2008).

Mercury

Mercury is among the prime heavy metal contaminant of the environment, which affects the health of vulnerable populations like antenatal women and is toxic to normal adults. It has been documented that chronic mercury exposure is responsible for developing diseases in the cardiovascular system such as coronary heart disease, hypertension, and myocardial infarction. It is hypothesized that the neurotoxic effect of mercury affects the cardiac autonomic function, as heart rhythm and function are controlled by the autonomic nervous system. Mercury exposure could have a prolonged impact on cardiac parasympathetic activity; moreover, it has been evidenced that heart rate variability might be affected by exposure to mercury (Genchi et al. 2020)**.**

Cadmium

Cadmium is a widely distributed metal all over the globe and is a potent toxicant that affects the cardiovascular system. It has been associated with hypertension, myocardial infarction, heart failure, moreover reported for cardiovascular mortality (Vaziri 2008; Tellez-Plaza et al. 2013). High cadmium exposure increases the thickness of intima-media, which causes endothelial damage and increases atherosclerotic plaque in animals (Messner et al. 2009).

Chromium

Limited evidence is available to show the association of chromium toxicity with cardiovascular disorders; however, hexavalent chromium (Cr(VI)), a most toxic form of chromium, has been reported to induce toxicity to the cardiovascular system. Though previous studies demonstrated that hexavalent chromium could disturb cytomembrane structure by exacerbating lipid peroxidation in the heart, the detailed mechanism behind the chromium-induced heart dysfunction is uncertain (Bagchi et al. 2002; Ray 2016).

Copper

Cardiovascular diseases are the prime cause of mortality and morbidity globally, and it has been reported that exposure to heavy metals like copper is associated with the pathogenesis of cardiovascular disorders. Based on the documented information it is hypothesized that divalent ion of metal like copper has the ability to catalyze highly reactive free radicals (hydrogen peroxide, superoxide anion, and lipid peroxide) via Fenton-type reactions which initiate lipid peroxidation which is a crucial event in the development of CVD like atherosclerosis (Alissa and Ferns 2011).

Manganese

Manganese is one of the potent toxicants which is harmful to many organ systems; however, less attention has been given to the causal association of Mn with cardiovascular dysfunction. Clinical and epidemiological evidence demonstrated the significant occurrence of abnormal electrocardiograms (ECG) such as sinus tachycardia, sinus arrhythmia, sinus bradycardia, and sinister megacardia among workers exposed to manganese Mn exposed workers showed a significant reduction in mean diastolic blood pressure. In vivo studies evidence that Mn can rapidly accumulate in heart tissues, which further induces mitochondrial disruption and interacts with the calcium channel in the cardiovascular system, developing acute or sub-acute cardiovascular disorders, such as hypotension and acute cardio-depression. (Jiang and Zheng 2005).

3.3.4 Renal

Heavy metals also affect the renal system of humans in different ways, some of which are described below:

Arsenic

Arsenic is one of the most abundantly found toxicants in water and soil, and inorganic arsenic is readily absorbed by the intestine via drinking water. The proteins like aquaporin-10 act as a transporter for the absorption of metals like arsenic in the intestine. Arsenic toxicity is mediated through the decrease in the Glutathione store (GSH), which is the protective mechanism of the cell against the heavy metal toxicity; Glutathione-mediates the methylation of arsenite, which earlier transformed from arsenate which reduces the toxicity and promotes the urinary excretion of heavy metals (Robles-Osorio et al. 2015).

Lead

Several studies documented the lead-induced nephropathy causing renal disease in humans. Both organic and inorganic lead causes toxicity to organ systems; organic lead compounds are absorbed via the dermal route, while inorganic lead is absorbed by ingestion and inhalation. Prolong occupational and environmental exposure to lead develops chronic nephrotoxic effects characterized by tubule-interstitial and glomerular alternations, resulting in chronic renal failure and hyperuricemia (Rastogi 2008).

Mercury

The route of absorption of mercury defines the intensity of its toxicity and its detrimental effects upon the respective organ. The retention of mercury is more in the kidney than in any other organ. The pathogenesis of the kidney is mediated through the damage to the secretory organ of the erythropoietin (the hormone that stimulates erythrocyte synthesis in the kidney) (Rastogi 2008).

Cadmium

Occupational and accidental exposure to heavy metals, including cadmium, causes renal dysfunction. The acute exposure of cadmium reduces phosphate and glucose transport which inhibits mitochondrial respiration, damaging the proximal tubular cells of the nephron. Cadmium is transported to the kidney and liver by binding with metallothionein after ingestion. The deposition of cadmium causes chronic tubular-interstitial nephropathy in the medulla and S1 segment of the proximal tubule (Lentini et al. 2017).

Chromium

Occupational and animal studies documented the association of chromium widely spared industrial and environmental contaminants with renal disorders. The co-exposure of chromium, cadmium, and lead are associated with the glomerular filtration rate decline. Chromium exposure via the skin, inhalation, and drinking water leads to acute renal failure and tubular necrosis (Tsai et al. 2017).

Copper

Copper has been reported to accumulate in kidneys and is the responsible nephrotoxic agent producing renal dysfunction like glycosuria, proteinuria, calciuria, and phosphaturia. Insufficient work has been done to study the role of copper in inducing nephrotoxicity (Kidneys 1961).

3.3.5 Neurological

Arsenic

Arsenic affects almost every organ of the body, along with the nervous system; as per the records of recent studies, even a low concentration of arsenic can interrupt the nervous system's functions and increase the susceptibility to cognitive dysfunction. Both organic and inorganic forms of arsenic can accumulate in most parts of the brain

with maximum deposition in the pituitary; moreover, it can cross the placenta in the embryonic stage, in high concentration, it induces defects in the neural network tube and delays growth (Tsai et al. 2017).

Lead

The capability of lead to cross the blood–brain barrier because it can substitute calcium ions. In the brain, lead causes disturbances in the hippocampus, prefrontal cerebral cortex, and cerebellum can develop various neurological disorders, such as behavioral problems, Parkinson's disease, brain damage, nerve damage, Alzheimer's disease, and schizophrenia. Lead can alter the regulatory action of calcium on cell functions and affects many intracellular biological activities at the molecular level (Sanders et al. 2009).

Mercury

The neurotoxicity of mercury depends on the bioavailability, its absorption through the membrane, distribution within the cell, and binding ability to the macromolecules. Both acute and chronic exposure to mercury vapors induces neurological defects such as axonal sensor motor polyneuropathy, malaise, gingivitis, hallucinations, malaise, mercurial erythrism, a syndrome that includes excitability, loss of memory, insomnia (Carocci et al. 2014).

Cadmium

Chronic cadmium exposure can lead to disorders of the central nervous systems such as olfactory dysfunction; moreover, cadmium toxicity induces neurotransmitter disruption, and stimulation of neural excitations, causing damage to the peripheral nervous system and many parts of the brain (Gao et al. 2017; Ma and Cheng 2005).

Manganese

Manganese is a well-known neurotoxic element that primarily enters the body through inhalation. Occupational exposure via mining, ferromanganese operations, alloy production, and welding causes various neurological defects such as irreversible parkinsonian-like syndrome (Levy and Nassetta 2003).

Nickel

Previous occupational studies have revealed that nickel is a potent neurotoxic element that causes neurologic effects, including weariness, giddiness, and headache among workers who consume nickel-contaminated water. It has been reported that disorders like homonymous hemianopsia can be induced due to the ingestion of nickel (Das et al. 2018).

3.3.6 Dermatologic and Allergies

Most of the heavy metals are considered allergens, and nickel is the most prominent element which causes cutaneous hypersensitivity. Prolonged exposure to nickel releasing items like jewelry, mostly in females, causes skin allergies, which are termed as "nickel dermatitis." Consumption of arsenic-contaminated water is reported to accumulate arsenic tissues such as the hair, skin, and nails. Long-term arsenic exposure produces non-carcinogenic dermal effects like spotted hyperpigmentation and palmar and plantar hyperkeratosis, which can lead to skin cancer. Exposure to Cr(III) and Cr(IV) can induce allergies to the skin. In some studies

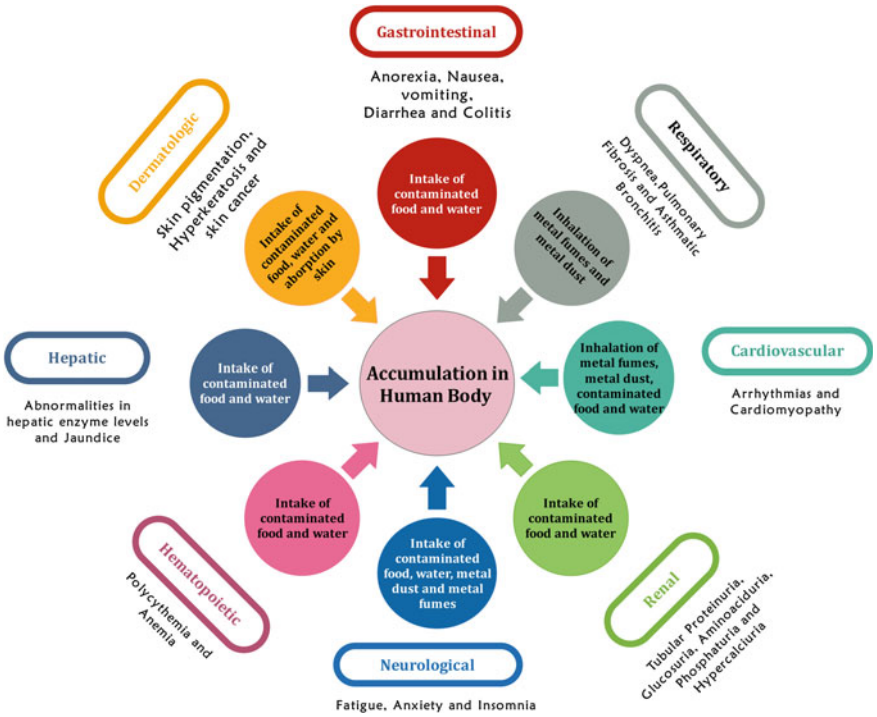

Fig. 1 Heavy metal induces health hazards in humans

is documented that occupational exposure to cement and leather has resulted in chromium allergy. Some other metals, including chromium, cobalt, and copper, cause skin hypersensitivity. (Gerhardsson and Kazantzis 2015; Ratnaike 2003). The Fig. 1 depicting the health hazard caused due to accumulation of heavy metals in human body (Fig. 1).

4 Diagnosis of Metal Toxicity

4.1 History of Exposure

Maximum environmental and occupational diseases also show some mutual medical symptoms, or they display unique nonspecific signs. It rarely occurs where the clinician's differential diagnosis for hazardous exposures enters into routine test procedures. So that there is a chance for clinicians that they might miss for making precise diagnoses that impact the course of the disease. Correct diagnosis assists in stopping the exposure and also prevent illness in others subjects by evading that specific exposure. To improve the diagnosis of the disease associated with recent or past exposures, the clinician should contemplate the prospect of the environmental and occupational factors of the disease and include an exposure history questionnaire into the clinical practice. Taking account of an exposure history may permit physicians to make more precise diagnoses, impact the course of the disease, prevent to spread of the disease in others by evading future exposure, and rapid workplace assessments and the safety of workers (ATSDR 2017).

4.2 Clinical Characteristics

4.2.1 Arsenic

The high toxicity of arsenic has been exposed globally, mainly by drinking water which develops various clinicopathological conditions. Symptoms of acute intoxication are diaphoresis, muscle spasms, nausea, vomiting, abdominal pain, diarrhea, anuria, dehydration, hypotension, cardiovascular collapse, aplastic anemia, and death (Tchounwou et al. 2004). The primary symptoms developed in the oral administration of inorganic arsenic were edema of the face and gastrointestinal and upper respiratory symptoms initially, followed by skin lesions and neuropathy in some objects. While in the long term, arsenic exposure produces non-carcinogenic dermal effects (spotted hyper-pigmentation and palmar and plantar hyperkeratosis) and skin cancer, cardiovascular and peripheral vascular disease, hypertension, noncirrhotic

portal fibrosis, nasal septum perforation, chronic bronchitis, developmental anomalies, neurologic and neurobehavioral complications, diabetes, hearing loss, hematologic abnormalities (like anemia, leukopenia, and eosinophilia), Blackfoot disease and carcinoma (Tchounwou et al. 2003; Ratnaike 2003). Workers exposed to organic arsenic through inhalation more often developed keratosis than nonexposed workers (ATSDR (Agency for Toxic Substances and Disease Registry) 2007).

4.2.2 Lead

Identification of lead toxicity is challenging because of its nonspecific nature of symptoms. The mild to moderate lead toxicity symptoms include fatigue, difficulties in concentration, memory loss, humor change, convulsions, sleep turbulences, headache, weight loss, nausea, and myalgia. In contrast, severe toxicity produces abdominal cramps, renal disease, encephalopathy, strokes, and peripheral neuropathy. Some other symptoms like muscle pain, droopiness, and work-related nasal symptoms are regularly observed in lead-exposed workers. In children, lead toxicity produces Fanconi syndrome and creates an adverse effect on neurological development. In some cases, lead also develops allergic symptoms by an increase or stimulate IgE production. Lead also shows the capability to replace the other divalent cations, such as calcium and zinc, in molecular machinery. Lead has a high affinity for thiol groups present on different functional proteins that affect the Central Nervous System (CNS), hematopoietic system, liver, and kidneys and produce severe disorders (Gupta and Gupta 2016; Cunningham 2007).

4.2.3 Mercury

The toxicity of mercury and its sternness depends on the chemical form of the Hg with its exposure path. Acute exposure to Hg can lead to brain damage, failure of the CNS, loss in memory, cardiac-related disease, liver damage, loss in vision, and loss of sensation. At the same time, chronic toxicity of mercury produces symptoms ranging from polyuria and proteinuria to nephritic syndromes in severe cases accompanied by hematuria and anuria. The vapors of mercury can cross the alveolar membrane and enter into the blood and afterwards in the CNS, leading to respiratory disease, erythrism, gingivitis, tremor, and other CNS-related disorders like Alzheimer's and Parkinson's disease. Methylmercury toxicity produces signs such as ataxia, peripheral neuropathy, choreoathetosis, visual loss, confusion, and prolonged mercury exposure produces lethal effects on fetal development and leads to neurological damage, behavioral problems, autism, and reproductive damage (Afrifa et al. 2019; Davis et al. 2017).

4.2.4 Cadmium

Clinical symptoms of cadmium toxicity are subject to the route, amount, and rate of exposure. Children and adults show a similar characteristic of cadmium toxicity. The first experimental toxicological studies were reported in 1919. Then after in the late 1930s–1940s, the first reports of pulmonary, bone, and renal lesions in industrial workers induced by cadmium toxicity, were published. In the 1960s, Japanese women exposed to cadmium toxicology were recognized as the major etiological factor in *itai-itai* disease, developed due to the consumption of cadmium contaminated rice and water (Rani et al. 2014). Consumption of very high cadmium contaminated food or drinking water can cause severe irritation in the stomach, leading to vomiting, diarrhea, and sometimes death. At the same time, lower levels of cadmium for chronic exposure may lead to a build-up of cadmium in the kidneys, leading to kidney damage. It also affects bones by creating them fragile and easily breakable (ATSDR (Agency for Toxic Substances and Disease Registry) 2020). Cadmium exposure has been paradoxically associated with blood pressure. If the U-Cd concentration is less than 10 μg/g creatinine, the kidney functions partially weakened, which might be changed after the exposure decreased. But, if cadmium exposure was higher than 10 μg/g, the kidney function may lose and which is irreversible or even failed after the exposure declined or null (Wu et al. 2016). Calcium toxicity, osteoporosis, anemia, non-hypertrophic emphysema, eosinophilia, anosmia, and chronic rhinitis will produce. Further, the cytotoxicity will lead to the apoptotic or necrotic event and create cancer; that's why International Agency for Cancer Research (IACR) classified cadmium as a Group-I carcinogen (Rani et al. 2014).

4.2.5 Chromium

To date, very limited human studies were conducted which show adverse health effects of oral exposure to chromium. Depends upon the industrial lung cancer incidents, in 1992, the U.S. EPA had informed that there is a chance of developing cancer in 1 human per million by chromium-containing air exposure in which Cr level at 80 pg/m^3 (which is 8×10^{-8} mg/m^3) (Costa and Klein 2006). The augmented lung cancer hazard has been observed between the workers where past contact to Cr(VI) has been more than 100 mg/m^3. It is found that by the intra-peritoneal injection of highly toxic doses of Cr(VI), Cr(VI) can be genotoxic and mutagenic in vitro and in vivo for humans. Although, Cr(VI) displays very partial genotoxicity via a natural exposure path and at environmentally relevant levels (Proctor et al. 2014).

4.2.6 Copper

Generally, copper toxicity is rare in the current industrial environment. Still, acute toxicity symptoms will be produced by moderately excessive doses (6 mg Cu/l equivalent to 0.14 mg Cu/kg body-weight/day), which generate gastrointestinal symptoms

like nausea, abdominal pain, diarrhea, lethargy, and anorexia are the other symptoms. While chronic or excessively high quantities display toxic signs, including haematuria, hepatic necrosis induced jaundice, and kidney damage. NOAEL (No observed adverse effect level) was found 4 mg Cu/l. In genetic conditions, like in Wilson's disease (an autosomal recessive disorder by non-functional ATPase, ATP7B) and Indian childhood cirrhosis is the leading cause of copper toxicity due to failure of incorporation of copper into the ceruloplasmin synthesis or to expel copper into the bile, so triggering an adverse hepatic copper build-up. Because copper comes under an essential dietary nutrient and is quickly supplied, therefore, copper deficiency is relatively rare, but it causes symptoms of anemia, leukopenia, and neutropenia. Menkes syndrome (reduction in copper transport) is an X-linked copper deficiency genetic syndrome that mainly occurs due to the defect in copper transporter proteins (Cu-ATP7A). And this syndrome produces symptoms like kinky hypopigmented hair, connective tissue abnormalities leading to aneurisms, loose skin, fragile bones, neurological degeneration, and ineffective temperature regulation (Tsuji et al. 2016; Taylor et al. 2020).

4.2.7 Manganese

Occupational exposure to manganese is one of the main sources of manganese neurotoxicity. In manganese neurotoxicity, workers have been exposed to manganese particulate (100-fold more than established safe limits) within mining, manufacturing, and welding industries. Inhaled manganese particles can generate inflammation in the lungs and respiratory system defect signs, including cough, bronchitis, pneumonitis, and impaired pulmonary function. Gasoline additive, methylcyclopentadienyl manganese tricarbonyl, is an additional latent environmental source for manganese exposure that releases phosphates, sulfates, and oxides of manganese atmosphere upon combustion, and 90% of its particle are in respirable size (Erikson and Aschner 2019).

4.2.8 Nickel

The nickel toxicity is dependent on nickel and its compounds' physicochemical characteristics, the quantity exposed, period of interaction, and route of exposure. Depend on the quantity and exposure time, it produces different health effects, like dermatitis, cardiovascular disease, asthma, and respiratory diseases, including cancer. Acute toxicity occurs by absorption through the GI tract or inhalation by the lungs. It produces nose and sinuses irritation, which leads to non-function of smelling ability and sometimes nasal septum perforation seen. Acute toxicity also has instant symptoms like nausea, vomiting, vertigo, irritation, etc. In contrast, late symptoms show stiffness of the chest, constant cough, dyspnoea, cyanosis, tachycardia, palpitations, sweating, visual disturbances, weakness, etc. It was also seen that about 1.5 months of exposure to nickel vapors (0.07–1.1 mg nickel/m^3) in welders leads to an increase

in breathing rate and vision dysfunctions with fatigue. Chronic exposure to nickel is accountable for many adverse effects in human beings, like lung fibrosis, respiratory disorders, asthma, bronchitis, kidney and cardiovascular diseases, and cancer of the nasal and respiratory tract. The insoluble nickel compounds can stay longer in the lungs and leads to responsible for cancer. Epidemiological studies also found that nickel refinery workers exposed to nickel-containing dust and fumes for a very long duration have a chance of increased mortality by lung and nasal cavities cancer. It was also reported that when nickel-containing objects are in direct and continuous contact with skin, nickel got corrosion by sweat and discharge nickel ion which taken up by the skin and generate an allergic effect, called nickel allergy. About 8–10% of women and 1–2% of men show sensitivity towards nickel (Das et al. 2018; Genchi et al. 2020; Cempel and Nikel 2006).

4.3 Analysis and Biochemical Assays of Toxicology

4.3.1 Arsenic

Arsenic toxicity studies progressively changed with time, and detection ranges from the analysis of oxygenated metabolites of inorganic arsenic to thiolated arsenic metabolites. These thiolated arsenicals are freely absorbed by the bladder cells and transformed into their corresponding trivalent oxygenated arsenic form. For detection of the arsenic presence, blood, urine, and hair samples are used. The estimation of exact arsenic species in urine is determined by atomic absorption spectrophotometry (AAS). Presently, the utmost sophisticated technology used to detect arsenic is HPLC equipped with either inductive coupled plasma mass spectrometry (HPLC-ICP-MS) or hydride generation atomic fluorescence spectrometry (HPLC-HGAFS), which provides an accuracy of more than 20 parts per trillion and linearity up to 10 ppm. Inductively coupled plasma atomic emission spectrometry (ICP-AES) and ICP-mass spectrometry (ICP-MS) offer lower detection limits than absorbance detection methods. In arsenic toxicity, the arsenic concentration id found in hair sample from 0.1 and 0.5 mg/kg for chronic poisoning while, 1.0 to 3.0 mg/kg shows acute poisoning (ATSDR (Agency for Toxic Substances and Disease Registry) 2007; Ratnaike 2003; Tchounwou et al. 2004; Davis et al. 2017).

4.3.2 Lead

In lead toxicity, the symptoms may develop according to dose; if dose levels of 4–5 μmol/l, then symptoms may develop in 1–3 days. While subacute and chronic exposure may take time to show the signs. Since about 90% of body lead concentrates within the skeleton, that's why the best measurement of lead load would be bone lead, which is measure by the X-ray fluorescence technique (Lockitch 1993). For

detection of lead concentration in blood serum, flame atomic absorption spectrometry (FAAS; detected up to ~1 μg/ml lead in the blood), Graphite Furnace Atomic Absorption Spectrometry (GFAAS; detection limit <0.1–0.2 μg/ml), Anodic Stripping Voltammetry (ASV; detection limit 0.2–0.3 μg/ml) and ICP-MS (detection limit ~0.01 μg/ml) were used. Basophilic stippling is also seen in the subject who has prolonged exposure to Pb (Barbosa et al. 2005; ATSDR 2017; WHO 2011).

4.3.3 Mercury

The blood containing mercury level represents the total mercury, which includes both elemental and methyl mercury. Primarily mercury exposure is observed by measuring mercury in urine, and about 95% of mercury (in the form of methylmercury) is taken up by the GI tract and transferred into the RBC and brain (Afrifa et al. 2019). In the case of inorganic mercury compounds (H^0) ingestion, a kidney-ureter bladder X-ray (KUB) is taken to track the movement of mercury through the GI tract (Ye et al. 2016). Mercuric species that bind with protein are presently approachable to an analysis by mass spectrometry, critical for act as predictive biomarkers of Hg-induced toxicity (Branco et al. 2017).

4.3.4 Cadmium

AAS and ICP-AES are the most preferred analytical techniques to detect the Cd quantity in biological samples. Graphite furnace atomic absorption spectroscopy (GF-AAS) having decent precision and duplicability (99–99.4%) to measure the Cd in blood, plasma, urine, and hair with a detection limit of about 0.4 μg/l. And by the modification in samples with an agent like diammonium hydrogen phosphate or palladium (Pd)-based modifiers increase the detection limits up to 0.1 μg/l. ICP Dynamic Reaction Cell Mass Spectrometry (ICP-DRC-MS) shows high sensitivity for detecting urine cadmium concentrations compared to ICP-MS. Radiochemical Neutron Activation Analysis (RNAA) is a rapid two-step solvent extraction method used to detect cadmium in tissue samples. The detection limits described for RNAA are about 2 mg Cd for the total kidney and 1.5 μg/g for the liver. Cadmium is preferentially accumulated, and concentrations in liver and kidney tissues quantify using in vivo neutron activation analysis and kidney by X-ray fluorescence analysis; however, the detection limit is very high. For cadmium analysis in teeth, Electrothermal vaporization ICPMS has been applied. Adsorptive cathodic stripping voltammetry (ACSV) and potentiometric stripping analysis (PSA) have been applied for hair analysis, animal tissues, and body fluids to detect the Cd level (ATSDR (Agency for Toxic Substances and Disease Registry) 2012).

4.3.5 Chromium

Size-exclusion chromatography coupled with ICPMS and electrospray mass spectrometry (ESMS) combined was used to preliminary recognize Cr-binding biomolecules. While advance spectroscopy, named X-ray absorption near edge structure (XANES) spectroscopy, was used to detect the coordinate environment of Cr in intact Cr-combined cells or tissues and subcellular or chromatographic fractions (Levina and Lay 2008).

4.3.6 Copper

The most common analytical technique for analyzing copper in the biological material are AAS or ICP-AES and ICP-MS. For ICP-AES, the detection limit for blood is 1 μg/100 ml, for tissue, it is 0.2 μg/g tissue, and for urine, it is 0.1 μg. While AAS equipped with a graphite furnace detect 0.25 μg/g wet weight in a tissue sample and 0.6 μg/g for toenail. ICP-AES is also suitable for investigating copper in groundwater, surface water, and drinking water (ATSDR (Agency for Toxic Substances and Disease Registry) 2004).

4.3.7 Manganese

For accessing the manganese levels in the biological and environmental samples, AAS and AES are the most common analytical procedures. AAS combined with a graphite furnace (GFAAS) is used, but it has a meager detection limit (<1 μg/l in urine, <1 μg/g in feces, and <0.2 μg/g in hair sample). Presently, the ICP-AES technique is regularly applied for manganese. The radioactive neutron activation analysis technique is also beneficial for quantifying the manganese concentrations in different samples. In neutron activation analysis, no reagents are required with minimum sample handling; thus, there is a low chance of contamination with exogenous sources of manganese, although this technique has a drawback: its low detection limit in biological tissues (4 ng/g) and but have high accuracy. Other methods by which manganese concentration is determined include mass spectrometry and X-ray fluorimetry. XANES and XAFS spectroscopy have been used the detect the presence of manganese- discharged from automobile exhaust containing MMT, Gas chromatography combined with laser-excited atomic fluorescence spectrometry (LEAFS) analyze Mn in range for different organo-manganese species is 8–20 pg while in MMT, it is 0.4 ng/ml (ATSDR (Agency for Toxic Substances and Disease Registry) 2012).

4.3.8 Nickel

Electrothermal atomic absorption spectrometry (ET-AAS), ICP-AES, or ICP-MS (detection limit of 5 ng/sample) was used to analysis of nickel in the air, which is absorbed on cellulose ester membrane filters (Templeton et al. 1994a). Presently, ET-AAS is the most popular technique to determine nickel in biological materials with detection limits of 0.4 mg/l for urine and 0.05 μg/l for serum (Templeton et al. 1994b; Sunderman 1993). The quantitative test (European Standard EN1811) for nickel ion release was used to detect the nickel concentration measured by AAS or ICP-MS (Genchi et al. 2020).

4.4 Physiological Investigation

Electrocardiography, respiratory function tests, electroencephalography, hematological test, and nerve conduction studies are examples of probable tests to diagnose the toxicity of specific heavy metals. The common symptoms in acute and chronic heavy metal toxicity are nausea, vomiting, loss of appetite, stomach cramps, constipation, sleeping problems, fatigue, mood swings, headache, joint/muscle aches, anemia, nervous system problem, genitourinary system problem, hyper-keratinization, wart formation, dermatitis, vasospastic, lung cancer, conjunctivitis, peripheral neuropathies, encephalopathy, laryngitis, bronchitis, rhinitis, blood-forming system problems, etc. Based on the symptoms that appear, physicians suggest suitable physiological investigation(s) identify the metal toxicity.

4.5 Indicators and Markers Used for the Detection of Metals

Biomarkers represent processes of the cellular or biochemical molecules or activities, structures, or functions (including neurobehavioral) quantify for any biological system and system contain indicator-signaling events. The change in any stage of a particular fundamental pathway can be used as a biomarker for exposure to the specific toxic compound. Preferably, biomarkers should be specific, profound, and non-invasive for the xenobiotic, which will be assessed. In the risk assessment, biomarkers perform an essential role by reducing the overall improbability (Branco et al. 2017).

4.5.1 Arsenic

Urine, blood, nails, and hair are the major human specimens used to estimate the internal dose of arsenic exposure. Upon ingestion, the inorganic-As (i-As) is rapidly converted into monomethylarsonic acid (MMA) and DMA inside the human body,

which are the end metabolites and excreted in the urine. Urinary arsenic concentration is a commonly used biomarker for short-term as well as long-term exposure (Tchounwou et al. 2004; Davis et al. 2017). For detecting long-term i-As exposure, human nail and hair have been widely taken as biomarkers. The unmetabolized i-As can bind with negative sulfhydryl-groups found in keratin-rich tissues. However, the quantification of total As in hair and nails (that represents primarily i-As) is possibly less sensitive than arsenic measured in urine (Slotnick and Nriagu 2006).

4.5.2 Lead

Lead disturbs numerous enzymes or processes accountable for heme synthesis, such as ferrochelatase, an intramitochondrial enzyme, which chelates the iron with protoporphyrin. In the case where Fe are unable to bind with protoporphyrin ring ultimately results in a formation of defective heme and an elevated level of this defective protoporphyrin chelates Zn instead of Fe. And due to the high level of Zn, at last, zinc replaces Fe and produces Zn-protoporphyrin. Lead also directly lowers or blocks the activity of some cytoplasmic enzymes like δ-aminolevulinic acid dehydratase (ALAD) and coproporphyrinogen oxidase. This will leads to alterations of some other metabolite concentrations in urine (ALA-U), blood (ALA-B), and plasma (ALA-P), coproporphyrin (CP) in urine. It is also seen that the activity of pyrimidine nucleotidase (P5´N) and nicotinamide adenine dinucleotide synthase (NADS) is altered in the blood after lead exposure. So, all these enzymes and metabolites are treated as a biomarker for lead toxicity (Barbosa et al. 2005). The most common and exact method of evaluating Pb exposure is the analysis of lead in whole blood. The amount of Pb in the blood imitates the current exposure type. Bone lead quantity is an indicator of cumulative exposure while quantifying the urinary and hair lead levels is also used to measure the Pb exposure, but they are not consistent (ATSDR 2019b).

4.5.3 Mercury

German toxicologists proposed using 2,3-dimercaptopropane-sulfonate (DMPS, as a chelating agent) as a biomarker for chronic mercury retaining and toxicity. They suggest that a tenfold rise between the pre and post urinary Hg levels or a post urinary level is more than 50 μg of DMPS, indicating an unusually elevated mercury burden. Both intravenous and orally administered DMPS is useful in vivo biomarkers for mercury accumulation (Godfrey et al. 2003). Nowadays, the total Hg levels in hair, urine, and blood are used as the most common biomarker in the absence of speciation analysis. For Me-Hg exposure, the mercury concentration in hair is a specific biomarker, while hair mercury levels are not considered for exposure to Hg^0 as the Hg^{2+}. The urine-Hg concentration (U-Hg) is the most suitable biomarker to determine inorganic mercury exposure (Hg^0) both in occupational exposures and in dental amalgams. At the same time, U-Hg levels are not considered for evaluating

Me-Hg exposure. The mercury concentration in the blood (B-Hg) is also considered a reliable biomarker of mercury exposure. But it has limitations due to short mercury kinetics in blood, and this biomarker is only valid for acute exposure or continuous (chronic) exposure. Selenoprotein (such as TrxR and GPx isoforms) is also considered among the acceptable biomarkers in Hg toxicity because of its promising endpoints in noninvasive biological samples (Ye et al. 2016; Branco et al. 2017).

4.5.4 Cadmium

To detect cadmium exposure, blood, urine, feces, liver, kidney, hair, and other tissues have been used as biomarkers. Blood Cd concentration is primarily suggestive for current exposure(s) to Cd either than whole-body burdens. Because the gastrointestinal tract poorly takes up dietary Cd, fecal Cd is a direct indicator of regular nutritional consumption of cadmium. Labors exposed to Cd by inhalation, fecal-cadmium were used to estimate the quantity of inhaled Cd transported to the gastrointestinal tract, and the amount of dust consumed incidentally at work. Cadmium levels in hair are also used to track the Cd exposure, even though due to the possibility of exogenous contamination, it creates confusion on the reliability of cadmium level in hair as a measure of absorbed dose. Metallothionein concentration may also be used as a biomarker of Cd exposure. In highly exposed workers, the raised level of metallothionein was detected in peripheral blood lymphocytes (ATSDR (Agency for Toxic Substances and Disease Registry) 2012). Urine cadmium is also used as a prominent biomarker for detecting acute and chronic cadmium exposure levels. β_2-microglobulin (BMG) and human complex-forming glycoprotein have been extensively used as a marker of tubular renal dysfunction caused by Cd exposure. N-acetyl-β-glucosaminidase (NAG, a lysosomal enzyme present in the proximal tubule) correlates with urinary cadmium levels as renal biomarkers in occupationally, and environmentally Cd exposed subjects (ATSDR (Agency for Toxic Substances and Disease Registry) 2012; Wu et al. 2016).

4.5.5 Chromium

The measures of different biological means, such as urine, plasma, erythrocytes, lymphocytes, exhaled breath condensate, etc., have been used as a biomarker of chromium exposure. For internal chromium exposure, the examination of urine-Cr (u-Cr) is helpful to measure the short-term high-level exposures of Cr(VI) in the workplace. Because in the bloodstream, the absorbed Cr(VI) can quickly enter into blood cells and inside it rapidly reduced into Cr(III) and stuck inside by binding with plasma protein. At the same time, the unbound Cr(III) is quickly evacuated in urine as cell membranes are impermeable to Cr(III). The biological half-life of u-Cr is very short, so it mainly imitates the maximum recent exposure and total chromium excretion in urine. Still, it does not use for the measurement of combined or cumulative exposures. It was found that the u-Cr concentration of 40–50 μg/l

chromium in urine resembled an approximate 50 μg Cr/m^3 workplace exposure. In erythrocytes, chromium levels were determined by graphite furnace AAS, and the detection limit was 0.3 μg/l (Qu et al. 2008; NIOSH 2013). The concentration levels of specific proteins and enzymes in the urine of workers may indicate the early effects of Cr(VI) exposure. Urinary β_2-microglobulins (β_2M) and urinary N-acetyl-β-glucosaminidase (NAG) were used as a marker in the worker who works in the field of hard-chrome plating, nickel-chrome electro-plating and, anode-oxidation (NIOSH 2013).

4.5.6 Copper

Altered copper levels can eagerly be measured in tissues, body fluids, and excreta. Elevated levels of copper in serum, urine, hair, and liver were found depending on the dose, exposure duration, and route of exposure (inhalation and oral). An elevated Cu level of whole blood (1.5–twofold) and serum Cu (1.5–threefold) concentration have been seen in humans after deliberately taken a single dose of 1–30 gm of Cu as $CuSO_4$ comparison to a non-exposed person. Copper levels in hair and nails can also be used to determine Cu exposure. In Cu toxicity, the liver is also affected by alterations in several serum enzymes, including serum aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase. An increase in serum bilirubin levels has also been detected in humans (ATSDR (Agency for Toxic Substances and Disease Registry) 2004).

4.5.7 Manganese

Anjum et al. (2019) studied the butyrylcholinesterase (BChE) activity in a blood sample of a subject in Bangladesh where they were exposed to manganese by contaminated drinking water. BChE is mainly activated in white matter, glia, and neurons in the human brain areas, which play a significant role in cognition and behavior. Therefore, BChE effectively controls the cholinergic system, and chronic manganese toxicity selectively affects the cholinergic mechanism of the central nervous system. Anjum and co-worker (Anjum et al. 2019) found a minor level of blood BChE activity and propose that continued drinking of Mn-contaminated water is related to decreasing plasma BChE activity. Pre-symptomatic neurochemical changes also occur after manganese exposure, which has been quantitated by magnetic resonance spectroscopy. It is found that workers exposed to airborne manganese, having doubled GABA (γ-aminobutyric acid) concentrations in the basal ganglia and thalamus. Another biomarker for airborne manganese exposure is the Mn: Fe ratio in RBCs and plasma; it associates with airborne manganese concentrations and with neurobehavioral changes. In occupationally exposed subjects, bone manganese concentrations were also found significantly higher than in nonexposed subjects (Livingstone 2018; Zheng et al. 2011; Hassani et al. 2016).

4.5.8 Nickel

Urine and feces are the main route where nickel is excreted, depend on its exposure route and chemical state. Nickel concentration in urine and serum consider as a biological indicator of industrial, environmental, and iatrogenic exposures to nickel compounds. Occupationally nickel exposed subjects have high nickel concentration in serum and urine than that non-occupationally exposed subject. Due to its short biological half-time present nickel concentrations in serum represent mainly recent exposure. If nickel is released into urine, it shows more prolonged nickel exposure and shows greater concentration than serum (Cempel and Nikel 2006). Higher levels of nickel oxide and sulfide in working air produce a comparatively low nickel concentration in plasma and urine than a corresponding level of soluble chlorides or sulfates exposed. Still, it shows a high concentration in the nasal mucosa and the lungs (Torjussen and Andersen 1979).

5 Therapeutics and Preventive Control of Metal Toxicity

5.1 Preventive Measures for Metal Uptake

Through the skin or mucosal absorption, breathing, and ingestion, toxic metal assimilates into the human body. Occupational exposure generally results in absorption after inhalation. The victims of high-level inhalation contact should be eradicated from the polluted environment without any delay. Several volatile metal compounds like mercury, stibine, arsine, alkyl tin, and modified metal compounds such as alkylmercury and alkyl lead may cause an emergency. These metals cause skin-related disease, and to minimize or avoid such risk, the contaminated belongings should be removed as soon as after exposure to lipid-soluble metal compounds, followed by decontamination of hair and fingernails. The contaminated body part should be thoroughly washed with cold water profusely. In chronic metal poisoning, the affected person should be quickly detached from the polluted area to avoid further exposure. In some cases, like mild poisoning after lead dust exposure or fumes, the worker may need to remove the contaminant through standard excretory mechanisms rather than therapy for recovery from mild toxicity. By assessing different absorption routes in a person, the risk of exposure by contaminated food and drink or clothing should be considered. Consumption of any food and drink at the work site should be strictly banned. The shower and changing room facilities for complete change should be provided after each shift (Järup 2003; Gupta and Gupta 2011).

5.2 Elimination of Absorbed Toxicants

5.2.1 Elimination from the Gastrointestinal Tract

In conscious patients, the stomach can be emptied to recover toxins by inducing vomiting within 4 h of ingestion. Pharyngeal stimulation and ipecacuanha emetic mixture are used to induce vomiting. The practice of gastric lavage is performed by skilled medical personnel in an equipped emergency unit. A cuffed endotracheal tube is to be lined first to protect the lungs in specifically unconscious patients (Gerhardsson and Aaseth 2016).

5.2.2 Diuresis

In diuresis, the unreceptive reabsorption in the proximal renal tubules of the kidney is decreased to remove toxins. Diuresis is performed by giving fluids combined with an osmotic compound like mannitol or through furosemide like a diuretic agent. The urine pH affects the excretion of some toxins because amplified ionization of the solute in the tubular fluid makes passive tubular reabsorption less effective. This method has limitations in metal poisoning; however, if a high movement of urine is maintained, excretion of the toxic metal fastens, which is also seen in acute poisoning by inorganic mercury and lead (Gerhardsson and Aaseth 2016).

5.2.3 Biliary Excretion

The prolonged presence of some toxic metals enters into enterohepatic circulation, where it is excreted into the bile due to the high concentration followed by intestinal reabsorption. The complex-forming agent bound with the metal compounds and defecated in the bile is given orally to avoid the reabsorption and thus improve the fecal elimination of the heavy metal compounds. The study has shown that adding this complex-forming compound like synthetic polystyrene resin with immobile sulfhydryl (-SH) in the diet at 1% concentration doubled the methylmercury excretion frequency from mice and also dropped the concentration in blood and tissue as compared with untreated controls. Similar studies in humans were also found by using these synthetic compounds that show the blood mercury levels were decreased and the fecal excretion of methylmercury was increased (Bakir et al. 1973; Ballatori and Clarkson 1985).

5.2.4 Dialysis

Toxic metals that do not bind to tissue irreversibly are removed by hemodialysis more efficiently than diuresis; however, metal ion content is low in the dialysate.

Metals like arsenic, copper, lead, lithium, magnesium, mercury, sodium, and zinc are dialyzable, and this practice is done when the subject took a possibly lethal dose, the clinical condition is worsening despite comprehensive treatment by other resources, and still, a problem like renal insufficiency exists. Peritoneal dialysis is one of the methods used when hemodialysis is not accessible. In verst case of acute inorganic mercury poisoning, DMPS is given followed by hemodialysis to remove the extract complex (Hsiao et al. 2019). When the toxic material is tough to dialyze, the exchange transfusion may be performed in the severe poisoning case. These compounds persist in the bloodstream in substantial amounts (Jagannati et al. 2016).

5.3 By the Deactivation of the Absorbed Toxin

Gastric lavage involves the channel is formed by the large orogastric tube with sequential administration and aspiration of small volumes of normal saline (10 ml/kg in a child; 200–300 ml in an adult), and subsequently the toxic constituents present in the stomach is removed. However, it may be caring for patients with a dangerous quantity of metal ingestion occurring within 60 min of evaluation whose airway is protected. Specific antidotes can inactivate some poisons (Christophersen et al. 2002; Mane and Patil 2017). However, treatment with lavage should not be late if the specific antidote is not available. The egg white or milk can also help inactivation of heavy metals like mercury and partially precipitation in the stomach. Activated charcoal has also been found effective for absorption of many poisons that persist in the stomach and disturb the enterohepatic circulation; the maximum dose of 50 gm is recommended at an interval of 20 min and in the dose of 5–10 gm in the form of thick suspension. A higher dose may persuade vomiting. The use of activated charcoal in iron poisoning is found futile (Zellner et al. 2019).

A very small and limited number of therapeutic agents (antidots) are reported for the human who might be given to overcome the effect of the toxic metal. These antidotes perform in the following ways:

- It might be interacting with the target toxic metals and convert it into the less harmful form or completely neutral antidot-metal complex, which might be quickly and effectively excreted in the urine;
- It can also compete with the toxic metal for attaching with their respective ligands. It can remove metals from its ligand site, or it may transport/relocate the toxic metals in a place inside the tissue, where it cannot show their poisonous effects. It was found that when the calcium gluconate intravenous administration, it will relocate the lead from its affected site and relieve for a slight period from the intense colic pain (Mayel et al. 2020).

5.4 Chelation of Metal Toxins

Chelating agents or chelators are those organic or inorganic compounds that can bind with metal ions (Na^+, Mg^{2+}, Cu^+, Cu^{2+}, and Zn^{2+}) and transition metals (like Mn, Fe, and Co) and form a ring-like structures complex. Ideal chelators are highly soluble in water, resistant to bioconversion, possess the capability to act on the metal deposition sites, the potential to keep chelating ability at the different pH of body parts, and the capacity to bind metals to form less toxic metal-chelator complexes than the free metal ion (Flora and Pachauri 2010). The fundamental concept behind the chelation is the chelating agent should have high-affinity electron donor or acceptor groups, so that specific metal which is likely to be removed, are easily bind. And after binding, the metal-chelating agent complex breaks with proteins or other endogenous ligands so that it can easily be excreted from the body. The chelating agent should also form a complex with the toxic metal in humans with high stability instead of essential metals for humans such as iron, calcium, zinc, or copper or relocate the poisonous metals to other tissues (e.g., the brain). A less toxic species which are formed after effective chelation may efficiently excrete; its efficiency relay on the physicochemical properties of metals and chelators, like the ionic size of metal, the ring structure of the metal-chelator complex, complex size and 3D structure, nucleophilic or electrophilic nature, the path of administration, availability to the cell, absorption, and metabolism, intra/extracellular localization and distribution in the target tissue and excretion. The chelating agent can show its most effective capability when the metals are still in the circulatory system or the extracellular fluid space because the intracellularly heavy metals are less reachable. Different chelating agents are available, in an ionized form and, so they have the very partial capability to cross the plasma/cell membranes (Andersen and Aaseth 2002; Lindsay and Kerr 2011). Some commonly used therapeutic chelating agent with their chemical formula and generic name is given in Table 1.

5.4.1 Dimercaprol

Dimercaprol is a commonly used chelator that acts as a precise antagonist for the treatment of Lewisite (vesicant arsenical war gases). Chemically, it is a dithiol compound that competitively binds to the protein sulfhydryl moiety of especially arsenic compounds and other heavy metals and forms a stable chelate. It is also effective against inorganic mercury, antimony, bismuth, and gold. In acute lead encephalopathy and increased intracranial pressure, dimercaprol treatment is reported with calcium EDTA. And the orally and intramuscular injection treatments were reported. It has a very short half-life (4 h). The patient with impaired renal function should be given a lower drug dosage. It will reduce the alkaline nature of urine during therapy, and acidic condition helps in the dissociation of the dimercaprol-metal complex. In some subjects, dimercaprol has been reported to produce minor side effects, while sometimes critical effects were seen by administering the full dose (Amadi et al. 2019a).

Table 1 List of some common chelating agents

Sr.no	Chelating agent	Generic name	Chemical formula	Metals
1	BAL (British anti-Lewisite)	2,3-Dimercaptopropanol	$C_3H_8OS_2$	Arsenic, Mercury, Lead, Gold
2	DMSA	meso-2,3-Dimercaptosuccinic acid; succimer	$C_4H_6O_4S_2$	Arsenic, Mercury, Lead
3	DMPS	2,3-Dimercaptopropane-1-sulfonic acid	$C_3H_8O_3S_3$	Arsenic, Mercury
4	$CaNa_2EDTA$	Edetate calcium disodium; sodium calcium edentate	$C_{10}H_{12}CaN_2Na_2O_8$	Lead, Calcium
5	Deferoxamine	Desferrioxamine	$C_{25}H_{48}N_6O_8$	Iron, Aluminum
6	Penicillamine	D-penicillamine	$C_5H_{11}NO_2S$	Copper

Dimercaprol is not used in the cadmium and mercury (aryl and alkyl) compounds poisoning. Dimercaprol is now considered only for temporary treatment of acute toxicity due to its side effects (Andersen and Aaseth 2002). Dimercaprol shows some significant drawbacks, like painful intramuscular injection, less safety, and proneness to relocate the arsenic to the brain (Flora and Pachauri 2010).

5.4.2 Sodium 2,3-Dimercaptopropane-1-Sulfonate (DMPS)

Sodium 2,3-Dimercaptopropane1-Sulfonate (DMPS), a chemical analog of dimercaprol, is a water-soluble and effective chelator for certain heavy metal poisoning. It shows less toxicity than dimercaprol. Some allergic adverse effects have been seen. DMPS offers efficiency in accelerating metal excretion in the case of acute and chronic toxicity produced by organic and inorganic mercury, arsenic, and lead, without producing any adverse health effects (Kim et al. 2019). DMPS can circulate not only in extracellular spaces but also in intracellular spaces. Humans biotransformed it into the cyclic and acyclic disulfides during its metabolism and are rapidly removed from the kidney. DMPS has effectively worked against several arsenic compounds' lethal effects and is reported for reducing both arsenic toxicity and regenerative spread of the bladder epithelium in rats (Suzuki et al. 2012). In West Bengal, chronic arsenic intoxication affected millions of people due to arsenic-contaminated water (Guha Mazumder and Dasgupta 2011). So, the treatment of DMPS in combination with a protein diet reported signs of reduction in affected subjects. The Soviet Union and Eastern Europe used DMPS against chronic lead poisoning. DMPS is effective against alkylmercury toxicity and inorganic mercury poisoning caused by mercury vapor inhalation and the ingestion of mercuric oxide. It is active increases

the mercury excretion from the kidney (Dargan et al. 2003). The studies in a gold-mining area in the Philippines show that an oral dose of DMPS positively affects mercury intoxication with significant improvement in symptoms like loss of memory, sleeplessness, metallic taste in the mouth, and fatigue and anxiety (Sears 2013).

5.4.3 Meso-2,3-Dimercaptosuccinic Acid (DMSA)

The chemical analog of dimercaprol, also known as "succimer," is the least toxic of the chelators. The drug binds to about 95% plasma protein where it binds with cysteine reside of albumin from its one side of sulfhydryl groups and leaving the other side for the chelate metals (Bjørklund et al. 2017). DMSA is quickly removed through the urine. DMSA also decreases the collection of both Pb and Me-Hg in the brain (Sears 2013). DMSA is less harmful than DMPS, and it is a frequently used antidote for lead toxicity in pediatric cases (Kim et al. 2015). The lead deposition in bone is also removed by the repeated chelation therapy where DMSA is useful. Some adverse effects were seen in lead toxicity treatment through DMSA, GI uneasiness, skin allergies, slight neutropenia, and hepatic enzyme concentration (Aaseth et al. 2018). Many studies demonstrate the efficiency of DMSA to bind and mobilize mercury in several animals (Aposhian et al. 1984). DMSA can also be applied against inorganic and organic mercury toxicity (Risher and Amler 2005).

5.4.4 DMSA Analog

Several new synthetic analog compounds like monoisoamyl DMSA (MiADMSA), monocyclohexyl DMSA (MchDMSA), and monomethyl DMSA (MmDMSA) has been derived from DMSA and successfully tested for their metal-binding ability. Some of these analogs also demonstrate better excretory efficiency than DMSA (Kim et al. 2019). MiADMSA is a water-soluble C5-branched chain alkyl monoester of DMSA. It is lipophilic, which allows it to cross the plasma membrane and go into the intracellular space to remove heavy metals. Current research has shown arsenic, lead, cadmium, and mercury are chelated by MiADMSA (Flora et al. 2008). MchDMSA is a cyclic carbon chain analog of DMSA, while MmDMSA contains straight and branched-chain methyl groups. Its lipophilic nature allows penetration inside the cells. MchDMSA and MmDMSA can be taken up by mouth, and studies on animal models showed that combination therapy of both agents reduces cadmium and arsenic levels significantly (Flora et al. 2011; Yadav et al. 2014).

5.4.5 Edetate Calcium Disodium EDTA

Calcium disodium EDTA salt ($CaNa_2EDTA$) is a derivative of EDTA that potentially chelates many divalent and trivalent metals in vitro. The $CaNa_2EDTA$ (or calcium EDTA) has been used as a therapeutic agent in lead poisoning. It will bind to lead and

displacing calcium from the chelator resulting in excretion of $PbNa_2EDTA$ complex from the body, leaving calcium behind. It also shows the dangerous toxic effects due to the chelation of essential metal, so it is mandatory to monitor its administration carefully. Calcium EDTA is weakly taken up from the gastrointestinal tract (<5%); therefore, intravenous administration is preferred. Its movement is mainly in the extracellular fluid and excreted by glomerular filtration quickly and is completely excreted within 24 h. The main toxic effect is on the kidney. Calcium EDTA may reallocate the lead to the brain after acute or chronic lead exposure (Kim et al. 2019). Several side effects like lacrimation, nasal congestion, mucocutaneous lesions, glycosuria, hypotension, and electrocardiogram irregularities are also seen during its treatment. Long duration treatment of calcium EDTA results in a reduction in trace metal due to specifically removing zinc. After a high dose of calcium EDTA, excessive chelation of essential metals was seen; thus, many adverse side effects arise in a concise duration, so DMSA now substitutes calcium EDTA against lead poisoning (Aposhian et al. 1995).

5.4.6 Penicillamine

Hydrolytic degradation of penicillin results in its dextro-rotatory isomer d-penicillamine or β,β-dimethylcysteine (Cuprimine), which works as a potent chelating agent for metals like Cu, Fe, Pb, Hg, etc. by increasing their elimination in the urine. In the case of inorganic mercury toxicity, N-acetyl-dl-penicillamine derivative was found more potent than d-penicillamine (Aposhian et al. 1995) because penicillamine is very well take up from the GI tract; in fact, 50% is absorbed orally and within 1 and 4 h maximum concentration was found in plasma. It also has a short half-life in the body (about 1–7 h) and is extracted in urine without any change. It also shows some adverse effects like fever, skin rashes, blood dyscrasias, renal tubular damage, and urine-related problems. During the treatment, the urine is examined for protein traces regularly, and a complete blood examination, including platelet count, is also performed. The mode of action of penicillamine is still to be decipher (Habib et al. 2006).

5.4.7 Tetraethylenetetraamine

In acute copper intoxication, tetraethylenetetraamine (TETA; trientine) is the preferred drug. The gastrointestinal absorption of TETA is poor, and the route of administration is oral. The two metabolites of TETA N_1-acetyltriethylenetetraamine (MAT) and N_1N_{10}-diacetyl triethylenetetraamine (DAT) perform an important role in the chelation of copper from the body. The drug is mainly excreted in urine as metabolites. The recommended dosage for the treatment is 0.75–2 gm/day (Flora and Pachauri 2010).

5.4.8 Deferoxamine (DFO)

DFO is the most suitable chelating agent for iron toxicity because it has a significant affinity for trivalent iron in other metals. DFO is administered by the subcutaneous, intramuscular, or intravenous route (most effectively other than two). Orally given DFO chelates remaining iron in the lumen and convert it into nonabsorbable form for the body, and thus it is nontoxic. Formed ferrioxamine complex is easily extracted from the body through urine. DFO is administered by slow intravenous infusion, and also gastric lavage may be performed. The DFO should be used carefully in patients who have weak renal function (Britton et al. 2002; Neufeld 2010).

5.4.9 Sodium Diethyldithiocarbamate (DDC)

Sodium diethyldithiocarbamate (DDC) chelating agent is mainly used for removing acute nickel carbonyl poisoning. DDC potentially removes the nickel from the body by increasing nickel evacuation in the urine (Elder et al. 2015). DDC can be administered orally in moderate to severe nickel poisoning. DDC is converted into ethylamine and carbon disulfide by the action of gastric juice, so the administration of sodium bicarbonate overcomes this reaction. The nickel toxicity in the lungs is reduced by the formation of lipophilic chelates with DDC and divalent nickel. However, due to its lipophilic nature, the complex also shows a high affinity toward lipid-rich brain tissue, thus also one of the causes of increased nickel concentrations in the brain. (Karimov et al. 2020).

5.4.10 Combinations Therapy of Chelating Agents

Co-administration of EDTA and dimercaprol is the most effective combination than EDTA alone, to treat acute lead toxicity where blood lead levels >10 μg/ml. To avoid relocation of chelated lead inside the brain tissue, dimercaprol should be administrated intravenously before 4 h of EDTA. It was also seen that DMSA and $CaNa_2EDTA$ combination in the treatment of chronic lead toxicity show more effective removal of the lead from the body and also show an improvement in transformed lead sensitive biochemical parameters (Flora et al. 1995). Combined treatment of DMSA and monoisoamyl DMSA (MiADMSA) has been found to efficiently decrease the arsenic-induced oxidative stress and decrease the arsenic load from the blood and soft tissues (Mishra et al. 2008). Recent studies stated that combined treatment of $CaNa_2EDTA$ and MiADMSA act against lead toxicity by shifting neurotransmitters' levels, which result in the induction of neurobehavioral changes (Flora et al. 2008). In lead poisoning, the combined treatment of DMSA with α-lipoic acid improves oxidative damage (Flora et al. 2003). Co-administration of MiADMSA (with thiol moiety) and antioxidants show improved efficiency against chronic arsenic intoxication. The Combination of vitamin E with DMSA/MiADMSA demonstrates improved results and decreases oxidative stress by diminishing lipid peroxidation

(Adonaylo and Oteiza 1999). This chelating agent combination therapy helps to reduce the duration and dose amount during the treatment resulting decrease in side effects and offers well clinical recoveries.

5.5 Antidote Therapy (Natural Antioxidants)

In chelation therapy, specific metal chelators have been used, which is the basis for the treatment of heavy metal intoxication. However, due to its several disadvantages, there is a need for search of any natural replacements. Different types of supplements, foods, and phyto-antioxidants from nature are identified to alleviate metal poisoning. They can serve as antidotes in developing nations and suit constraints like affordability, availability, and almost negligible side effects. Natural antioxidants may serve as a defensive measure in contrast to chronic and acute heavy metal intoxication and act as a new area for the future research and development of new antidotes with minor side effects (Amadi et al. 2019b).

5.6 Alternate Therapy for Heavy Metal Poisoning

Plasma exchange/plasmapheresis procedures can be preferred as replacement therapy in an emergency case due to high metal toxicity. Few studies have publicized that plasma exchange is most effective for removing inorganic mercury when applied in combination with chelation therapy but in the early phase of intoxication. The hemodialysis has been performed to treat mercury toxicity but was found to be ineffective (Nenov et al. 2003). In induced sweat, known as sauna therapy, where sweating is likely to be induced is a natural phenomenon to excrete toxins. The studies have demonstrated the elevated concentration of Cd, Ni, Pb, Al, Mn, and Co in sweat. Future studies should discover clinical health outcomes of induced sweating programs in patients with metal intoxication (Genuis et al. 2011).

6 Summary and Conclusion

Heavy metals naturally occur in the earth's crust and are essential for numerous modern industrial and economic development; humans are directly involved in their exploitation. All these heavy metals create a direct or indirect impact on the human body. They play an important functional role by driving various physiological and biochemical activities in the body or produce adverse side effects by altering these processes. In humans, heavy metals like arsenic, lead, cadmium, mercury, chromium, manganese, and nickel can produce euphoric effects in the human body, causing acute and chronic toxicities. There are different mechanisms present by which these

heavy metals cause generate neurotoxicity, inflammation, and free radicals, which promote oxidative stress, damaging lipids, proteins, and DNA molecules. Further, these generated free radicals propagate into carcinogenesis. Acute or chronic heavy metal toxicity leads to several organs such as the brain, lungs, liver, and kidney, damage or failure and causing different diseases in humans. Symptoms regarding heavy metal toxicity may begin after a few hours, can be non-specific, and are not easy to interpret at first glance. Different biochemical and biomarker tests are helpful in the diagnosis of acute and chronic exposure to heavy metals. Chelating agents, gastric lavage, and oral doses of other chelators are helpful procedures in reducing metal toxicity in humans.

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The Scope for Early Diagnosis of Noise-Induced Hearing Loss Among Mine and Industrial Workers: A Brief Review

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1 Introduction

Noise-Induced Hearing Loss (NIHL) is a widespread occupational disease associated with mine workers and various other occupational settings where there is high-intensity exposure to noise. These occupations are printed materials, metal products, railways, aerospace sites etc. NIHL is classified as a notified disease under the Mines Act, 1952 and Factories Act, 1967 and is categorised as a major occupational disease in India along with silicosis, Coal worker pneumoconiosis, lung disease by International Labour Organization (ILO). It is a type of sensory deficit that is caused by exposure to loud noise for many years and leads to bilateral and symmetrical Hearing Loss (HL) (Mcbride 2004). According to the National Institute of Occupational Safety and Health (NIOSH), the United States, the maximum permissible noise level in a shift of 8 h for unprotected ear is 85 dB(A) (decibel in A-weighting) while Occupational Safety and Health Association (OSHA) has given 90 dB(A) as max permissible noise exposure limit (Mahdieh et al. 2012; Chepesiuk 2005). NIHL causes irreversible permanent changes in the ear but it can be preventable. A minimum exposure period of one to five years can lead to the development of NIHL, however, if the magnitude of the noise is too high above 96 dB(A) for eight hours, NIHL can

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_8

occur at an early period. It is usually detected by the Pure Tone Audiometry (PTA) technique where the audiometric notch is usually observed at 4 kHz which recovers at higher frequencies. However, the notch at 6 kHz is also considered as NIHL notch (McBride and Williams 2001).

Noise is considered as the second most common environmental pollution which is known as an 'unwanted sound' and it is measured in A-weighted Sound Pressure Level (SPL). SPL or acoustic pressure level is a logarithmic measure of an effective pressure of a sound relative to a reference value which is measured in decibel dB(A). High-intensity noise occurs in a wide range of workplaces, including manufacturing industries for food, printed materials, metal products, pharmaceutics, ceramics, machinery factories and the mining sector. Noise prone workplaces have a heavy health impact on the auditory sensation of workers around the world. Millions of healthy lives become partially or fully deaf due to occupational NIHL (McBride and Williams 2001; Jain et al. 2018).

1.1 Symptoms of NIHL

NIHL symptoms can be subtle and practically unnoticeable at an early stage but the damage could be worse and become irreversible and permanent if left unchecked (McBride and Williams 2001).

- Struggle to hear and understand conversation in a noisy environment.
- The sufferer can't pick up on normal household sounds.
- Telephone conversation becomes increasing difficult for understanding.
- The sufferer can't hear properly when their back is turned away from the noise.
- Experience of tinnitus i.e. ringing, buzzing or fluttering in one or both of the ears.
- Interpretation of sound becomes difficult for the person.
- Ear discomfort after exposure.
- Loss of sensitivity i.e. temporary or permanent threshold shift.

1.2 Health Hazards Caused by Exposure to Noise

Exposure to noise may lead to severe health complications which include sleeplessness, deafness, communication problem by speaking loudly or shouting even in normal conversation, speech blurring, mental and physical deterioration in health. Following are the major health hazards caused due to noise exposure to high frequency for a short duration or at low frequency for a long time (Ryan et al. 2016; Wang and Puel 2020).

1.2.1 Temporary Threshold Shift (TTS)

TTS is defined as an exposure to noise in which ears sensitivity threshold decreases after exposure. This process is referred to as a shift in the threshold of hearing. During short exposure to noise, most people experience a rise in auditory threshold which normally disappears in 24 h but, may last as long as a week. TTS may include intracellular damage in sensory cells, cochlea and swelling of auditory nerve endings. Exposure to noise decreases the sensitivity of auditory sensory cells which is proportional to the duration and intensity of exposure. The decreased sensitivity of auditory sensory cells increases the auditory threshold. In its early stages, this increase in auditory threshold also known as auditory fatigue or TTS is entirely reversible but persists for a certain time after continuous exposure.

1.2.2 Permanent Threshold Shift (PTS)

Exposure to high-intensity sound stimuli over the years may lead to permanent HL. This is referred to as a permanent threshold shift. PTS is characterized by degeneration of hair cells, complete auditory cell destruction and degenerative loss of stereocilia.

1.2.3 Hearing Loss (HL)

The mechanism of HL arises from trauma to degeneration of stereocilia in the cochlea. Continuous exposure to a high level of sound i.e. above 85 dB(A) can lead to permanent HL. Substances like VEGF, nuclear factor, glucose transporter 1 are thought to be the cause of NIHL. The increase in sound intensity causes trauma to the cochlear structure in the inner ear which may result in irreversible HL. The immediate effect of exposure to sudden impulsive high-frequency noise may lead to rupture of the eardrum and traumatic damage to the middle ear.

1.2.4 Age-Related Hearing Loss (ARHL)

HL due to aging is known as ARHL or Presbycusis and it is a combination of alteration in the structure of the inner ear, change in the rate of blood flow to the inner ear and the degeneration of auditory nerve. Presbycusis is typically a high pitched gradual HL that can be noticed by the changes in hearing threshold over a period of time. Common symptoms of Presbycusis include difficulty in hearing and perceiving voices and background noises, with loss in clarity of speech. Aging HL can be worsened by other factors like diabetes, poor circulation, noise exposure and certain medications (More details on Sect. 4).

2 Classification of HL

2.1 Based on the Position of Damage, HL Can Be Characterized into Three Categories (Waleed et al. 2015; Wahid et al. 2020)

- Conductive Hearing Loss
- Sensorineural Hearing Loss
- Mixed Hearing Loss

2.1.1 Conductive Hearing Loss (CHL)

CHL occurs when the sound is not properly transmitted through the auditory system. CHL affects the passage of sounds between the eardrum and the inner ear. It involves in reduction of sound intensity threshold or the ability to hear a whisper or faint sound. This type of HL can be treated medically or surgically.

Causes of CHL

- Fluid in the middle ear due to cold
- Ear infection (Otitis media)
- Poor Eustachian tube function or blockage in the Eustachian tube
- Malformation or absence of the outer ear, ear canal, or middle ear
- Inflammation in the outer or inner ear
- Trauma that leads to injury in the tympanic membrane and/or ossicles
- Allergies/ Drug allergies or use of external reagents in the ear like mustard oil or other oils
- Benign tumors.

2.1.2 Sensorineural Hearing Loss (SNHL)

SNHL occurs due to the inner ear or auditory nerve dysfunction. The inability of hair cells to stimulate the nerve endings or damaged organs of Corti may be the reason for SNHL. It can be mild, moderate or severe including total deafness. Even at audible loud speech, the interpretation of the word is still unclear. This type of HL cannot be corrected by medical or surgical- intervention.

Causes of SNHL

- Genetic factor i.e. HL runs in the family
- Aging
- Head Trauma or neurological disease
- Exposure to loud noise
- Poorly congenital development of inner ear

- Meniere's disease
- Drug-induced Ototoxicity-
- Tumors such as acoustic neuroma
- Prenatal infections such as rubella, cytomegalovirus, herpes virus, toxoplasmosis etc.

2.1.3 Mixed Hearing Loss

When the CHL and SNHL are detected in the same ear then it is known as mixed type HL. The conductive component can be treated by doctors but the treatment of the sensorineural component is more challenging. The causes could be both reasons which are mentioned in CHL and SNHL.

2.2 Classification of HL Based on the Severity

According to the classification by the National Standard Association (NSA) and Ear, Nose and Throat Academy (ENTA) of the United States of America, fall of 25–40 dB(A) is negligible HL, 40–55 dB(A) is soft HL, 55–70 dB(A) is moderate HL, 70–90 dB(A) is severe HL and fall of more than 90 dB(A) is considered as permanent HL. The minimum level of sound pressure that can cause temporary HL is 65 dB(A). Normally, the acceptable limit is exposure to 85 dB(A) for daily 8 h work and with either 3 or 5 dB(A) exchange rate, the period of exposure for every increase of 3 or 5 dB(A) should be halved (Fuente and Hickson 2011; Piatto et al. 2009).

3 Global Scenario of NIHL

Around 10% of the world population work in hazardous levels of noise-causing NIHL which is the second most common form of acquired HL after Presbycusis, with studies showing that people who are exposed to noise levels above 85 dB(A), suffered from NIHL. It affects 1.86 newborns among 1000 around the world of which half the NIHL is due to genetic factors. Nearly one hundred and twenty million people suffer from hearing impairment around the world. It is a worldwide problem in the industry and it contributes to 16% of HL among adults, ranging from 7 to 21% in various sub-regions and higher in developing countries as reported by World Health Organization (WHO) (Jain et al. 2018).

The effects of exposure to occupational noise in all sub-regions are depicted in Fig. 1. A global annual incidence rate of NIHL is 16, 28,000 cases, which means an annual incidence rate of almost two new cases per 1000 older workers. As depicted, South Asia shows the higher prevalence (27%) across the world, whereas the Middle East and North Africa Region has the lowest prevalence rate. It is estimated that from

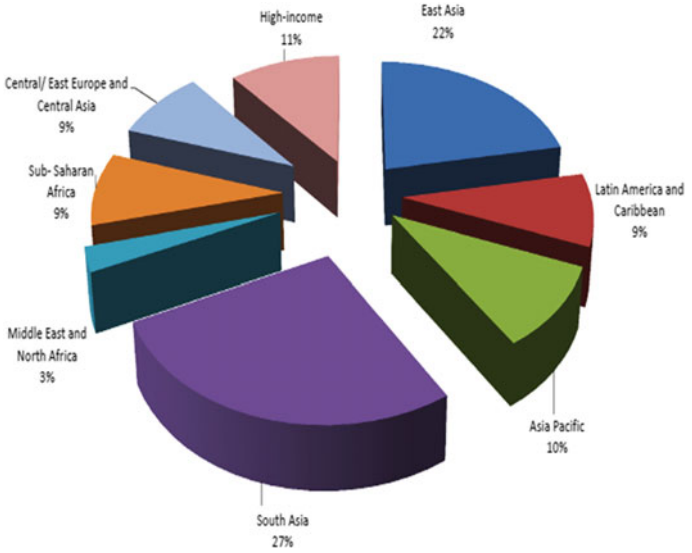

Fig. 1 Pie chart showing disabling HL across the world (Disabling hearing loss adult threshold is ≥ 41 dB, adults of 15 years or older) (*Source* WHO 2012)

2011 to 2031, people with HL would increase from 10 to 14.5 million. As per the estimates of WHO, the current global labour force having deafness is about 2600 million and it is growing continuously. According to statistics, in the year 2018, HL was detected among 466 million people around the world and by 2050, 900 million people will be suffering from HL (Jain et al. 2018; Manar et al. 2019; Global estimates on prevalence of hearing loss. Mortality and Burden of Diseases and Prevention of Blindness and Deafness 2012).

Asia is the largest and populated continent in the world. Its population is estimated at four billion people, representing 60% of the world's current human population. NIHL in Asia shows a complex scenario due to the industrialisation and economic growth of many developing countries. The workers of mining, construction, printing, crushers, drop forging, iron and steel companies are highly vulnerable to NIHL (Fuente and Hickson 2011; Singh 2012).

In India, it is reported that Occupational Permissible Exposure Limit (OPEL) for 8 h Time Weighted Average (TWA) is 90 dB(A) according to DGMS (Directorate General of Mines Safety) technical circulars. Major industries responsible for excessive noise intensity exposure are shown in Table 1. According to the survey conducted by National Sample Survey Office (NSSO) in the year 2002, 291 persons per one lakh have a hearing disability in India while according to a recent report in Feb 2020 by Central Pollution Control Board (CPCB) New Delhi, *Chennai city* is the noisiest among the six metro cities (Singh 2015; Henwasin 2019).

Table 1 An overview of Noise levels in a different area in India

Industries	Range dB(A)
Textile industries	102–114
Pharmaceutical firms	93–103
Oil and natural gas complex in Bombay high	90–119
Road traffic in Ahmedabad city	60–102
Surface rail traffic	90–102
Metro rail	70–111
Air traffic	90–112
Fertilizer plants	90–102

4 Factors Contributing to the Development of NIHL

The factors contributing to NIHL disease conditions are environmental factors, genetic factors and many other factors like ototoxic drugs, chemical toxicity and even age of an individual act on to make the condition of NIHL even worse. An overview of these factors is described below.

4.1 Environmental Factors

Among the environmental factors, noise intensity is the main cause of HL. The construction and mining industry workers experience high exposure to environmental noise compared to other industrial units. Exposure to noisy mining operations during heavy metal extraction work worsens the condition of auditory senses in miners (Ohgami et al. 2013).

4.2 Genetic Factors

Genetic susceptibility plays a significant role in the development of NIHL. According to Steyger (2009) congenital HL is often observed by sensory defects among the neonates affecting approximately every third child among the thousand live births (Steyger 2009). The recent study conducted by Zhang et al. (2019) reported that seven genes namely EYA4 (codes for EYA transcriptional co-activator and phosphatase 4 protein), MYO1A (Myosin), CDH23 (Cadherin 23), PCDH15 (Protocadherin related 15), KCNMA1 (Potassium calcium-activated channel subfamily M alpha 1) and OTOG (Otogelin protein of the inner ear) are involved in the development and onset of NIHL (Zhang et al. 2019). The mutation in GSTM1 (Glutathione S-transferase Mu 1) and GSTT1 (Glutathione S-transferase theta 1), CAT (Catalase), SOD1, SOD2 (Superoxide Dismutase) and other oxidative stress genes are also associated with

NIHL. Gap junction proteins such as GJB2 (Connexin 26), GJB3 (Connexin 31), GJB6 (Connexin 30), Potassium voltage-gated channel protein-encoding genes such as KCNE1, KCNQ1, and KCNQ4 which helps in potassium recycling plays a key role in cell to cell communication. Mutation of these genes causes syndromic and nonsyndromic HL (Wong et al. 2013).

Some animal model genetic studies were conducted to find the role of certain genes which causes NIHL. For instance, in mice models study the mutation in the MYH14 gene (which codes for myosin protein) causes autosomal dominant hearing impairment (DFNA4). It has been observed that OHC loss was comparatively higher among MYH14-/- mutated mice than in the wild type (Fu et al. 2016). Heterozygous mutation in the DNMT1 gene (codes for DNA methyltransferase 1 protein) causes Deafness and Hereditary Sensory Neuropathy type IE (HSN1E) which is responsible for bilateral as well as unilateral HL (Kniffin 2015). There are many other genes responsible for HL as per the available database in National Center for Biotechnology Information (NCBI). Information for all such genes can be found in the book titled 'Genetic Hearing Loss and Gene Therapy' authored by Carpena and Lee (2018).

4.3 Other Factors

The other factors which could cause NIHL are **ototoxic drugs**, the age of an individual etc. The ototoxic drugs like high doses of aspirin, loop diuretics, some antibiotics, some chemotherapy drugs, and some anti-inflammatory drugs, antineoplastic cisplatin and bactericidal aminoglycoside antibiotics are responsible for the development of NIHL (Steyger 2009). The clinical signs of NIHL could be:

- The onset of tinnitus in one or both ears.
- Escalation of prevailing tinnitus over a period.
- Experiencing pressure or fullness in the ears (if not an infection).
- The progression of existing HL or increase in habits of listening to loud noise.
- Experiencing dizziness or whirling sensation.

According to Steyger (2009), chemical ototoxicity like exposure to paint solvents, gas stations, propane, kerosene, diesel, petrol, spray adhesives, alcohol use etc. may not directly cause HL but may initiate a cascade of physiological events. Chemical ototoxicity generation of reactive oxygen species can interfere with normal biochemical processes affecting the blood labyrinth barrier, causing a blockage in ion channels, DNA damage etc. It may worsen the situation in cases where an individual is continuously exposed to noisy working environments (Steyger 2009).

There are many diseases that get worse over age or appear when people attain a certain age. In the case of HL, age is a crucial factor that exacerbates the situation. Presbycusis or ARHL is a condition that is usually observed among elderly people who have attained >50 years of age. Elderly people who have reduced blood circulation or diabetes are at higher risk of developing this disease. According to WHO, by the year 2025, more than 500 million elderly populations would develop ARHL.

The degeneration of stria vascularis, injury in the IHC or OHC, thickening of basilar membrane or loss of sensory elements at the basal end of the cochlea are the major cause of ARHL. Apart from these, slight variation in peripheral and central auditory systems could also be a cause of ARHL (Thakkar et al. 2015). Apart from all the above-mentioned risk factors, vibrations and lifestyle habits like smoking, alcohol, tobacco chewing are factors that may accelerate the development of NIHL (Zhang et al. 2019).

5 Pathophysiology of NIHL

5.1 Brief Hearing Mechanism

The human ear is a sensory organ responsible for hearing, maintenance of posture and equilibrium, by detecting body position and head movement. The mechanism of hearing is dependent on series of complex events. The ear has three anatomical parts including the outer, middle and inner ear (Figs. 2 and 3). The external ear which is composed of the auricle, ear canal and eardrum membrane collects sound waves and transmits them to the eardrum. Three tiny bones of the middle ear (the ossicles) act as levers and conduct the sounds to the oval window, and finally through the cochlea (a snail-shaped organ) which has the auditory receptors (the organ of Corti) in the inner

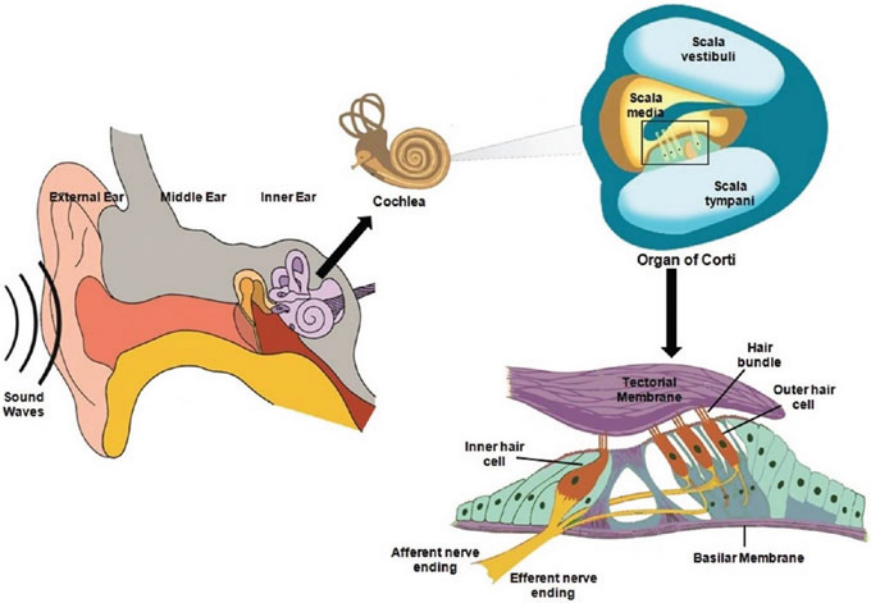

Fig. 2 Mechanism of hearing (*after* Jain et al. 2018)

Fig. 3 Mechanism of hearing

ear. A collagen-based extracellular matrix called the Tectorial membrane on top of the hair cells is vibrated by sound waves. Within the organ of Corti, physical vibrations produce mechano-electrical transduction which is detected by hair cells and these cells respond by producing electrical impulses. Nerves transmit these impulses to the brain where they are interpreted. Different sound frequencies stimulate the hair cells in different parts of the organ of Corti and interpret the various sound frequencies. The auditory pathway conducts the sound impulse to both sides of the brain but the interpretation of specific sounds takes place on the left side of the brain. Sounds are heard at normal hearing thresholds between 0 and 20 dB(A) across the 125–8000 Hz range while the symptoms of HL start at more than 20 dB(A), which is confirmed by measuring pure tone average (average hearing sensitivity at 500, 1000, 2000 Hz) (Jain et al. 2018; Manar et al. 2019; WHO 2012).

5.2 Mechanism of NIHL

Exposure to noise can physically damage the structural integrity of the ear (affecting the tympanic membrane, middle ear and inner ear), which alters the intracellular pathways and causes cell necrosis or apoptosis and induces HL which may make ear conditions worsen as depicted in Fig. 2. The micro-machinery of the inner ear has a vital role in the processing of sound within the cochlea. Hair cells function as mechano-sensors for the perception of sound, acceleration and fluid motion. Excessive auditory stimulation damages fragile inner ear sensory hair cells which lack regenerative potential (Steyger 2009). Noise-induced damage can cause biochemical changes like enhance oxidative stress and diminish the cochlear blood flow by the production of isoprostanes (a vasoactive lipid peroxidation product). The presence of reactive nitrogen product peroxynitrite (ONOO–) has been seen in the cochlea post noise exposure. Peroxynitrite is produced by the combination of Nitric Oxide (NO) with superoxide (O_2^-), which is a perilous free radical. Few pro-inflammatory mediators are also associated with cochlear damage (Kurabi et al. 2017). Various other factors involved in noise-induced cochlear damage are apoptosis factors Bcl2 associated X (Bax), Bcl2 associated death promoter (Bad), B cell lymphoma 2 (Bcl2), Bcl2 related gene (Bclx), Cytochrome C, Apoptotic protease activating factor 1 (APAF), Caspase 1, Caspases 3,6,7. These factors are involved in caspase-mediated cell death either by intrinsic or extrinsic pathway. Other cell signalling network molecules are Nuclear Factor kappa B (NF-kB), Focal Adhesion Kinase (FAK), Kirsten RAt Sarcoma viral oncogene homolog (KRAS), Ras-related C3 botulinum toxin substrate (Rac), Cell division control protein 42 (Cdc42), Mixed Lineage Kinases (MLKs), Jun N-terminal Kinase (JNK), Activator Protein 1 (AP-1) etc. which functions as mediators of sensory hair cell damage (Kurabi et al. 2017). Moreover, the parameters of exposure i.e. intensity, frequency and spectrum of noise, duration of exposure etc. play a significant role in the pathophysiology of noise trauma and the hazardous effect of sounds on the mammalian inner ear.

The possible mechanism of acoustic trauma and metabolic exhaustion in the inner ear after continuous and impulsive noise stimulation was studied by many researchers. Prolonged exposure to noise produces recognizable pathological changes in the cochlea with substantial damage to hair cells of the inner ear. Proteins present in the inner ear are disturbed by loud sound through multiple mechanisms like loss of protein–protein interactions, aberrant accumulation, targeted degradation, mechanical damage, excite-toxicity, ischemia, metabolic exhaustion, ionic imbalance and structural derangements. Specific proteins are known to be associated with HL and show related dysfunction in the human cochlea due to noise stimulations (Jain et al. 2018).

Despite several studies done so far, the onset mechanism of NIHL is still not fully resolved. To inspect the potential mechanism of NIHL, scientists are using recently developed technologies like OMICS. The detection of proteins and pathways perturbed within the micro-machinery of the ear and the cause and effect relationship

study on these proteins would reveal multifaceted properties of these molecules (Zheng et al. 2000; Yeo et al. 2011).

6 Diagnosis of NIHL

NIHL has been well recognized since the industrial revolution. Exposed workers to excessive noise should be screened by audiometry. When HL is suspected, a thorough history, physical examination and proper diagnosis should be performed. If these examinations disclose evidence of HL, referral for full audiometric evaluation should be recommended. The available diagnostic tests are as follows (McBride and Williams 2001; Wahid et al. 2020; Kong and Fowler 2020; Mathers et al. 2000; Rabinowitz 2000).

6.1 Weber Test

It is a simple and quick screening test to evaluate unilateral CHL and SNHL. When someone has asymmetric HL, it can be detected by this test. To test, the physician strikes a tuning fork (of 512 or 1024 Hz) and places it in the middle of the head of the patient. The patient can share his experience that by which ear (either left or right) he can hear better.

Interpretation of Weber Test

Equal sound is heard by the patient means he has a normal ear. In the case of CHL, a sound is heard better in the abnormal ear. In the case of SNHL, a sound is heard better in the normal ear.

6.2 Rinne Test

The test was named after Heinrich Adolph Rinne (1819–1868), a German otologist who proposed the test. In this test, a comparison was made between Air Conduction (AC) and Bone Conduction (BC). In the case of AC, the ear canal and eardrum are involved. The sound waves pass through the outer ear then the middle ear and lastly to the cochlea in the inner ear. In the case of BC, vibration signals are directly transmitted to the inner ear without the involvement of eardrum.

In this test, the physician strikes the tuning fork (512 or 1024 Hz) and keeps it to the mastoid bone behind the ear. The patient responds when he no longer hears the sound. Then the physician moves the tuning fork to the ear canal, again he signals when he no longer hears the sound. The length of time taken by the patients is recorded.

Interpretation of Rinne Test

Normal hearing patients have AC twice than BC i.e. the AC time is twice as long as the BC time. The patient can hear the sound adjacent to their ear twice as long as he hears the sound behind his ear. An abnormal result is when BC is better than AC. In the case of abnormal CHL, the BC sound is twice than AC time and in the case of SNHL, AC time is longer than BC time but not twice as long as BC. The Rinne test should be performed with the Weber test to confirm the diagnosis.

6.3 Audiometry Analysis

It is necessary to confirm a hearing deficit because physical tests of hearing, such as the whispered voice and the figure-rub test are not as reliable. Audiometry is sufficiently sensitive and specific to serve as a screening method. Audiometers must be calibrated regularly and used in a quiet room. The pure-tone hearing levels can be measured at frequencies of 0.25, 0.5, 1, 2, 4, 6 and 8 kHz. AC is measured by earphones placed on the ears, while bone conduction is measured by placing a vibrator in contact with the skull behind the ears. Each ear is evaluated separately and test results are reported on a graph known as an audiogram. Comparison of AC and BC allows the classification of HL. As exposure to excessive noise intensity continues, neighbouring frequencies are progressively affected and the notch broadens, intruding into neighbouring frequencies. NIHL is usually bilateral and shows a similar pattern in both ears. The difference between the two ears should not exceed 15 dB(A) at 0.5, 1, 2 kHz and 30 dB(A) at 3, 4, 6 kHz, respectively. The extent of HL can be assessed using the grading system proposed by the WHO: up to 25 dB(A) (normal), 26–40 dB(A) (mild), 41–60 dB(A) (moderate), 61–80 dB(A) (severe) and above 81 dB(A) (profound). When the audiogram hearing threshold level exceeds 20 dB(A) then it is considered abnormal. Figures 4 and 5 respectively show the audiometry booth and audiogram. The audiogram shows a notch at 4 kHz which recovers at a higher frequency.

7 Which is a Characteristic Notch for NIHL: 4 or 6 kHz?

Even though audiometry is considered as the gold standard method for the detection of NIHL, however debate is still going on about what should be the characteristic frequency either 4 kHz or 6 kHz? There are many studies around the world on detection of NIHL cases in which scientist has observed either 4 notch or 6 kHz notch or both in their studied population. For instance, Ketabi et al. (2010) who worked on 245 Iranian axial parts factory workers found a 4 kHz notch as characteristics frequency of NIHL while, the findings of Satish et al. (2008) is opposite the above-reported study. They observed a 6 kHz notch among their studied population. Though

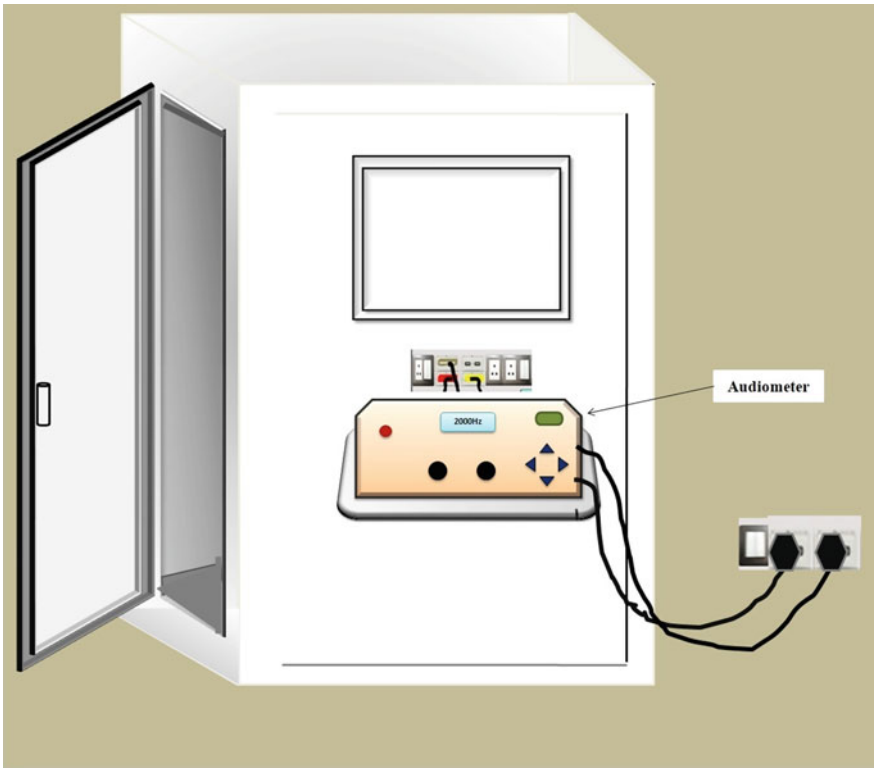

Fig. 4 Image showing audiometry booth

the 4 kHz notch was also found in their study, the significance of the 6 kHz notch was comparatively more than 4 kHz (Ketabi and Barkhordari 2010; Satish and Kashyap 2008). Similarly, Majumder et al. (2018) found both the notches in their study group comprised of 64 men and 33 women administrative workers of Ahmedabad city (Majumder et al. 2018). According to Bhatt et al. (2017) identification of audiometric notch at either of the frequencies i.e. 3, 4 or 6 kHz is suggestive of NIHL. To confirm the NIHL, apart from audiometric analysis, high-intensity noise exposure history is an important parameter to be considered. Though there are differences in opinion about the characteristics notch of NIHL, notch at 4 kHz is considered as the most acceptable frequency for the identification of NIHL which recovers at higher frequencies. To describe the theory behind notch at 4 or 6 kHz observation made by Bhatt et al. (2017) and Aggrawal et al. (2015) can be considered. As we know that the outer ear canal length varies from person to person. The NIHL frequency is dependent on outer ear canal length. When an individual is exposed to huge noise, it may show a notch at any frequency. If the ear canal is short, a notch would have appeared at 6 kHz and if it is long, the individual may exhibit a notch at 3 kHz when exposed to the same impulse of noise (Bhatt and Guthrie 2017; Aggarwal et al. 2015).

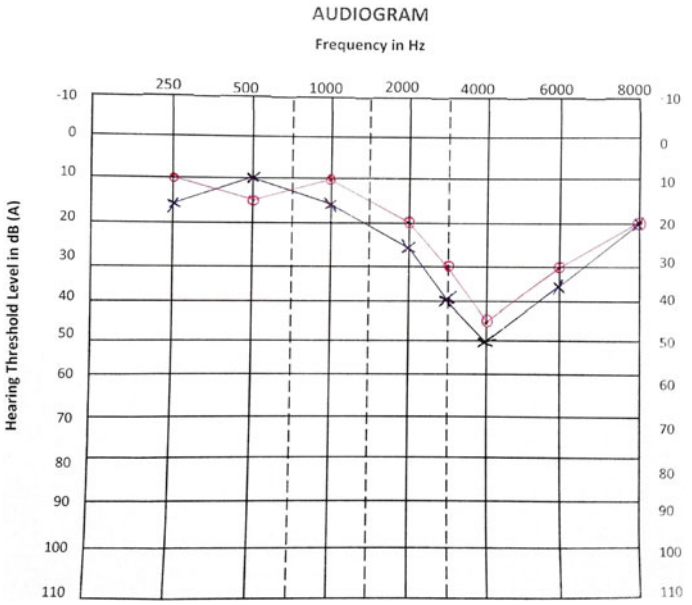

Fig. 5 Representative audiogram showing 4 kHz notch (*Note* X = Left Ear Air Conduction, O = Right Ear Air Conduction)

8 Novel Diagnostic Techniques for the Detection of NIHL: Insights of Proteomics and Multiplex ELISA

The disadvantage of routinely available techniques is subjective (Audiometric test) which suffers from lots of limitations and it is incapable of early and stage-specific diagnosis of NIHL. Regardless of the strict standards for hearing protection, extensive public health awareness campaigns and effective legislation programmes, diagnostic tests are needed to ensure rapid and accurate detection (McBride and Williams 2001; Tanaka et al. 2018). Due to the limitation of available diagnostic tests, scientists are trying to search for potential biomarkers which play an important role in the diagnosis of NIHL.

8.1 Biomarker Study to Detect NIHL

Biomarkers are indicators of any disease which may be protein, gene or other biomolecules. It is synthesized by the host and/or by the pathogen or by both before the onset of any disease or afterwards. A biomarker can be; either a biomarker of exposure or a biomarker of effect. They are necessary to improve diagnosis, guide and monitor activity of molecularly targeted therapy and therapeutic response across a

wide range of diseases (Rifai et al. 2006). Moreover, in the discovery and development of drugs, biomarkers are the prime target by which pharmaceutical companies could hope to find a diagnostic solution for disease (Qoronfleh and Lindpaintner 2010). Many biomarkers for infectious diseases have been identified but for occupational diseases, very few biomarkers are known. In India, very few studies are available on biomarkers related to exposure to noise. Most of the studies are concerned with animal models as subjects but very little are known about proteomic techniques using human as subjects (Jain et al. 2018).

Biomarkers, as applied to a given disease, have utility in one or more of the following areas (Qoronfleh and Lindpaintner 2010):

- Can act as a diagnostic tool. A panel of biomarkers is more specific and reliable than a single biomarker.
- Can inform us about disease biochemical pathways that may lead to the development of novel therapeutic targets.
- Can act as pharmacodynamic biomarkers to monitor the safety and efficacy of a new treatment.
- Can act as surrogate biomarkers to anticipate or predict the later clinical benefit of an intervention.
- Molecular biomarkers are unbiased compared with questionnaires and other tests imposed on patients, especially in paediatric patients.

Biomarker discovery and validation studies can be performed by various techniques but the two methods which are more commonly used, first is proteome profiling and second is affinity multiplexing assays. The study of protein biomarker of Occupational Noise-Induced Hearing Loss (ONIHL) will help to identify the hidden biochemical pathway involved in this disease leading to loss/overexpression of proteins. The individual or panel of biomarkers can be used for the early detection of ONIHL (Qoronfleh and Lindpaintner 2010).

Proteomics in one sense means the basic study of proteins and enzymes while in another it is the integrated study of entire sum of all proteins produced by an organism or group of organisms. But proteomics is a tool used for protein analysis of the mass without cell destruction of cell structure as it gives information about the biochemical processes involved in disease. It also helps in monitoring cellular processes and identifies protein expression levels. Through the proteomics, approach one can understand the pathophysiology by analysing the proteins involved in disease which includes One-Dimensional (1D) and Two-Dimensional (2D) electrophoresis, DIGE (Differential Gel Electrophoresis), MALDI-TOF–MS (Matrix-Assisted Laser Desorption Ionization-Time Of Flight Mass Spectrometry), LCMS, iTRAC (Isobaric Tags for Relative and Absolute Quantitation) based analysis, SELDI-TOF (Surface-Enhanced Laser Desorption/Ionization Time of Flight) and many more. By employing 2D electrophoresis proteins are identified as a spot based on IEF (Iso Electric Focusing). The differentially expressed spots can be the novel biomarkers that may be used as a tool for the early detection of disease. Proteomics efforts are an important component of functional genomics and it is critical to understand and synthesize the information generated by the human genome project. Historically, an effort to discover novel

biomarkers in body fluids, especially in plasma or serum, have been challenging owing to the large dynamic range of the proteome and the moderate resolving power of early instruments.

8.2 ELISA

Enzyme-linked immunosorbent assay (ELISA) is a biochemical technique used mainly in immunology to detect the presence of an antibody or an antigen in a sample. ELISA has been used as a diagnostic tool in medicine and plant pathology, as well as a quality control check-in of various industries. Of today's available tests, ELISA has evoked considerable interest among investigators as it has been found to be potentially valuable and simple to aid in the early diagnosis.

In the case of Direct ELISA, an unknown amount of antigen is affixed to the surface of the microtiter plate, and then a specific antibody is applied so that it can bind to the antigen. This antibody is linked to an enzyme and a substance containing the enzyme's substrate is added. The subsequent reaction produces a detectable signal, most commonly a colored product, indicating the presence of antigen and antibody binding. It is used for quantitative analysis of cytokines and other biomarkers (Elshal and McCoy 2006).

8.2.1 Multiplex ELISA

Recent advancement in ELISA technology is the multiplex array which measures multiple proteins simultaneously by using a single sample. Because of this technology, there is a reduction in sample volume, time and material costs, while the sensitivity of reaction increases over a single ELISA. Multiplex bead array assays provide quantitative measurement of large numbers of analytes using an automated 96-well plate. It can be utilized for the studies of high throughput analysis of numerous analytes. The development of multiplexed immunoassay provides multiple, parallel protein measurements by using a single specimen (Elshal and McCoy 2006; Trune et al. 2011; Ellington et al. 2009).

8.2.2 Multiplex ELISA Assay for the Early Diagnosis of NIHL

After the standardization of NIHL specific primary and secondary antibodies, the method can be used for the detection of NIHL using serum samples of the exposed subjects. If the specific antibody in the serum sample is detected above the cut-off, it could be considered as NIHL positive. The sequence of antibodies coated in each well is shown in Fig. 6. The concentration of each antibody may vary. There are two Phosphate Buffer Saline (PBS) wells that act as a negative control. The method is simple as shown in Fig. 7. Briefly, the plate with serum sample is incubated at

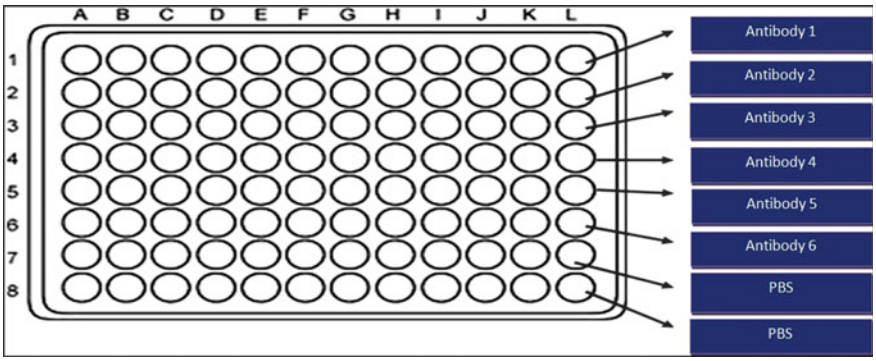

Fig. 6 Sequence of antibodies in multiplex ELISA

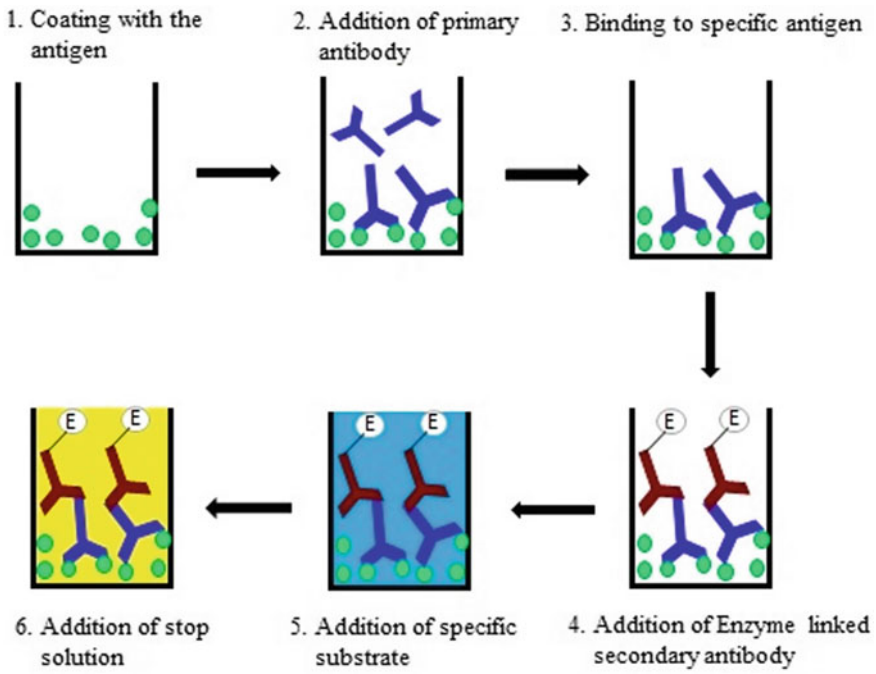

Fig. 7 Systematic representation of ELISA

37 °C for 90 min. The excess uncoated antigens are washed with a washing solution (preferably 1X PBS Tween 20) and a blocking buffer is added. The plate is further incubated at 37 °C for 45 min. After washing, primary antibodies are added which allow them to fix with the antigen by incubating at 37 °C for 45 min. Post washing the unbound antibody is removed and primary antibody specific secondary antibody is added and the plate is further incubated. After washing the substrate and after

5–10 min, the reaction is stopped by the addition of 2.5 N H_2SO_4 (Sulphuric acid). The absorbance can be read at 450 nm on an ELISA plate reader. By this method, six antibodies or antigens can be detected in a single sample at one time. Multiplex ELISA is rapid, cost-effective and easy to perform. It shows good sensitivity and specificity. The panel of cochlear proteins may be useful as early diagnostic and prognostic biomarkers of NIHL.

8.3 Proteins Associated with NIHL

Proteins are a vital component of the cell, involved in various cellular activities. The degeneration or overstimulation of the proteins of the cochlea may lead to a non-perception of sound. Aberrant accumulation, loss of protein–protein interactions, metabolic exhaustion, targeted degradation, mechanical injury, excitotoxicity, imbalance of ions of perilymph and endolymph and structural derangements mechanism may be caused by excessive noise exposure leading to disturbance in proteins' structural integrity. Targeting the cochlear proteins by applying high-end proteomic techniques before and after excessive noise stimulation may give substantial information about the cochlear proteome and hidden physiological pathways. The underlying mechanism can be unveiled by the application of the OMICS approach and novel bioinformatics tools. There is an urgent need for extensive research on NIHL due to the availability of only a few studies in this line. The detailed analysis of all the proteins mentioned here and for those which are yet to be identified is warranted for the effective clinical solution for HL and this techniques like proteomics and ELISA would be of scientific interest (Jain et al. 2018; Zheng et al. 2000). Table 2 shows few proteins, their location, functions and effects in case they get damaged. The detailed explanation of all the cochlear proteins involved in the hearing mechanism is already described in our previous articles and is available online (Table 3) (Jain et al. 2018; Meshram et al. 2019; Urade et al. 2020).

9 Preventive Measures for NIHL

NIHL has been classified among the top occupational health issues which need extensive research according to WHO and NIOSH (Zhang et al. 2009). The situation is alarming, therefore the Center for Disease Control and Preservation (CDC)-NIOSH and OSHA has made certain guidelines for the workplace safety of workers. Indian Government's DGMS, a regulatory agency for the safety of miners and oil field workers has also made certain guidelines to prevent noise pollution at the workplace. Brief information of all the guidelines as mentioned below.

To reduce the noise hazard at the workplace, occupational health professionals have been suggested to follow the Hierarchy of Controls (Fig. 8) (Noise and hearing loss prevention, National Institute for Occupational Safety and Health 2018). It shows

Table 2 Expression of proteins in cochlear hair cells associated with NIHL (after Jain et al. 2018)

S. No	Protein name	MW (KDa)	Location	Function	Causes
1	Harmonin	284	Ribbon synapses	It provides understanding of pathogenesis	Prelingual and severe deafness
2	α-tectorin	239	Tectorial membrane	It helps to convert sound waves to nerve impulse, a critical process of normal hearing	Damage to α-tectorin protein can cause nonsyndromic sensorineural and moderate-to-severe prelingual deafness
3	Protocadherin 15	214–742	Towards steoreocilliary tip	Calcium-binding domains	Nonsyndromic prelingual hearing loss
4	Stereocilin	193	Stereocilia	It converts vibration and motion into electrical current, which in turn alters the cross-membrane potential	Bilateral, non-progressive, sensorineural hearing loss with onset in early childhood
5	Diaphanous	141	Inner hair cells, outer hair cells and external supporting cells	Involved in cell-cell polarization and cytokinesis	Progressive low-frequency and post lingual hearing loss
6	Otoferlin	140	Inner hair cells	Involved in vesicle membrane fusion	Prelingual profound hearing loss involving all frequencies, starting at birth or before the age of 2 years
7	Myosin 1b	132	Tip of stereocilia	Actin dependent motor protein responsible for intracellular movement	Hearing loss in variable degree
8	Wolframin	100	Inner hair cells, outer hair cells and external supporting cells	Participate in regulation of cellular calcium homeostasis at least partially, by modulating filling state of endoplasmic reticulum calcium store	Autosomal recessive syndrome and low frequency sensorineural hearing loss

(continued)

Table 2 (continued)

S. No	Protein name	MW (KDa)	Location	Function	Causes
9	Whirlin	97	Tip of stereocilia	Coordinate polymerization of actin for the growth of membrane in stereocilia	Loss of this protein causes recessive hearing loss in rats and human
10	Prestin	81	Inner hair cells	Essential for auditory function. Inbuilt amplifier, plays important role for electromotility that drives cochlear amplification and produces acute sharp turning curve	Loss of this protein disturbs the balance in cochlea. Characterized by moderate to severe hearing loss and deterioration of frequency sensitivity which is voltage-dependent across the OHCs
11	Radixin	80	Inner hair cells	Important in linking actin to the plasma membrane	Nonsyndromic prelingual hearing loss
12	Connexin 26	26	Tip of stereocilia	Forms gap junction between adjacent cells and allows intracellular communication	Loss of this protein is responsible for severe to profound nonsyndromic hearing loss
13	Cadherin 23	23	Towards steoreocilliary tip	Involved in organization of hair bundles of stereocilia in IHCs and OHCs. Important for delivering mechanical signals to the mechano-electrical transducer channels	Loss of this protein causes moderate to profound high-frequency progressive sensorineural prelingual hearing loss

that eliminating the hazard causing machine is going to sort the issue of noise exposure. In case elimination of the source in not feasible, it can be substituted with a less noisy system. Moreover, Engineering and administrative controls must be applied like the development of less noisy equipment, creation of a device that can prevent noise to reach the workers. Among the administrative controls, a manager should make sure that the workers get least affected by noise by rescheduling their working time. Further use of Personal Protective Equipments (PPE) must be made compulsory.

Table 3 Cochlear proteins involved in the hearing mechanism

S. no	Proteins (Gene)
Stereocilia proteins	
1	Stereocilin (STRC)
2	Whirlin (WHRN)
3	Myosin 1b (MYO1B)
4	Fimbrin also known as Plastin (PLS)
5	Epsin (ESPN)
6	Villin (VIL)
7	Cadherin 23 (CDH 23)
8	Connexin 26 (GJB2)
Tectorine Membrane proteins	
9	Otogelin (OTOG)
10	Alpha Tectorin (TECTA)
11	Beta Tectorin (TECTB)
Inner Ear Cell proteins	
12	Prestin (*SLC26A5)*
13	Wolframin (Also found in Outer Ear Cells) (WFS)
14	Radixin (RDX)
15	Otoferlin (OTOF)
Other proteins	
16	Transthyretin (Retinol Binding Protein or Prealbumin) (TTR)
17	Transferrin (TF)
18	Kininogen 1 (KNG1)
19	Calmodulin also called as Enkurin (TRPC)
20	Lysine (K)-specific methyltransferase 2D (KMT2D)
21	Alpha 1 Anti Chymotrypsin (α1AC) (SERPINA3)
22	Plexin-A3 (Plxna3)
23	DNA methyltransferase protein (DNMT1)
24	Adenosine Kinase (ADK)
25	Protein UNC45 (homolog B) (UNC45B)
26	Alpha protein kinase 2 (AKPK2)
27	Coiled coil domain containing protein (CCDC50)
28	Harmonin (USH1C)
29	Ezrin/Cytovillin (EZR)
30	Moesin (MSN)
31	Claudin 14 (*CLDN14)*
32	Tricellulin (TRIC also known as MARVELD2)

(continued)

Table 3 (continued)

S. no	Proteins (Gene)
33	Cochlin (COCH)
34	Collagen IX (COL9A1)
35	Proto Cadherin 15 (PCDH15)
36	Actin Gamma 1 (ACTG1)
37	SERPIN (SERinePeptidase Inhibitor) Proteins

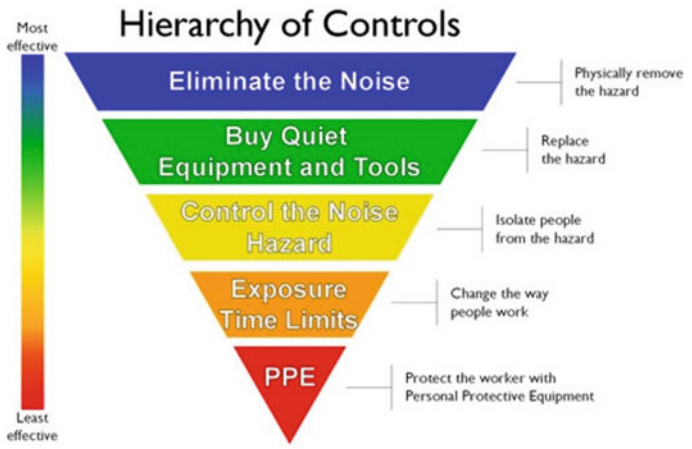

Fig. 8 Showing Hierarchy of controls. *Source* NIOSH (www.cdc.gov/niosh) (Noise and hearing loss prevention, National Institute for Occupational Safety and Health 2018)

In order to map the area noise level, NIOSH has developed a mobile app known as Sound Level Meter (SLM) which is a combination of noise dosimeter and professional sound level meter devices. The app is developed by acoustic engineers and experts in the detection of HL and is freely available and easy to use. The key features are as follows:

- It is in compliance with the Type 2 requirements of IEC (International Electrotechnical Commission) 61672:3 SLM standard in case used with an external microphone.
- Tested and validated by NIOSH with accuracy ±2 dB(A).
- Provides all the relevant data matrix-like threshold sound with averages such as LA_{eq} (Equivalent continuous sound level) and TWA (Time Weighted Average), L_{Max}, L_{Min} and L_{Peak} in linear scale dB(Z) Levels, Noise Dose and Projected Noise Dose according to NIOSH and OSHA standards, and all three major weighting networks (A, C, and in linear scale Z).
- Easy to calibrate with an internal or external microphone.

- Clear step by step guidelines for selection of protection device, conducting noise monitoring, range of hazardous noise etc.
- The data can be shared and is has direct technical support from NIOSH hearing experts.
- User has to select the measurement criteria whether they want to go by NIOSH or OSHA as both have a different set of standards. The app then automatically selects the threshold level.

The drawback of this app is:

- It is only available for iOS device users.
- It can't be used in India.
- Workers don't have enough money to procure expensive smart iOS devices hence its usability from the economic point of view is highly limited.

To protect the workers from getting NIHL, DGMS has made certain guidelines by which the workers' safety could be established at the workplace and noise pollution could be reduced at source, at media and personal protective level (DGMS Annual Report 2007).

The key points of the guidelines are as follows:

- The government has made it mandatory to perform the noise intensity surveys periodically which are comprised of area noise monitoring and personal noise monitoring.
- Engineering and administrative controls must be done in every mining work setting.
- Workers must be supplied with PPE kits and they must follow the guidelines.
- Audiometric examination of the workers must be performed in a periodic manner as per Form 'O' of mine rules 1955 under Mines act 1952.
- Noise intensity survey records must be maintained by the mining agencies.
- Awareness and health promotion programmes must be conducted on the effects of noise on health.
- Periodic monitoring and review of the hearing conservation programme must be done.

10 Summary

NIHL is one of the most leading occupational diseases which contributes to social isolation and leads to degraded quality of life. Worldwide 16% of the disabling HL in an adult is due to excessive exposure to noise in the workplace. Noise exposure is considered as one of the most persistent health hazards in mining occupations. Workers who are exposed to a high level of noise, more than $\geq$85dB(A) are prone to the onset of NIHL. Noise damages key molecules such as proteins present in the micro-machinery of the ear which is required for the mechanoelectrical transduction

of sound waves. Exposure to a high level of noise causes hearing impairment due to both mechanical and metabolic exhaustion in the cochlea.

NIHL can be detected by various methods of which audiometry is considered as the gold standard technique but the limitation of this technique is that it can detect the HL when someone has already developed NIHL. It can't be used for the onset and early diagnosis of NIHL. Hence there is a requirement of such methods which could detect the NIHL at the early stages of its onset. A biomarker study using proteomics could be helpful for this analysis.

The cochlea is the major organ responsible for the resilience of sound. There are key cochlear proteins present in TM, IHCs, OHCs and Stereocilia which gets damage by impulse noise. Thus, the proteins that are up and down-regulated during noise exposure should be analysed to elucidate the pathogenesis of NIHL.

Detailed proteomic analysis using robust techniques like MALDI-TOF, LCMS, iTRAQ 150 based identification, SELDI-TOF etc can be used to get information about the structural component of the ear and study their mechanism. Multiplex ELISA technique is rapid, easy to perform and cost-effective. It can be used for improved early and stage-specific diagnosis for understanding the pathophysiology of NIHL.

It can be speculated that these reviewed proteins play a vital role to protect the structural integrity of the inner ear. The potential biomarkers along with clinical assessments correlation may be utilized for achieving an effective diagnosis of disease. Comprehensive understanding of inner ear proteome will accelerate the biomarker study required for the diagnosis of NIHL and its early detection and prevention of its onset to exposed workers.

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Noise Mapping: An Effective Tool for Monitoring Noise-Induced Health Hazards in Active Mines

Veena Manwar and A. K. Pal

1 Introduction

India occupies a prevalent place in the production of minerals over the globe enclosing as many as 95 minerals. These include 3 atomic minerals, 4 fuels minerals, 33 metallic and non-metallic minerals and 55 minor minerals (including building and other materials) (Government of India 2018–19). Thus mining sector, being one of the leading sectors of the economy, provides basic raw materials to many major industries like iron and steel, power generation (thermal), cement, petroleum and natural gas, fertilizers, petrochemicals, precious and semi-precious metals/stones, electrical and electronic equipment, glass and ceramics, etc.

Apart from large leasehold areas, the Indian Mining industry is also distinguished by a large number of small operational mines with approximately 1405 mines reported during 2018–19 and are involved in mineral production activities (excluding atomic, fuel and minor minerals) (Government of India 2018–19).

1.1 Workforce in Mines

The mining industry represents an important part of the economic system. All other industries directly or indirectly use mining products. A considerable number of permanent/contractual employees are required to run the mining operations round

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_9

the clock. As per the Indian Bureau of Mines (IBM), Nagpur the average day-to-day employment in the mining industry (except atomic and minor minerals and petroleum (crude) and natural gas) in 2013–14 was 512,270 persons (Indian Minerals Yearbook 2014). According to the Directorate General of Mines Safety (DGMS), the average daily employment in opencast mines in the year 2013 was 391,126 persons (Director General of Mines Safety 2016). But as per Mine Labour Protection Campaign (MLPC), 2013 report, there were 2.5 million workforces engaged in over 30,000 small and large unorganized mines in Rajasthan alone (Mine Labour Protection Campaign (MLPC) 2013). Hence, the actual population working in Indian mines is not properly documented. However, according to World Bank reports (The World Bank 2013; Hentschel et al. 2002), around 100 million people (workers and family members) depends on artisanal mining as compared with about 7 million people worldwide in industrial mining. Besides this, a large number of mines outsource their work. However, most of the mining activities are confined in remote areas or villages with tribal populations.

1.2 Noise and the Mining Community

The harmful effects of mining on the mine workers and surrounding population are well known. Major health threats faced by miners are due to exposure to noise, dust and vibration, breathing of many harmful and toxic substances. The movement of various heavy machineries, air blasts during excavation and operation of other processing plants give rise to vibration and high noise. Loud noise and vibration from the blast adversely affect people in the surrounding communities. High noise exposure damages the auditory system, produce cracks in buildings, and gives rise to stress and discomfort (Stewart 2020; Gad et al. 2005). Animals or birds population living near the mine are also adversely affected (Berrios et al. 2016). Noise is a critical issue when we talk about the adverse effects of mining on the mining community. Usually, mines are operating continuously for 24 h which produce wide fluctuations in noise level. During the nighttime, it is a matter of greater concern to the villagers or people living in nearby areas. Das in 2015 reported that six villages were affected due to mining activity in three adjacent opencast mines in Odisha (India) (Das 2015). A noise study from opencast mines in and around the Belpahar and Brajarajnagar area of Ib river coalfield in the state of Odisha reported that 81% of students had been disturbed by frequent air horns of vehicles. The same study also revealed that 26% of local inhabitants of nearby villages complained about sleep disturbances due to road traffic noise produced by movements of heavy dumpers and trucks transporting coal at night (Mohapatra and Goswami 2012).

2 Mining Industry and Its Associated Noise Problems

2.1 Noise as Occupational Hazards in Mines

In the mining industry, noise pollution is not a new concept. The mining community has the highest and persistent hazardous level of noise exposure to which workers are exposed when compared with other industries. This is due to various noise sources in mines, e.g., excavators, dumpers, dozers, loaders, drilling machines, ventilation fans and blasting. The noise occurring due to various extraction processes and operation of Heavy Earth Moving Machinery (HEMM) in mines are matters of serious concern for workers' health and safety. Practically noise is associated with every process carried out in mines, and when assessing its impact on humans it is usually classified as occupational noise. The workers in these industries are often exposed to high noise doses, thereby risking harmful auditory and non-auditory consequences. Around 30 million workers were exposed to high noise levels indicating 70–90% of miners' are suffering from noise-induced hearing loss (NIHL) (NIOSH 1976; Franks 1996; Bauer and Kohler 2000). According to Scott et al. (2004), cases of Coal Worker's Pneumoconiosis (CWPs) and NIHL were highest in U.S. mining from 1983 to 2001 (Scott et al. 2004). The surveys conducted by various national institutions have indicated that noise exposure levels among workers in most mining activities are greater than the suggested limit of 90 dB(A). In some of the operations, the noise levels are as high as 115 dB(A) with peak levels often crossing 140 dB(A). Kumawat and Yadav (2016) in their study showed that noise levels in the mine and nearby locations were beyond permissible limits during day and night time (Kumawat and Yadav 2016). Based on surveys conducted by DGMS in different mines, it was observed that operators of pneumatic jackhammer drills, rock breakers, shovels, mechanical loaders, and the persons working in adjacent areas are exposed to sound levels higher than those prescribed by DGMS (Table 1).

National Institute of Miners' Health, Nagpur (NIMH) conducted a study in various mines from 2010 to 2015 revealed that the operators of various equipment and persons working in nearby areas are exposed to high noise levels. Tables 2 and 3 reveal some

Table 1 Noise levels measured in Indian Mines (DGMS Circular, 2013)

A	In an underground metalliferous mine	
(i)	Jack Hammer drills	106 dB(A)
(ii)	Rock breaker	106 dB(A)
(iii)	Rocker shovel	104 dB(A)
B	In an opencast mine	
(i)	Near drill	111 dB(A)
(ii)	In dumper cabin while moving	103 dB(A)
(iii)	diesel shovel (in cabin)	89 dB(A)

Table 2 Noise levels measured at 5 m distance from mine equipments (2010 to 2015)

	Shovel	Drill machine	Dozer	Dumper	Conveyor belt	Crusher plant
ACC mines	80–90	85–100	80.5	75–85	80–90	85–95
NMDC mines	80–90	80–90	85–95	80–85	NA	85–95
Ultratech mines	90–95	90–95	NA	75–85	NA	NA
ACL Mine	80–85	80–90	80–95	75–85	NA	85–95
NALCO	80	80–90	80–90	80–85	80–90	86.2

Table 3 Records of personal exposure Time Weighted Average (TWA_8)[a] of workers to noise in dB(A)

	Shovel	Drill machine	Dozer	Dumper	Conveyor belt	Crusher plant
ACC mines	88.3	85.1	89.4	89.1	85	88
NMDC mines	89.3	97.2	87.1	90.8	84.3	89
Ultratech mines	90	87.1	80.9	81.9	NA	NA
ACL mine	81.5	84.7	92.0	87.3	NA	NA
NALCO	84.3	88.1	98.7	89.4	87	NA

[a] Eight hours time weighted average

records of area noise monitoring study and personal noise monitoring study (National Institute of Miners' Health 2010–2015).

A recent study conducted by Deshmukh et al. (2018) on occupational exposure to noise in opencast iron ore mines in India observed that workers working in the crushing plant and nearby area were exposed to 81.64 dB(A), operators operating HEMM equipment were exposed to 86.10 dB(A). Similarly, in the loading plant, workers were exposed to 83.76 dB(A), in the screening plant it was 87.62 dB(A) and in other mine operations and workshops, it was 84.92 dB(A) (Deshmukh et al. 2018).

To ascertain the extent of occupational illness among miners, NIMH, Nagpur in 2012 carried out a medical examination of 1270 employees from various mines in the state of Gujarat. Audiometry results showed 337 (26.5%) workers were having various degrees of Noise-Induced Hearing Loss (NIHL) (National Institute of Miners' Health 2010–2015). A survey conducted by the same institute in 2011 among 682 workers in various mines of Rajasthan, revealed that 20–25% of workers had evidence of NIHL (Sishodiya et al. 2013). In both these studies, NIHL was found to be the leading occupational illness among the miners. Various studies conducted by DGMS also indicated that a large proportion of workers involved in mining may be suffering from NIHL. This proportion could vary from 25 to 75% depending on the nature of exposure in mining operations. The Central Government in their notification published in February 2011 declared NIHL as notified disease under the Mines Act, 1952.

2.2 Legislative Frameworks for Occupational and Ambient Noise Exposure

Depend on the study carried in the different parts of the world with respect to the harmful consequence of noise exposure, it was realized by the DGMS to frame the noise limits in order to achieve the following objectives:

- Prevent the risk of hearing problems,
- Prevent communication interference, and
- Eliminate mental/fatigue.

Based on the above-mentioned objectives and the International Labour Organization ILO Code of Practice, the following standards and guidelines have been provisionally recommended [DGMS Circular No.18 (Tech), 1975] (Directorate General of Mine Safety 2013).

- 85 dB(A) as a warning limit for an eight-hour exposure.
- 90 dB(A) as danger limit for an eight-hour exposure.
- However, during emergencies and unforeseen technical reasons, this daily dose may be permitted to exceed only if, the maximum weekly dose should not exceed the value specified above.
- Workers should not be exposed to a noise level of 115 dB(A) or more without proper ear protection.
- Workers shall not be allowed to expose to noise levels more than 140-dB(A).
- Speech intelligibility at a distance of 50 cm or less need to be an important criterion for noise measurement.
- Noise and vibration control criteria should be incorporated at the design stage of equipment and machinery.

Following protective measures may be taken in case of a situation where noise and vibration levels can't be brought below the danger limit by suitable design or installation.

- Provision of suitable partially or totally soundproof booths
- Provision of suitable hearing protection and anti-vibration device
- Provision of anti-vibration working platform; or
- Reducing exposure time.

In India, indeed, ambient noise pollution did not receive the kind of attention it deserved. The noise was considered as an air pollutant in the Air (Prevention and Control of Pollution) Act, 1981 (The Air (Prevention and Control of Pollution) Act 1981). This was further stressed in the Environment Protection Act, 1986. Based on this Act, the Central Government made The Environment (Protection) Rules, 1986 and with notification No. G.S.R. 1063(E), dated 26th Dec 1989, the ambient air quality standards in respect of Noise were specified in Schedule III (Rule 3) as given in Table 4. The above standards were adopted by the Ministry of Environment, Forest

Table 4 Ambient air quality standards in respect of noise

Area code	Category of area	Limits (Leq) in dB(A)	
		Day time	Night time
A	Industrial area	75	70
B	Commercial area	65	55
C	Residential area	55	45
D	Silence zone	50	40

Note • Daytime is reckoned in between 6 am and 9 pm
• Nighttime is reckoned in between 9 pm and 6 am
• Silence zone is defined as an area up to 100 m around such premises as hospitals, educational institutions and courts. The silence zones are to be declared by competent authority. Use of vehicular horns, loud speakers and bursting of crackers shall be banned in these zones
• Mixed categories of areas should be declared as one of the four above mentioned categories by the competent authority and the corresponding standards shall apply

and Climate Change (MoEFCC) vide their notification dated 28th June 1999 under Environment Protection Act (EPA), 1986.

2.3 Traditional Methods of Noise Monitoring

Various methodologies are used for assessing noise levels in mines. Personal noise monitoring and area noise monitoring are undertaken by mining companies to ascertain the level of noise generated by heavy earthmoving machinery or noise doses received by mine workers (Manwar 2018).

2.3.1 Ambient Noise (Community Noise) Monitoring

Objectives

- To determine the existing noise status and to compare the same with existing noise standards/norms set by statutory bodies.
- To identify the possible reasons/causes in case of the noise status exceeding the prevailing noise norms.

Monitoring procedure

- Identification of strategic residential, commercial and sensitive areas within mining complexes.
- Monitoring of noise levels at each location covering four cardinal directions. The monitoring should facilitate the evaluation of daytime and nighttime noise

levels as per Central Pollution Control Board (CPCB) norms (The Noise Pollution (Regulation and Control) Rules 2000). Hence, it is advisable to undertake at least six sets of readings [Maximum Peak Level (MaxP), Maximum RMS Level (MaxL), Minimum RMS Level (MinL) and Level of Energy Equivalent (Leq)] covering 24 h, keeping a gap of four hours in between two consecutive readings

- Determination of average values of Leq for both daytime and nighttime [Leq(d) and Leq(n)] at each location.
- Determination of Ldn value on the basis of the average value of Leq(d) and Leq (n).
- Monitoring of meteorological parameters, e.g., wind speed, wind direction, humidity and temperature levels as these parameters influence the propagation of sound as well as density of sound waves at the monitoring locations.
- It is important to find out the major noise sources and their locations, i.e., the direction and approximate distance of the major noise sources from the monitoring location.
- 1/1 octave frequency spectrum analysis of the community noise in order to evaluate annoyance/irritation capability of community noise.

2.3.2 Work Zone Noise Monitoring

Objectives

- To determine the existing status of equipment/machinery noise and whether the present status is exceeding the prevailing warning level [85 dB(A)] set by DGMS.
- Characterization of existing equipment/machinery noise to evaluate noisy components of the equipment/machinery.
- Frequency spectrum analysis to identify alarming and dominant frequencies so as to take appropriate control measures.

Monitoring procedure

- Selection of different noise equipment/machinery of the mine/industrial complex, workshop, material handling plant, etc.
- Identification of appropriate location for setting noise monitoring instrument (operator's position, within 1 to 3 m of the noisy equipment) (see Fig. 1)
- Determination of Leq level for each equipment/machinery
- Frequency spectrum analysis of the equipment where the Leq level exceeds 85 dB (A). Initially, 1/1 octave band analysis needs to be conducted in order to identify alarming sound frequencies where the sound levels are quite high. This is then followed by 1/3 octave band analysis within these alarming frequency ranges for evaluating dominating frequencies. This facilitates in selecting appropriate control measures.
- Noise dose analysis of machinery operators exposed to high noise levels is carried with the help of a noise dosimeter instrument. Dosimeters are useful in areas where

Fig. 1 Area noise monitoring in an opencast mine

the noise levels are variable or when workers move in different areas of a plant or mine during the course of a working shift.

- Noise dose is expressed as a percentage of an acceptable or criterion noise dose. It depends not only on the levels of the noise at various frequencies but also on the duration of exposure of the employee. The exposure index in terms of percentage noise dose should be correlated with the studies on hearing loss or hearing threshold shift to understand the possible implication of noise exposure in a given situation. Estimation of hearing loss due to exposure to noise can be carried out by audiometry (see Fig. 2).

2.3.3 Audiometry

An audiometer is a tool to measure an individual's hearing threshold as a function of frequency (pure tone). Such assessments are used to identify possible hearing loss or hearing defects. The evaluation process for hearing capability is undertaken by measuring air conduction by an audiometric test with an audiometer. The test is conducted in an acoustic room with pure tones at predetermined frequencies and intensities. The test is conducted using headphones for sound frequencies ranging from 0.5 to 8 kHz and a minimum level from 15 dB linear. The subject person has to respond when the particular frequency sound is audible. The responses of the subject are recorded in the audiogram datasheet. A range of tests is then performed with responses noted in the audiogram datasheet. For the purpose of detection and classification, the maximum loss of hearing in any of the frequency bands is compared to the criteria for NIHL as shown below (see Fig. 3).

Fig. 2 Personal noise dosimeter of a mine employee

2.4 Problems with Traditional Methods and Necessity of Noise Mapping

Existing noise monitoring techniques are targeted to evaluate either an area or personal noise exposure which is easily manipulated by the subjects under study. This can considerably modify the results unless a large number of samples is observed under strict supervision.

In mines, various noise sources are working simultaneously. Noise sources may be stationary or moving. With existing techniques, we cannot say with confidence that all these noises sources are distinguished properly and how much noise is being produced by each of the noise sources in a particular area.

Under these conditions, noise mapping is considered as an effective and advanced method to estimate the noise level in a study area by considering all the acoustical parameters. Noise mapping prefers better visualization of the influence of noise and its propagation in the form of noise contours in the area under study. Detailed noise mapping can also be used to locate the areas where the levels of noise exceed the legal limits.

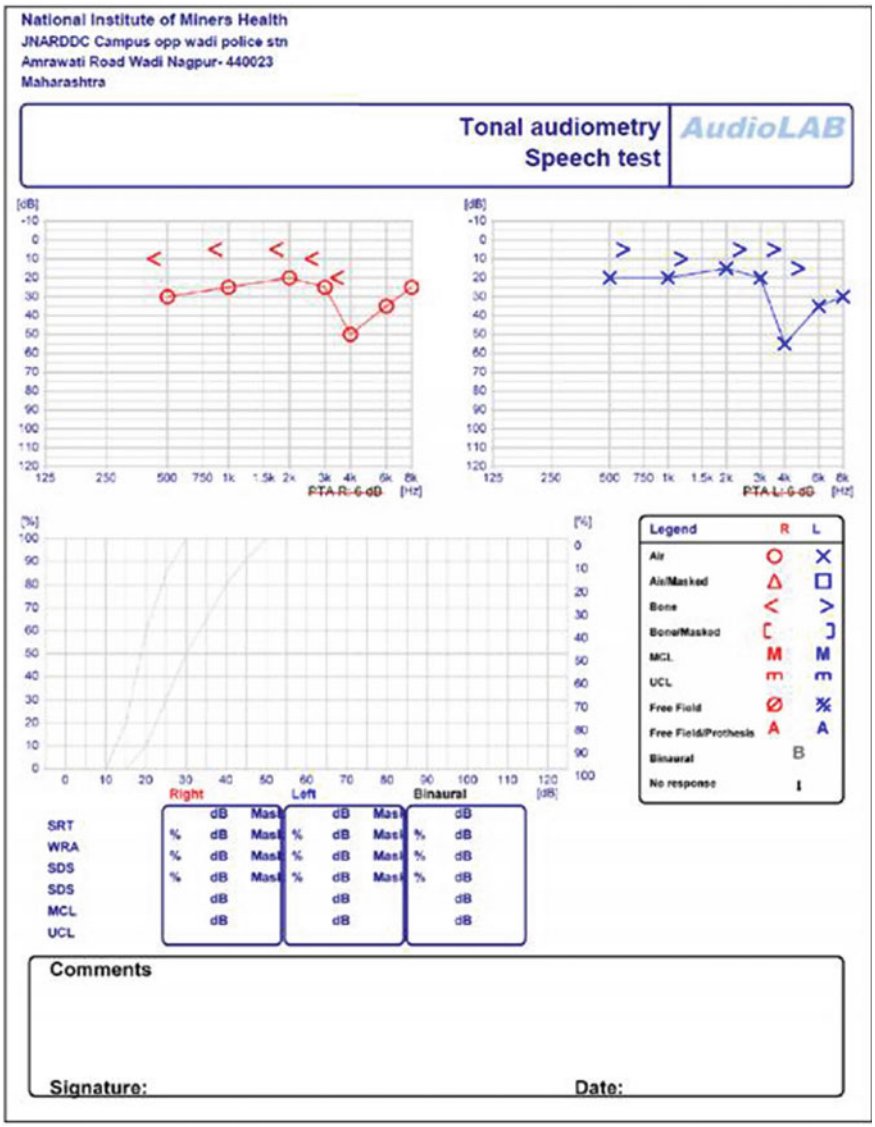

Fig. 3 An audiogram showing hearing threshold shift at 4 kHz. (*Source* Department of Occ. Health, NIMH)

3 Noise Mapping—Its Importance and Procedure in the Light of Environmental Noise Propagation

3.1 Environmental Noise Propagation

Many factors need to be considered in order to calculate, predict or effectively visualize the pattern of propagation of noise in a given environment. For estimating the noise level at any location there are several important environmental factors that affect the spatial pattern of noise propagation. The most important factors are types of sources—whether it is point, line or area sources. It is very important to study the source, how it is emanating and propagating the sound energy around it. If the source is a point source, the sound energy spreads out spherically, so that the sound pressure level (SPL) is the same for all points at the same distance from the source, and decreases by 6 dB per doubling of distance. If it is a line source then the sound level spreads out cylindrically and decreases by 3 dB per doubling of distance. The reduction of noise as it passes through the atmosphere is dependent on many factors like distance from the source, frequency content of the noise, temperature, humidity and wind velocity. The complexity of atmospheric conditions makes it impractical to accurately define all relevant environmental parameters that may influence local sound speed along all possible sound propagation paths between source and receiver. Therefore, an appropriate sound propagation model is required which will consider all these factors while calculating noise propagation. In the dynamic scenario, therefore modeling of sound propagation supported by corresponding information about noise sources, meteorological data and other influential parameters can provide an effective solution for this. Thus, noise mapping has been described as the completeness of an acoustic model and provide a useful link between the technical parameters and the resulting noise exposure of affected people (Probst et al. 2010). Noise mapping shows not only the present noise level but also increased noise levels due to planned expansion or continuous change in mine workings by considering acoustic phenomena like multi-reflections, diffractions and absorption that arise due to the complex topographic configurations.

3.2 Noise Mapping

Noise mapping is a paradigm shift from traditional methods. Noise mapping indicates necessary visualization and evaluation of noise pollution in a particular area thereby pinpointing the area/locations where the noise levels are exceeding the legal limits. The noise indicators for noise mapping are L_{day}, $L_{evening}$, L_{night} and L_{den} (day-evening-night). According to END (Environmental Noise Directive 2002/49/EC) 'noise mapping' provides a necessary presentation of data on an existing or predicted

noise situation in terms of a noise indicator. Noise mapping also indicates breaches of any relevant limit in force, the number of people affected, or the number of dwellings exposed in a certain area (EU 2002; Murphy and King 2010).

3.3 Geographic Information System (GIS) Integrated Noise Mapping

New mapping techniques, integrated with GIS features, enhance the quality of noise maps. This when integrated with GIS and other facilities can effectively predict the extent to which internal noise affects the outside community thereby presenting a holistic view of the problem. GIS works as spatial data analysis and prediction software for mathematical modeling which in combination improves the quality of maps and provides a spatial presentation of the acoustic situation. GIS thus provide a spatial decision support system for the decision making process. Noise effect can also be assessed by evaluating noise levels with exposed population and their sensitivity to noise (De et al. 2000). Prediction maps are produced by using software that is capable of implementing a number of calculation methods. It is a useful management tool to protect the mining community from the adverse effects of exposure to loud noise.

The demand for noise mapping from the mining industry is increasing due to the recent directives of DGMS. Standardisation of the technology is urgently required to comply with the directive as this would in turn provide noise environmental management planning in a simplified way in India.

3.4 Legislative Frameworks for Noise Mapping

Noise mapping is used in most European countries. In 2002 the European Union (EU) passed Environmental Noise Directive (END) (EU 2002). This Directive dealt with four key areas, i.e., strategic noise mapping; estimating population exposure; noise action planning and dissemination of results to the general public (Murphy and King 2010).

The Environmental Noise Directive stipulates the following Salient features:

- Undertake strategic noise mapping to determine exposure to environmental noise as it represents a global assessment of noise exposure in a given area due to different noise sources.
- Strategic noise mapping is carried out after every 5 years for major roads, airports, railways, and agglomerations.
- As per EU Directives, determination of exposure to environmental noise through indicators Lden (day-evening night equivalent sound pressure levels) and Lnight (night time equivalent sound pressure levels) and provide estimates of the number of people exposed to the values Lden and Lnight by member State.

- Ensure that all the details on environmental noise and its effects is made available to the public;
- Based on noise mapping results, adopt action plans so as to prevent and reduce environmental noise particularly where the noise levels have harmful effects on human health and to preserve environmental noise quality.
- Member states of the EU used different calculation standards for calculating road traffic, aircraft, railway and industrial noise. Due to this, the results from different states are difficult to compare directly.
- Therefore, there is a need for a common and standardized noise assessment methodology for all major noise sources so that it would be easy to compare different noise results.
- A Harmonised method was selected by the European Commission in cooperation with the Member States as a common method to evaluate the noise levels from the main sources like road traffic, industrial noise, railway traffic and aircraft.

DGMS guidelines in India for noise mapping

DGMS has circulated recommendations of 10th and 11th National Conference on Safety in Mines held on 26th–27th December 2007 and 4th–5th July 2013 at New Delhi where (Sect. 4.1) it has been stipulated that (DGMS 2008):

> Noise Mapping should be made mandatory of various places in the mine premises based on the various machines being used in concerned mines along with personal noise dosimetry of individual workmen exposed to the noise level above 85 dB(A).

Though DGMS has issued directives for noise mapping studies in mines, the environmental policy/legislation in regard to noise mapping in the mining industry are not detailed like European Directive. It is observed that a time has come to recommend some general noise guidelines for conducting noise mapping in mines so that steps to be taken to control noise levels (Kaku 2013). A detailed study of the propagation of noise from various sources to the entire mine and nearby residential areas using noise mapping technology is essential not only for a better understanding of the subject but also for the utilization of such technologies for the management of environmental noise.

4 Noise Mapping in Mines

4.1 Studies Undertaken in Different Countries

Boddington Mine in Western Australia applied noise mapping techniques to solve issues related to community concerns in respect of environmental noise. After noise mapping study the Boddington mine has modified the day-night scheduling of work. A noise monitoring network has been established to collect real-time noise and weather data, transmitted to the mine for operational purposes. A community website

has been developed to display time-weighted noise data overlaid on an aerial map of the mine using GIS. Measures taken to reduce the impact of noise on neighbours included purchasing equipment with low noise rating, using rubber truck trays to reduce rock noise, using cab-to-cab silent horns and replacing reversing beepers with quieter reversing alarms (Successfully responding to community concerns about noise 2011). Further, the Environmental Impact Assessment (EIA) of the **Eagle field mining expansion project** was evaluated by Noise Mapping Australia (2010). Utilizing available mining noise data from existing mines and considering a large number of variables, **virtual noise maps** were produced using PEN3D and CONCAWE. Among various measures suggested, the dump truck route to the out-of-pit dump needs to be close to the natural surface. The ideal position of the overburden dump was also evaluated. The proposed pit and operational design were found helpful in controlling noise at all locations except one (Eaglefield Expansion Project 2010).

A number of noise mapping applications in western countries are undertaken to tackle environmental noise problems in European cities. Accordingly, appropriate scoring techniques have been developed and are used to evaluate hot spots. However, applications of noise mapping in the mining industry are limited, but the considerable scope does exist for viable alternatives for environmental noise management.

4.2 Studies Undertaken in India

Mohalik and Pal in 2003 developed a noise model of a mining complex based on noise attenuation parameters like geometric spreading, barrier, air absorption, ground effect and meteorological effect. Algorithms were evaluated considering all the noise sources as a point source and programming was written in C language. Accordingly, noise maps were generated using state-of-the-art technologies. This research study also includes simulation of virtual mining situations for impact assessment of project implementation (Mohalik and Pal 2003).

In recent times, a number of studies related to noise mapping of mining and its surrounding area have been reported. Lokhande, et al., 2018 conducted noise mapping in different opencast mines in Keonjhar, Sundergarh and Mayurbhanj districts of Odisha, India using the ISO 9613-2 method to assess the effects and impact of noise on the residential area (Lokhande et al. 2018). Similarly, Manwar et al. (2016) in their studies depicted a pattern of noise propagation through noise mapping in a mining area based on ISO 9613-2 calculation method (Manwar et al. 2016). However, that study demands an appropriate and more efficient noise calculation method for use in mining projects.

In her Ph.D. thesis (Manwar 2018) she conducted a systematic noise propagation and distribution study through noise mapping in and around two mechanized limestone surface mining complexes. Here different mining activities as per their types and characteristic were identified as stationary area sources, moving sources,

point sources or line sources. Noise measurements were carried out as per the standard procedure of ISO 9613-2:1996 and other related standards (ISO 9613-1:1993 1993; ISO 9613-2:1996 1996; ISO 6395:2008 2008; ISO 3028:1998 1998; ISO 3744:2010 2010). Measurements were taken with Type 1 Sound Level Meter (SLM) using A-weighting scale (ISO 1996-1:2003 2003; ISO 1996-2:2007 2007). Noise mapping and modeling were carried out in Predictor LimA software for both the mines using two principal calculation methods, i.e., ISO 9613-2 and Harmonise. ISO 9613-2 provides a set of oldest and most widely used procedures whereas the Harmonoise sound propagation model considers the combination of well-known models and algorithms for complex situations.

The research study thus provided detailed measurements of outdoor noise levels at limestone mining areas and assesses the noise impact on the surrounding locality by predicting the noise levels for different situations. The field restrictions were understood and alternative methods were adopted wherever applicable so as to suggest which options would be better in practical mining conditions. Later on, the captured data were utilised also for virtual conditions assuming enhanced productivity either by an increased level of mechanisation or by extending working hours. The extent of the impact on the population living in nearby mining areas was visualised through mapping. Also, different calculation methods were applied to find out a better choice of methods for the assessment of noise propagation in surface mines.

Separate noise maps were produced using indicators L_{den}, L_{day} and L_{night}. Predicted noise levels in dB(A) was plotted versus observed L_{den} values at selected validation points within the study area to evaluate the level of accuracy. The statistical study showed that the observed values and predicted values in both ISO 9613-2 and Harmonise methods had positive correlations. When compared, correlation in the Harmonoise method was found better than it was in ISO 9613-2 method (Manwar 2018; Predictor V9.10–Software for Noise Prediction (Bruel & Kjaer); Bruel & Kjaer, Acoustic Determinator (V1.40); Bruel & Kjaer 2001). Figure 4 is one of the representations of the noise map of a limestone mine in North India. To develop a noise model, all the noise sources of the mines and meteorological parameters were taken into consideration and accordingly noise map was generated by using ISO 9613-2 calculation method.

5 Standardized Procedure for Conducting Noise Mapping in Mines

5.1 Noise Inventory

The process of noise mapping starts with documentation of noise sources and their type with location. Machines and installations are primarily divided into stationary and moving sources. Later, they need to be categorised as point, line or area sources. Obstacles/hindrances for measurement of noise, if any, are to be clearly documented

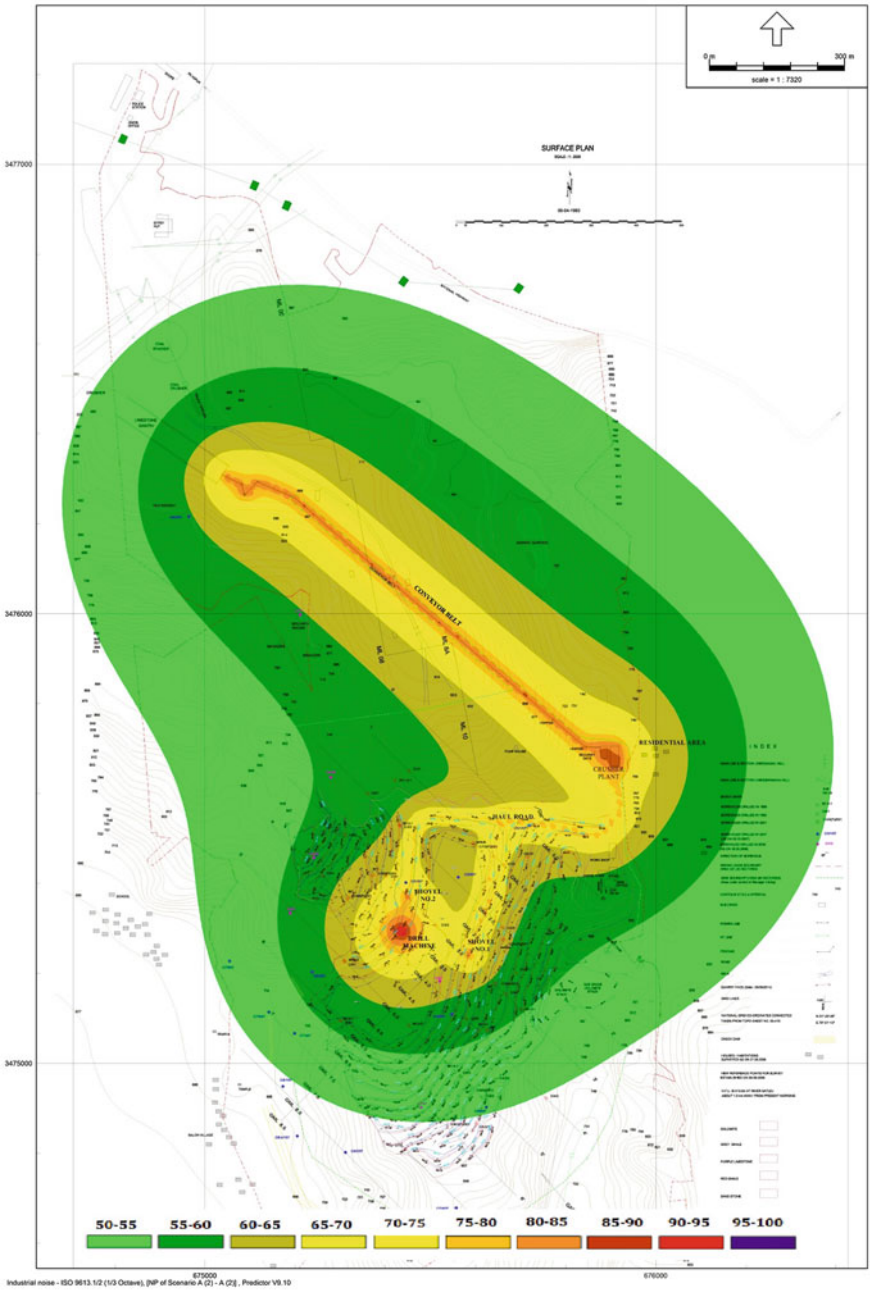

Fig. 4 One of the representations of noise map of limestone mine in India (Manwar er al. 2016)

for taking precautionary measures during evaluating the SPL around any source. Geographical locations of sources are to be noted for including them in the mapping software later.

5.2 Surface Plans

Surface plans in.dwg format are immensely helpful for easy implementation. In case such drawings are not updated or found faulty in nature, satellite images of the study area can be downloaded from Google Earth or Bhuvan (Indian portal) for noise mapping.

5.3 Step by Step Procedure (Manwar 2018)

- Sound sources in and around the mine are identified and a noise inventory is built.
- Plants such as crushers are identified as area sources, dumpers moving on haul roads were taken as moving sources. Shovels and drilling machines are identified as point sources. Belt conveyors are treated as a line source in the noise model.
- Noise measurements are carried out according to ISO 8297:1994 (Acoustics—Determination of sound power levels of multisource industrial plants for evaluation of sound pressure levels in the environment—Engineering method), ISO 9613-2:1996 (Acoustics—description, measurement and assessment of environmental noise) and ISO 6395:2008 (Earth Moving Machinery—Determination of sound power level—Dynamic test conditions) and other related standards (ISO 9613-1:1993 1993; ISO 9613-2:1996 1996; ISO 6395:2008 2008; ISO 8297:1994 1994).
- Noise measurements are to be taken with the help of a Sound Level Meter (SLM) using A-weighting scale and at the same locations coordinates are to be taken with a GPS device.
- Meteorological parameters like wind direction, temperature and humidity are to be collected from the mine office.
- The surface plan of the mine leasehold areas is taken from the mines in DWG file format.
- The surface plan (DWG file format) is imported to ARCMAP 10.2 software. Coordinates of noise sources taken with the help of GPS are imported on the surface plan. Shapefiles of noise sources (crusher plant, dumper, haul roads, shovels and drills) are digitized and stored as shapefiles (Environmental System Research Institute (ESRI)).
- Noise prediction software uses sound power levels of the noise sources for the calculation of noise levels at the receiver points. The sound power levels are calculated in the Acoustic Determinator taking the sound pressure level of noise sources as input data.

- Then all these data are imported in Predictor LimA and used as attributes to corresponding noise sources.
- The surface plan of the mine is imported in Noise Predictor software as a background image before implementing the evaluation procedure for ascertaining noise propagation.
- All the shapefiles created in ArcMap10.2 are now imported as noise sources in the project within Predictor LimA.
- Individual attributes contain a description of the source, type of source, coordinates, emission level (power level data) and working hours.
- Computed sound power level data are then added as attributes to the respective individual sources.
- Considering all these parameters, the propagation of noise levels at usually 10 m $\times$ 10 m grid intersections are calculated using the Harmonoise calculation method and noise maps are produced.
- Noise maps are generated with different indicators like L_{day}, L_{night} and L_{den}.
- Different colours may be assigned to indicate different noise levels in dB(A) in a noise map. For example, noise levels ranging from 50 to 55 dB(A) and 55 to 60 dB(A) are indicated by different shades of green, 60–65 dB(A), 65–70 dB(A), 70–75 dB(A) and 75–80 dB(A) are indicated by different shades of yellow, 80–85 dB(A) is indicated by orange colour, 85–90 dB(A) is indicated by maroon colour, 90–95 dB(A) is indicated by red colour, 95–100 dB(A) is indicated by violet colour.
- The above description is based on the use of ArcGIS 9.0 (ESRI) and Predictor LimA (B&K) software.

6 Summary

Acoustic emission (noise) has only lately being considered as a serious occupational health hazard for the people working in mining industries. Increasing automation, mechanization, and deployment of heavy machinery has significantly aggravated this problem. In opencast mining, the availability of large diameter, high capacity pneumatic drills, blasting of hundreds of tonnes of explosives, round the clock operation of dumpers, dozers, and tippers are identified as noise-generating activities. In a pit-crushing system with a mobile crusher and large capacity materials handling instruments are being installed to facilitate the speedy movement of large quantities of ores and overburden. All these activities are major sources of noise pollution in and around the active mining areas. Therefore, noise has emerged as one of the most prevalent environmental stressors in the mining industry.

The acoustic emission inevitably leads to the NIHL. In addition, the noise influences work performance and make communication more difficult. Besides, the fauna (wildlife) in the surrounding areas also gets significantly affected by noise. Many countries and communities have introduced legislation making it a legal requirement to measure occupational and community noise levels in a systematic manner. In a

developing country such as India, not much attention has been paid to noise pollution and its consequences on human health. Although the standards for environmental noise monitoring is well stipulated by the CPCB, New Delhi, mitigation measures are taken especially when there is a complaint raised by the affected community. Proactive and voluntary efforts are still rare. One of the reasons is a lack of scientific projections on the impact of noise of any project before its implementation, i.e., at the planning stage before execution. Unless noise management strategies are successfully implemented, environmental noise will remain a major concern for the health and wellbeing of the mining community throughout the life cycle of the mine.

The DGMS and IBM in India have realized the hazards of noise and vibrations and framed the noise limits based on the ILO code of practice in order to provide noise-free occupational noise exposure status. Further, DGMS has circulated Recommendations of 10th National Conference on Safety in Mines held on 26th and 27th Dec 2007 at New Delhi and it was also further stressed in 11th Conference on Safety in Mines which was held during 4th and 5th Jul 2013 at New Delhi, where it has been stipulated that noise mapping of various places in the mine premises should be made mandatory based on the various machines being used in concerned mines along with personal noise dosimetry of individual workmen exposed to the noise level above 85 dB(A). During these conferences, along with safety aspects of different mining activities, emphasis was put on the safety of workmen exposed to high levels of noise in mines.

Noise mapping is an advanced technique, preferred for visualization of the influence of noise and its propagation in the form of noise contours in the area under study. Detailed noise mapping can be used to identify the areas where the noise levels exceed the legal limits. The main noise indicators for noise mapping are L_{day}, $L_{evening}$, L_{night} and L_{den} (day-evening-night). Understanding the probable effects of a noisy environment through mapping enables us to design and implement preventive control measures for the future. The END (Environmental Noise Directive 2002/49/EC) is a directive for the European Union that gives a common and standardized assessment methodology to avoid, prevent or reduce harmful effects of noise levels on human health. Similarly, the DGMS in India has issued directives for conducting noise mapping studies, but these are not detailed enough like European Directive.

Effective management of occupational health hazards thus needs to be identified in the mining industry with a view to eliminate them or minimize them to such an extent that these do not pose any serious threat to health, productivity and overall quality of life of miners as well as the surrounding community. This is possible only when all existing noise sources are identified and their characteristics are fully understood. In a virtual scenario, the noise sources are to be assumed along with their sound power levels in accordance with the mining plan. Once we fully delineate the source, their characteristics and the environmental conditions, etc. propagation of noise can be modeled using acoustic laws. Eventually, it will come out as a powerful tool for the control and management of noise propagation in mining areas.

Given a situation where noise management is limited to noise measurements and dosimetry, noise mapping is envisaged to be of great help in the context of Indian mining industries where a large community is usually affected by the noise created

by mining activity. We need to address the problem of noise management for a mining community with the latest tools and technologies available utilizing the fast computational capabilities of modern computers and software which are built with an integrated development environment. In this article, we provide an overview of the noise policies for conducting noise mapping in mines, so that concrete steps can be taken for the prevention and control of noise pollution.

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Postural Injuries and Associated Pain in Earth Moving Machinery Operators

N. P. Kulkarni, S. Gangopadhyay, and J. Bharshankar

1 Posture, Injuries and Musculo-Skeletal Disorders

Mining, by definition, can be classified as a complex and hazardous work domain with further classification into sub-domains like exploration, mine development, mine operation, decommissioning and land rehabilitation. That mining holds immense promise towards industrial development is well documented, but it cannot be negated that this activity is inherently dangerous, in terms of the likelihood of accidents as well as ill-health. The answer towards mitigation of these health issues lies in the knowledge of the hazard as well as concern for the welfare of others on the part of workers, management and also the legislators (Murray 1988).

Irrespective of the shift towards mechanization in mining, human touch cannot be but ruled out. While some tasks in mining require manual material handling others require the operation of machine controls in constrained spaces and/or head-rooms since space is but a premium. It is the neglect of ergonomic considerations and/or improper postures during such activities which contribute to incidences of Musculoskeletal Disorders (MSD).

Technically speaking, MSD can therefore be defined as injuries or dysfunctions affecting muscles, bones, nerves, tendons, ligaments, joints, cartilages and spinal discs (Lost-work time injuries and illnesses: characteristics and resulting days away from work 2016) as a result of improper/incorrect postures wherein correct postures

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_10

can be said to be the ones which involve proper manipulation of joints to make possible for the human body to attain a sustainable, comfortable, non-health affecting body position (Sahu 2009).

Factors responsible for these injuries and dysfunctions are varied, and range from over-exertion, cumulative load, contact of body parts with equipment or furniture, or even something as basic as a fall. But then it is mostly the demands of an activity that cause or aggravate MSD, based on its repetitiveness (Sarkar et al. 2016; Das and Gangopadhyay 2018).

Research has proven that MSD can be caused by a single trauma as well as by cumulative trauma. Single trauma and thence an injury is caused when there is an exposure of large amounts of energy for a duration as short as 48 h. Contrastingly cumulative trauma results when there is low magnitude energy transfer over a prolonged period and, exceeding a latency of 48 h (Riihimäki 2000).

Work-related Musculoskeletal Disorders (WMSDs) can be differentiated over MSDs as covering the medical conditions of the musculoskeletal system acquired by a worker exposed to specific working conditions, contemplating inflammatory and/or degenerative disorders which affect the tendons, nerves, muscles and joints, among others (Brasil 2010). These injuries can be attributed to repetitive work or overload, to environmental factors and/or organization, inappropriate use of equipment, etc. to name a few (Caetano et al. 2008). Such attacks result, usually in pain, numbness, heaviness, tingling, fatigue and functional disability (Alencar et al. 2009), thereby significantly reducing the ability to work and also the worker's quality of life.

It is essential to realize that WMSDs are by nature heterogeneous, primarily due to their multi-causation pathways. This makes prevention and control of WMSDs a challenge which is not easy to understand or accomplish. Studies have shown that working conditions (environment and organization), biomechanical, psychosocial and individual factors such as improper posture are oft associated with the occurrence of symptoms indicative of MSD. Physical discomfort (Dusane et al. 2017), longer commutes to work, inadequate and poorly designed workstation, intense work rhythms, invariance of tasks, repeatability of movements, physical exertion, sustaining poor posture for longer periods of time, mechanical pressure on certain segments of the body, static muscular work, shock and vibration, are some of the collaborative factors responsible for the onset of WMSDs (Melzer and Iguti 2010; Silva and Jesus 2013; Cabral et al. 2012; Trindade et al. 2012; Branco et al. 2011).

Considering the epidemiological data available, it can be easily argued that WMSDs are an important occupational health hazard today (Gangopadhyay 2019). Several previous observational studies have shown a strong association between physical demands of a job, its corresponding exposures and work environment, as being major contributory factors towards the development of WMSDs.

However, it may also be noted that compared to epidemiological research carried out on chronic diseases, the epidemiology of MSDs has a relatively short tradition and the interest has only peaked during the past thirty years (Riihimäki 2000).

2 Assessment of Pain and Postures

A neutral body posture involving non-health affecting body position has been theoretically defined to be a good posture (Sahu 2009). Research carried out over a period of time has identified compromised workplace factors as often being causative towards awkward and static postures, which are in turn associated with upper extremity pain and discomfort in different body parts among the working class (Putz-Anderson et al. 1997; Ohlsson et al. 1995; Punnett et al. 2000). Over a period of time not just do these risk factors alter the neutral posture but when coupled with workspace constraints of an informal workstation along with high muscle exertion, these lead to a forced back bent sitting work posture which increases the likelihood of fatigue thereby decreasing the capability of the tissue to recover. And this in turn ultimately leads to more pain and discomfort (Silverstein et al. 1987; Alcouffe et al. 1999; Treaster and Burr 2004) thereby manifesting as musculoskeletal problems (Chavalitsakulchai and Shahnavaz 1993; Tiwari et al. 2003; Singh et al. 2005). Armstrong et al. have even reported a critical review of epidemiological studies wherein the relationship between work postures and MSD was examined (Armstrong et al. 1993).

For surveillance purposes, using symptoms to ascertain health outcomes is inexpensive. Not only is data acquisition quick and easy but is also suitable for large studies thereby making standardization easy. One of the most commonly used standardized symptom questionnaires is the Nordic questionnaire (Kuorinka et al. 1987). It has been observed that not just is it suitable for surveillance purposes, but can also be developed for ascertaining symptom-based musculoskeletal syndromes.

However, it also has its set of cons, in that, subjective perception plays a huge part in such symptom-based disorder ascertainment. This is especially a matter of concern since it runs the risk of being influenced by several extraneous factors such as other concomitant diseases, physical activity level at work and leisure; individual characteristics such as pain and illness, behaviour or mental state, and cultural factors. And no doubt, therefore, validity can become questionable.

Therefore, in addition to the standardized symptom questionnaires wherein there is a need for attention to verbal expressions, differences in dialects or cultures as also the inclusion of Visual Analogue Scales (VAS) and pain drawings (Riihimäki 2000), observational methods need to be included here. These methods being capable of assigning a numerical value to diverse work postures and also the severity of postural risk, enable designers and/or decision-makers to articulate changes in the work process as well as in that of the workspace design. Ovako Working Posture Analysis System (OWAS) (Karhu et al. 1977), Quick Exposure Checklist (QEC) (Li and Buckle 1998), Rapid Upper Limb Assessment (RULA) (McAtamney and Corlett 1993) and Rapid Entire Body Assessment (REBA) (Hignett and McAtamney 2000) are a few noteworthy observational methods for evaluating working postures (Mandal 2014).

3 Pain as a Precursor to MSD

3.1 Low Back Pain

Low Back Pain (LBP), often the most identifiable trait of MSD, has been observed to be so common in the population today that it is often difficult to define a healthy subpopulation. But then, most data on back disorders are based on questionnaire surveys with only a few community studies having used clinical examinations to verify its existence (Bigos et al. 1994).

Based on a review of 40 studies for back disorders; of physical factors, the strongest evidence was found for lifting and forceful movements whereas the evidence was found to be insufficient for static postures. Of psychosocial factors, evidence was not considered as strong for any of the risk factors (Riihimäki 2000).

Clear cut demarcation of causative factors towards LBP and therefore also towards MSD underlines the importance of a questionnaire that is clear cut and well defined to the aims of a study. Epidemiology of symptom-based MSD can be improved by amending questionnaires and classification of disorders, and by also validating these classifications. Operational case definitions can be based on pain localization, pain characteristics (intensity, type), duration of pain, frequency of pain episodes and occurrence of other symptoms.

Review studies carried out in 1997 and 1999 pointed towards a strong manifest for manual materials handling, twisting and bending and Whole Body Vibration (WBV) as being risk factors for back pain. Moderate evidence was found for arduous physical work, whereas practically no evidence was found for sitting, standing or walking, sports, and other leisure-time physical activity (Hoogendoorn et al. 1999). Evidence was also found to be mixed for psychological factors, stress, job dissatisfaction, work pace, monotony, etc. with there being no association found for lack of job support (Burdorf and Sorock 1997). Research has also shown that the prevalence of LBP increments with increasing age until 55–64 years following which there is a decline (Heliovaara et al. 1993; Deyo and Tsui-Wu 1987).

In studies exclusively aimed at studying the correlation between MSD and WBV exposure for Load Haul Dump (LHD) operators in underground mines (Grenier et al. 2010), it was observed that reported discomfort was poorly correlated to International Organization for Standardization (ISO) discomfort scores. Further, MSD scores produced stronger relationships with already reported discomfort scores than did vibration exposure values. Similar studies in India and focused especially on HEMM operators in opencast mines hinted towards the prevalence of musculoskeletal pain as being a manifestation of MSD as also for a significant erosion in the quality of life (Mandal and Srivastava 2010; Mandal and Manwar 2017).

In a study focused on WMSD in US mines during the period from 2009 to 2013, it was observed that the days lost at work was highest for shoulder and knee injuries. Further, this was found to also increase with the age of the workers (Weston et al. 2016). In a similar study based in China and covering about 1900 underground coal miners, the morbidity of MSD was significantly higher when compared to ground

workers. Logistic regression analysis hinted at repetitive operation and awkward posture, as being the primary risk factors for MSD in neck, shoulder and upper limbs; whereas repetitive operation, moving heavy loads and stooping posture were observed to be significantly related to lumbago. MSD in lower limbs was observed to be associated with standing for long times as also being in awkward postures (Weston et al. 2016). Frequent occurrences of pain in the back, knees and feet due to the repetitive nature of the work as well as due to maintaining static positions for prolonged time periods has also been reported (Durlov et al. 2014; Mukherjee et al. 2019). Overall a significant correlation has been observed between occupational factors and MSD in coal miners (Xu et al. 2011).

With regards to the severity of patients with LBP alone, as against those with LBP accompanied with pain radiating to the leg due to nerve root involvement, there was reported increased pain and disability, poor quality of life and increased use of health resources for the latter, thereby necessitating the need for early identification of MSD symptoms and for pursuing effective treatments (Konstantinou et al. 2013).

Clinical validation of the prevalence of MSD and its deteriorating effects has also been concluded by Lawrence in his study wherein radiography of miners and heavy manual workers pointed towards lumbar disc degeneration as a result of their occupation. A similar effect was however not significantly pronounced in the light manual workers or sedentary workers (Lawrence 1955).

3.2 Pain and Impaired Sleep

Musculoskeletal pain is an acknowledged cause of sleep disruption, and individuals with WMSDs frequently report more pain (Li et al. 2017; Zhang et al. 2018). MSD of the bones, joints, and muscles is known to result in pain that leads to micro-arousals with movement. This in turn interferes with the ability to sleep which in turn leads to fatigue and thereby interfering with the person's quality of life makes his/her pain worse (Institute of Medicine (IOM) et al. 2006).

Sleep disruption is commonly considered to be an aftermath of the pain experience. Sleep disturbance has been frequently reported by people with chronic LBP usually exceeding twelve weeks (Van de Water et al. 2011). Research has also indicated that one in twenty of all new cases of chronic pain in the population can be attributed to sleeping problems (Catarina et al. 2008). Also, subjects who reported increased pain severity have reported greater sleep deterioration than subjects with low pain severity (Wilson et al. 1998). Studies have also reinforced the view that sleep disturbance could have a bidirectional relation with other features of chronic pain. While an initial study (McCracken and Iverson 2002) reported no confirmation about repairing disrupted sleep leading to melioration in patients' daily activity as also a reduction in their suffering, another study (Harrison et al. 2014) reaffirmed the necessity of considering sleep as a potential therapeutic target in both, prevention and management of musculoskeletal conditions. A similar finding was echoed by Sali et al., who felt that although insomnia was traditionally assumed to be simply a

symptom of pain or depression, there was a need for specific insomnia assessment and treatment for those with chronic musculoskeletal pain (Sali et al. 2014).

In a study involving elite athletes of Santa Catarina, there was observed a correlation between the poor quality of sleep and pain which was significantly evident as the count of affected body parts increased. Athletes with poor sleep quality suffered more pain as compared to those with sleep duration changes, thereby suggesting that musculoskeletal complaints were associated with athletes' sleep quality as against their sleep duration. The study also established that athletes with higher nighttime awakenings had pronounced nighttime pain (Bleyer et al. 2015).

In a study spanning nine years and covering 1941 subjects, Saad et al. reported an estimated prevalence of sleep disturbance of 58.7% and concluded that sleep disturbance was dependent on pain intensity, whereby every increase by a single point on a ten-point VAS was found to be associated with a 10% increase in the likelihood of reporting a disturbance in sleep (Saad et al. 2011). This underlines the fact that overloaded tissues need recovery time and that work-rest schedules could do with the incorporation of stretch routines (Costa and Vieira 2008) for pain alleviation.

4 Mining and MSD

With mining jobs today being partially or fully mechanized, more time is spent driving vehicles and operating Heavy Earth Moving Machineries (HEMMs) viz. Dumpers, Dozers, Loaders, Excavators etc. (McPhee 2004). While the shift towards mechanization has boosted production many folds, it has also brought with it, the prevalence of newer occupational hazards along with varied safety concerns, one of them being MSD (Mandal 2014).

Data from the Second European Survey on Working Conditions (Paoli 1997) identified mining as being amongst those industries wherein 40% or more of the workers are exposed to three or more of the following risk factors (working in painful positions, moving heavy loads, short repetitive tasks and repetitive movements) for at least 25% of the working time (Buckle 1999). This is known to overload the tissues and cause delayed muscle soreness due to micro-injuries of muscle fibres, resulting from unfamiliar and mainly eccentric exercises (Connolly et al. 2003) as there is often no time for recovery from stress offered by these repetitive tasks.

As mentioned earlier, back injuries are one of the most recognisable traits of MSD. A graphical overview of back injuries reported by Mine Safety and Health Administration (MSHA), USA from their studies carried out over a period from 1996 to 2005 is presented below. While Fig. 1 (Gallagher 2008) illustrates back injury rates per 100 Full-Time Equivalents (FTEs) of underground and surface mines, Fig. 2 (Gallagher 2008) illustrates back injuries reported by commodity and mine type per 100 FTEs of underground and surface mines.

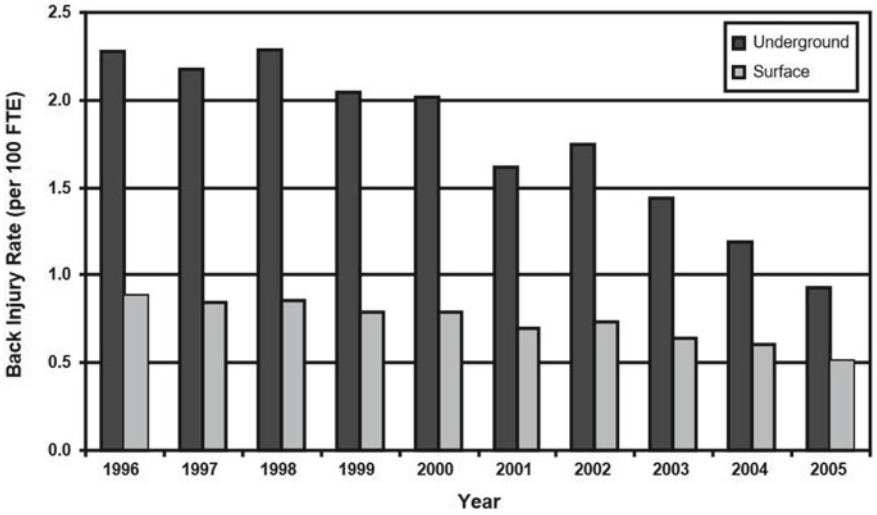

Fig. 1 Back injury rates per 100 FTEs (underground v/s surface) for the period from 1996 to 2005

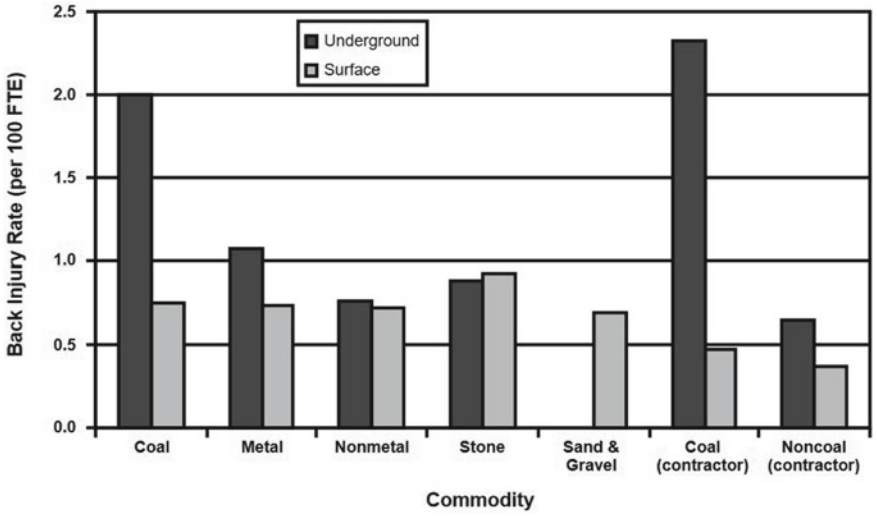

Fig. 2 Back injury rates by commodity and mine type (underground v/s surface) for the period from 1996 to 2005

The prevalence rate of back injuries in both the types of mining—underground and surface, is self-explanatory. However, what stands out is the quantum being significantly higher in underground mines chiefly due to the unique environmental restrictions which force the adoption of awkward working postures.

5 Studies on International Front

In a study carried out amongst Brazilian miners, musculoskeletal symptomatology was observed to have been reported by a majority of employees in one or more body segments with the lumbar region being the most affected. Also, operators of older age reported more MSD in various body segments as compared to young miners. The operators working more hours or those with a longer service duration were observed to report a higher prevalence of MSD in some body parts with most of them being in the lumbar and dorsal regions (Bleyer et al. 2015).

A postural analysis study carried out in a Canadian underground mine revealed that Load Haul Dump (LHD) operators spent over 94% of their time with the neck rotated in excess of 40º when operating their respective HEMMs. This was indicative of posture adoption being directly influenced by visual cues and available line-of-sight (LOS) (Godwin et al. 2008) for these operators.

6 Studies on Indian Front

Kittuswamy examined using a computer-aided system, the dynamic jobs of fifteen excavator operators and computed the percentage of time, the operator adopted a neutral posture. The amount of time the back was observed to be in neutral posture ranged from 32 to 100%; shoulder (irrespective of the side) from 29 to 99%; and the neck 55 to 97.5%. This indicated that operators were necessitated to assume awkward postures for considerable periods of time during the course of their jobs. Also, these postures were notable for their contribution to neck, shoulder and back (descending order) pain. Deviation of the back could be explained by the integral nature of the job; workers bending over to observe the ground that they were digging or moving, deviation of the shoulder explained by the requirements of operating various controls (i.e., levers and gears) located inside the cab and deviation of the neck being chiefly due to the operator maintaining eye contact with his work, located at or below ground level (Kittusamy 2003).

LHD operators too have been observed to report higher incidences of musculoskeletal injury. Poor LOS and awkward postures adopted by the LHD operators heighten the risk of driving-related accidents and also of musculoskeletal injury. The design of the LHD vehicle mostly dictates what the operator can see which in turn has a direct influence on driving postures adopted by them thereby resulting in several risk factors for musculoskeletal injury (Godwin et al. 2008).

In a study of dumper operators, the problem of LBP was significantly higher (85%) in the exposed population when compared to controls (20%). Similarly, pain in the ankle (37.83%), neck (37.5%) and shoulder (30%) too were higher among exposed personnel when compared to the control population (Mandal and Srivastava 2010). However, while this was but a pilot study and limited to occupational exposure to equipment vibration and not postural risk per se, it provided only a brief about

postural injuries HEMM operators are exposed to, thus necessitating the need for an in-depth study on the prevalence of MSD in mining and the contribution of associated risk factors.

7 Guidelines in India

During the deliberations at the Tenth Conference on Safety in Mines held at New Delhi, India from 27 to 28 November 2007 the need for ergonomic assessment of all machinery employed in the mines was felt. The recommendations of the said conference (Recommendations of the Tenth Conference on Safety in Mines held on 2007) thereby explicitly stated the need for e*rgonomic assessment of all latest machines (so as to include work process, working aids/tools and work posture), before their introduction into mining.* The same was also reiterated in the Eleventh Conferences on Safety in Mines held in 2013 as well (Recommendations of the Eleventh Conference on Safety in Mines held on 2013). And this has undoubtedly been due to the importance attached by the Directorate General of Mines Safety (DGMS), the regulatory authority in India, to incidences of MSDs in mining.

8 Findings from Our Recent Study

Research studies on WMSD in India related to mining occupations are usually rare. One such study titled "*Postural risk analysis of mining equipment operators and its relation to musculoskeletal disorders*" was conducted by the authors under the aegis of National Institute of Miners' Health (NIMH), Nagpur posts its sanction by the Ministry of Mines (MoM), Government of India (GoI) for assessing the prevalence of injuries that could lead to the development of MSD amongst operators of commonly used loaders in underground coal mines.

Popularly known as the Side Discharge Loader (SDL), this crawler mounted versatile task-master is known for its inherent ruggedness and ease of operation in slushy terrains. Commonly found in coal mines, post-blasting SDLs of the respective sections engage in a number of trips ferrying coal from the face to the tubs before the same is hauled up to the surface. However, the immense utility of the SDL of being able to work in gradients up to 1 in 4 (and a cross gradient of 1 in 8) (Sarkhel and Dey 2015) is also accompanied by uncomfortable working postures for its operators since its dimensions are defined by the height of the coal seam. While research has proven the existence of musculoskeletal discomfort due to uncomfortable working posture for SDL operators (Sharma et al. 2016; Dey et al. 2017) little attempt has been made at posture analysis and studying the factors contributing to this discomfort.

The afore-mentioned study was therefore conducted and encompassed a total of one hundred and fifty-nine SDL (Model 611 and Model 635; Make: M/s. Eimco Elecon (India) Ltd.) operators (National Institute of Miners' Health 2019). Operators

Fig. 3 SDL operator during operation of his HEMM

were observed to be in the age bracket of 23–59 years with their exposure to SDL operation ranging in a period from 6 months to 19 years. On average, an SDL operator (Fig. 3) was observed to be engaged in 48.03 ± 9.08 trips during his working shift with the approximate distance travelled per trip being 86.95 ± 23.81 m (National Institute of Miners' Health 2019).

Interviewing the operators and body mapping the pain pointed to prevalence rates of pain being the highest for the lower back (69.81%) followed by the neck (63.52%). This was followed only by pain in the left shoulder (28.93%) and left elbow (18.87%) with the prevalence of pain in the rest of the body being comparatively marginal.

A detailed figurative description of the presence/occurrence of pain in various parts of the body for the operators (n = 159) studied is shown in Fig. 4.

Pain prevalence in the lower back and neck could be attributed to the fact that the SDL operators had to almost continuously twist their lower back and neck in both the left and right directions intermittently while moving in the reverse direction to ensure that the path was clear of obstruction. Additionally, there was also a repetitive strenuous movement of the neck towards the left to ensure the absence of obstruction while moving forward. Further on, straining of the back and more pronouncedly of the neck was repeated during loading of the bucket with coal (at the face), and its subsequent emptying in the tubs. Alarm, air filter and lights were observed to be the cause of complaint about their interference in the LOS especially for the extra low height SDL operators, thus further straining their lower back and neck.

On average, an SDL operator was engaged in 6 h of activity in the allotted panel and there was observed repetitive straining and twisting of the lower back and neck

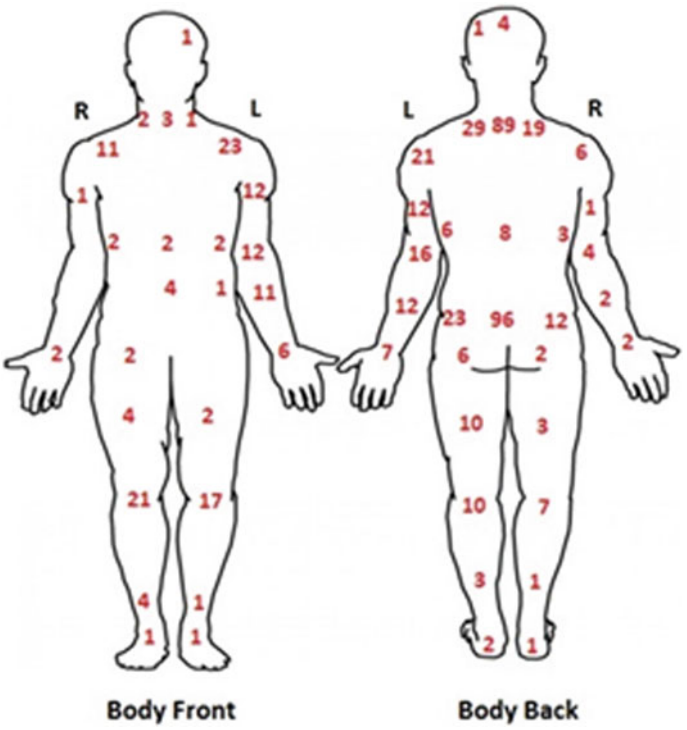

Fig. 4 Distribution of pain prevalence on various parts of the body

during this period. SDLs being crawler mounted are prone to more vibration being transmitted to the operators via their seats. That the seats had minimal cushioning and an absence of pneumatics meant that the transmission of vibration to the operator was not being regulated or minimized which also explained the additional load on the lower back and neck via transmitted vibration in addition to its repetitive twisting in the course of duties. Both these factors were observed to play a vital role in the increased prevalence of LBP and neck pain for these operators.

Classification of SDL operators on the basis of occurrence of LBP and/or neck pain with reference to the duration of time (years) engaged in operating SDL is as depicted in Table 1.

Analysis of the data gathered in the course of the study indicated that operation of SDL was the primary contributory factor for LBP and/or neck pain with there being an increasing correlation for it with a corresponding increase in the duration of operating the SDL. Elevated RULA and REBA scores too were observed indicating a substantial contribution of neck and trunk twisting as well as bending.

Further, the absence of arm rests on the seats of the operator accentuated incidences of pain in the left hand (shoulder and elbow). This could be explained by the fact that the left hand was comparatively more occupied in SDL movement since the

Table 1 Relation between years of working as SDL operator and pain in lower back or/and neck region

Pain in body part	Presence of pain across years of experience as SDL operator		
	0–5 (n = 48)	6–10 (n = 90)	≥11 (n = 21)
LBP	27 (56.25%)	69 (76.67%)	17 (80.95%)
Neck pain	23 (47.92%)	64 (71.11%)	15 (71.43%)
LBP and Neck pain	16 (33.33%)	54 (60.00%)	13 (61.90%)

directional and movement control levers were positioned on the left side. Contrastingly the right side of the SDL had fewer levers and also had the presence of hoses in the nearby periphery which acted as occasional support for the right hand.

Overall the study hinted towards an increase in the prevalence of pain with an increase in age, total mining experience and duration of employment as an SDL operator. There was also observed a positive correlation between duration of exposure towards operating an SDL and the intensity of pain with prevalence rates being considerably higher after six years of working as an SDL operator. Association and negative correlation were strongly observed between the intensity of pain and quality of sleep corrected for age in these operators.

Whilst the study was effective in establishing a relationship between the occurrence of MSD and its associated risk factors, ergonomically friendly intervention strategies too were suggested for the operators.

9 Summary

Over a period of time, several interventions have been proposed to reduce WMSD occurrences. These include work adjustments, re-engineering type modifications, exercise programs and training in ergonomic principles (Vieira et al. 2008). Evidence present also points to the effectiveness of strengthening exercises in reducing WMSD (Gundewall et al. 1993; Mooney et al. 1995). However, it is imperative to note that reducing exposure to risk factors associated with the initial onset and development of postural injuries needs to be the prime focus at any workplace. And only when this can't be achieved in totality should linkage of varied research disciplines be attempted to develop and implement operator-friendly intervention programmes.

Acknowledgements The authors are thankful to the Ministry of Mines, Government of India for sanctioning and funding the study on "Postural risk analysis of mining equipment operators and its relation to musculoskeletal disorders". We are thankful also to Director, NIMH for his support during the course of the study. We also owe our gratitude and acknowledge the support received from Director, ICMR-NIOH. We also acknowledge the assistance of the project staff during the course of the study.

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Ergonomics in Mining: Current Status and Future Challenges

Urmi R. Salve and Arunita Paul

1 Introduction

Mining is the process of extracting minerals and coal from the earth. The importance of this industry is enormous in the terms of materialistic advancement of human civilisation. Several major activities together are needed for mining operations. These are exploration, mine development, mine operation, decommissioning and land rehabilitation (Donoghue 2004).

Mining is an activity that is going on through ancient periods of time. The oldest mine activity was found in Ngwenya heritage site in Swaziland (https://whc.unesco.org/en/tentativelists/5421/#:~:text=Ngwenya%20Mine%20is%20situated%20on,the%20world's%20earliest%20mining%20activity). The mine was active 42,000 years ago for haematite extraction (whc.unesco.org, accessed 14.06.2020). Being an ancient industry mining is always associated with the extensive activity. The working environments in mines are complex and very demanding. Thus, the human interaction in such an environment is complex and strenuous too (Dempsey et al. 2018). Moreover, mining being an extensively multidisciplinary industry caters to several occupations together. Understanding of all the activities and tasks associated with the full process is, thus, absolutely necessary (Donoghue 2004).

By definition, "*Ergonomics is the scientific discipline concerned with the understanding of interactions among humans and other elements of a system, and the profession that applies theory, principles, data and methods to design in order to optimise human well-being and overall system performance"* (Imada 2007). Ergonomics cater for the limitation and capability of human components in a work system. Thus, instead of asking the worker to accommodate beyond their capacity, this discipline emphasizes on providing better intervention to optimize both productivity and human comfort and safety (IEA 2020). The complexity of the man–machine-environment

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_11

system in mines provides a major opportunity for ergonomics and occupational health-related research and intervention in this area (Dempsey et al. 2018). To optimise the balance between the job demand and miners capabilities ergonomic intervention is required. There is a considerable amount of research on the application of ergonomics in the mining industry (Dempsey et al. 2018). National Institute of Occupational Safety and Health (NIOSH), International Labour Organization (ILO) published various categorised ergonomics guidelines for this industry. Some of the recent trends include developing ergonomics assessment tools for this industry (Dempsey et al. 2017), participatory ergonomics in the mining industry (Burgess-Limerick et al. 2005) and mining instrument design with an ergonomics approach (Steiner and Burgess-Limerick 2013) etc. With the evolving digital and virtual technology, Industry 4.0 is also starting to influence the mining industry like the others (Bertayeva et al. 2019; Loow et al. 2019). With the change of the work pattern that Industry 4.0 brings, the ergonomic challenges faced are also evolving. Thus, there is a need to review all the existing challenges and scopes of ergonomics in this particular industry.

Indian mining history dates back to the ancient Harappan times. India is rich in its off-shore and on-shore deposits of crude oils, coal, bauxite, copper, iron, mica, gold etc. (www.mines.gov.in). The total number of minerals produced by India is eighty-eight. Among these four fuel minerals, three atomic minerals, twenty-six metallic and non-metallic minerals and fifty-five minor minerals are there (www.mines.gov.in). Thus, mining industry is a major contributor to India's growth and development and the general scopes and challenges there is evolving as same as the other countries. However, some aspects of the Indian mining sector are typical of its unique status. The typical geography, demography, organizational structures and psychosocial context develops into some unique problems and scopes in the Indian mining industry. Thus, the application of ergonomics in the Indian context should emphasise those particular needs.

The aim of the current study is to review and discuss the overview of present ergonomics challenges in the mining industry, with an emphasis on the Indian context.

2 Methodology

The related academic and non-academic literature were obtained for the scope of the study. The literature was obtained with the help of different keywords, for example, ergonomics and human factors in mining, Indian mining sector, ergonomic intervention in mining, future scopes of ergonomics in mining, future mining technologies, Industry 4.0 and mining etc.

Based on the keywords developed published studies were searched using different search engines such as Google Scholar, PubMed, Science Direct etc. Also, the Central Library of the institute was accessed for the same purpose.

The inclusion criteria are:

- Systematic reviews on the topic
- Primary studies focussed on the general topics
- Government and administrative reports
- Related technological studies from mining and other industries

The exclusion criteria are as follows:

- Any study before the year 2000 was excluded to understand the recent changes

Based on the above-mentioned criteria around 60 studies were selected and reviewed.

3 Result and Discussion

3.1 General Overview of Ergonomics and Occupational Health Challenges in Mining

Mining industry is undoubtedly a very hazardous working environment (Dempsey et al. 2018; Kramer et al. 2017; Verma and Chaudhari 2017). The source of morbidity and mortality in this industry can be of two types (Kramer et al. 2017):

i. Accidents such explosions, leakage of poisonous gases, collapsing of mine stopes, flooding or general mechanical errors etc.
ii. Cumulative effects of different exposures including silicosis, asbestosis, mesothelioma, lungs, nasal and gastro-intestinal cancers etc.

Comparison between these two showed that from earlier times, accidents and safety system failures were the major cause of fatality and compensation demand. However, the current situation is changing, specifically for developed countries and organised mining sectors. Due to the advancement of safety technology and analysis, the number of accidents is significantly less than that of cumulative disorders resulting from chemical and biological exposures (Kramer et al. 2017; Bianco and Demers 2013; Driscoll et al. 2005).

The hazards present in the mining industry can be of several types. The understanding of these provides insights for risk assessment and prevention.

Physical hazards contribute in a major proportion to both accidental injuries and cumulative disorders. The effects can be ranged from minor to fatal (NIOSH 2000). Acute injuries may be caused by different situations such as rockfall, fires, explosions, mobile equipment accidents, falls from height, entrapment, electrocution, flooding of underground workstations etc. (Donoghue 2004; NIOSH 2000).

3.1.1 Physical Hazards in Mining Industry

For the mining industry, noise is a universal physical hazard that plays important role in the development of noise-induced hearing loss (NIHL). The noise is created

from blasting, crushing, drilling, cutting, material handling, ventilation and other activities required for extraction and processing of the ores. Noise and NIHL control is a difficult task and needs more extensive research in the context of mining (McBride 2004). However, with the development of noise mapping techniques identification and control of noise is moving towards a more comprehensive direction. In the context of India, noise mapping and related research are being excessively done by several researchers and agencies (Manwar et al. 2016).

Another important physical hazard present in almost all mines is vibration. Whole-body vibration is generated from mobile equipment such as trucks, scrapers, diggers etc. The condition of roads and vehicles also contribute to the intensity of the vibration. Whole-body vibration can lead to the development of spinal disorders or alleviate the pre-existing symptoms (Donoghue 2004). Hand-arm vibration is experienced from operating hand-held vibratory devices such as air leg rock drills. The classical manifestation of this kind of vibration is observed in hand-arm vibration syndrome (HAVS) or vibration white finger (VWF) (Donoghue 2004; Shen and House 2017). This effect is more prominent in cold regions (Shen and House 2017). Effective control and equipment interface design such as handle, seat is having a significant effect on the management of vibration-related problems. However, India being a tropical country VWF is not prominent in most cases, thus the HAVS is often underestimated (Mandal and Srivastava 2006). There is a lacuna of vibration-related research in the Indian mining context. The exact impact of vibration is needed to be evaluated for Indian miners (Mandal and Srivastava 2006).

Environmental factors such as heat and humidity play an important role in deep underground mines and in tropical regions. Air temperatures increase with geothermal gradient and increased barometric pressures in deep underground mines (Donoghue and Bates 2000). The increased heat can cause severe problems such as heat stroke in deep underground mines of tropical countries. The underground mines in Africa and India is particularly important in this aspect (Donoghue 2004). Heat stress management in the mines is an intriguing topic. The step by step models developed by some researchers during ventilation design can be effective to control this issue (Anderson and Souza 2017).

Other than these major physical hazards, several radiation-related problems may also be present in some mines. For example, Radon daughter present in underground mining may lead to lung cancer. This problem can be encountered with proper ventilation design (Donoghue 2004). Different studies from other industries have led to the assumption that solar ultraviolet exposure may increase the risk of squamous cell and basal cell carcinoma (Armstrong and Kricker 2001).

Barometric pressure can be an important factor for deep underground mines and high-altitude mines. Chronic intermittent hypoxia is common in high altitude mines in South America leading to the manifestation of acute mountain sickness (AMS) (Richalet et al. 2002).

3.1.2 Chemical and Biological Hazards in Mining Industry

The range of chemical hazards in mines is diverse; the material to be mined often being the hazard itself. Exposure to this type of hazard most of the time leads to cumulative diseases such as cancers, respiratory diseases etc. Some of the critical exposures and their effects are discussed as follows:

One of the most problematic exposures till date has been crystalline Silica (Donoghue 2004; Donoghue 2004). Inhalation of this material for a long period of time leads to the development of silicosis. Exposure to a large amount of Silica may not be noticeable because it is colourless, odourless and does not have any immediate health effects. However, chronic inhalation leads to massive lung fibrosis (http://nhp.gov.in/disease/non-communicable-disease/silicosis). Other than that, silica exposure leads to silico-tuberculosis, chronic obstructive pulmonary diseases (COPD), renal problems and lung cancer (Steenland and Sanderson 2001). Extensive research in this area has led to the development of several control measures. Some of these are axial water-fed rock drills, wet techniques, ventilation, enclosed cabins and respiratory protections (Donoghue 2004). However, in India, the problem of silicosis still remains in large part due to several reasons. In a 1999 report published by the Indian Council of Medical Research (ICMR), it was estimated that around 1.7 million workers in mines and quarries are affected by Silica exposure (http://nhp.gov.in/disease/non-communicable-disease/silicosis). This is a prevalent problem in mines of Gujarat, Rajasthan, Pondicherry, Haryana, Uttar Pradesh, Chhattisgarh, Bihar, Jharkhand, Orissa and West Bengal (http://nhp.gov.in/disease/non-communicable-disease/silicosis). Extensive research emphasising on Indian context should be undertaken to curb this major problem of the Indian mining industry.

Coal dust produces similar problems in mines leading to 'black lung' that is COPD and another spectrum of related lung disease. This is recognised as coal mine dust lung disease (CMDLD). This is particularly prevalent in coal mines of the US in recent years. However, India and China also face similar conditions and in the Indian context, studies should be conducted for the management and prevention of this disorder (Laney and Weisman 2014). The risk can be managed by dust suppression, ventilation and respiratory protection (Kizil and Donoghue 2002).

There are several other chemical hazards present in different mines. One of the very harmful such material is asbestos which leads to asbestosis, a lethal lung disease. Although in 1986 India placed a moratorium on asbestos production, the effects are still manifesting in the former mining areas. One of the probable reasons may be the lack of clean-up after the mines stopped functioning. The left-over hill-like dumps are leading to chronic exposure for the nearby villagers as reported by different agencies (https://medicalxpress.com/news/2014-12-abandoned-asbestos-hazard-india.html).

Diesel particulates, lead, cadmium, manganese, cobalt, aluminium etc. also lead to cumulative diseases. The metallurgical processing of different ores also requires several chemicals that can be hazardous. For example, cyanide is used as a solvent for copper and mercury. Mercury is still being used in some gold mining operations to produce mercury-gold amalgams (Bose-O'Reilly et al. 2003). These materials are harmful to different systems including the respiratory system, reproductive and

renal systems. Also, the presence of irritant dermal exposures increases the occurrence of dermatitis (Donoghue 2004). Design of workstations and personal protective equipment (PPE) with ergonomic considerations can be of immense help for risk management (Dempsey et al. 2018).

Mining industries also suffer from biological hazards. The remote location mines in tropical countries suffer from the recurrence of tropical diseases such as malaria and dengue fevers (Donoghue 2004).

3.1.3 Biomechanical Hazards and Fatigue in Mining Industry

Miners across the world use to suffer different biomechanical problems also despite the more and more mechanised industry. The work itself is substantially strenuous with a large portion of manual handling. Cumulative trauma is still a major problem in the mining industry (Donoghue 2004). Mines in sub-continental countries such as India often practice the traditional methods of mining. These practices are specifically prone for developing musculoskeletal disorders of the shoulders, spine, knees etc. (Ijaz et al. 2020).

Most mines are needed to remain operative all the time, thus shift work is very common. A fair amount of research was done to investigate fatigue in this work pattern (Baker et al. 2003). However, the detrimental effects of longer shift lengths, higher workloads, less task variation, decision latitude in mining industries are not well investigated (McPhee 2004). The contribution of slips, trips, falls and increasing age of miner population is also not well established (McPhee 2004).

3.1.4 Role of Organizational and Cognitive Ergonomics in Mining Industry

Psychosocial and organisational factors also play an important role in the safety and wellbeing of the miners. It was found that organizational factors such as task diversity apparently influence the safety parameters (Page 2009). Organizational deficiency in terms of resource management, organizational climate, operational processes results in an increased rate of accidents (Aliabadi et al. 2018). However, awareness at the organizational level contributes positively towards occupational health (Kramer et al. 2017).

Mining is a complex industrial system, where it is very critical and challenging to understand the interaction among cognitive processes, working environment and available equipment (Demir et al. 2017). It can be safely assumed that like other complex sociotechnical systems, mining activities are also associated intricately with cognitive processes such as decision making, reasoning, problem-solving, human errors and resilience etc.

Cognitive ergonomics is closely associated with automation and semi-automation processes. The effectiveness of these systems is largely dependent on their capacity to interact properly with human cognitive capabilities and limitations (Mehta and

Parasuraman 2013; Parasuraman 2011; Parasuraman et al. 2000). The future scope in mining technology is mostly based on automation, virtual and digital technology etc. Thus, it is important to understand the role of cognitive ergonomics in this aspect. This is discussed more elaborately in the section about the future challenges.

In recent years, a branch of cognitive ergonomics has emerged, which leads to a more objective measurement of several cognitive parameters. To understand mental workload or vigilance more effectively these methods are being widely used nowadays. This branch is called neuroergonomics, and it has already gained popularity in several safety-critical sectors (Mehta and Parasuraman 2013; Parasuraman 2011; Parasuraman et al. 2000).

Mining is also a safety-critical sector like the nuclear and aviation sector. Thus, human error and reliability assessment methods are important in this sector. It is important to apply cognitive ergonomics concepts and task analysis methods in this area (Demir et al. 2017; Horberry et al. 2013). In a recent study by Demir et al. (Demir et al. 2017), the cognitive work analysis (CWA) method was applied for different operations and organizations in the mining industry. The authors proposed a five-level quantification model for observation of the overall cognitive quality of a mining operation (Demir et al. 2017).

3.1.5 Safety and Accident Analysis in Mining Sector

All over the world, to provide a better working environment and to optimise the man-machine-environment interaction, different legislations were developed. Like other industries, this is true for mining also. In those entire legislatures, safety is the term of utmost importance. Safety implies the control of risks that can negatively affect occupational health (Joy 2004). For this purpose, the risk assessment methods are very important. The general steps for risk assessment are described below (Joy 2004):

i. Risk Identification- identifying the hazards and the situations (unwanted events)
ii. Risk Analysis- calculating the magnitude of these unwanted events
iii. Risk Control-formulating suitable measures
iv. Implementing and monitoring control measures

There are different risk assessment techniques available. Each of these has its typical purpose. Some of these are the following (Joy 2004):

i. Informal Risk Assessment (RA): general identification and communication of risks in a task
ii. Job Safety/Hazard Analysis: general identification of risks and controls in a specific task following a standard work practice
iii. Preliminary Hazard Analysis/ Hazard Analysis/ Workplace Risk Assessment and Control: general identification of priority risk events
iv. Hazards and Operability Study (HAZOP): systematic identification of hazards in a process plant design

v. Fault Tree Analysis (FTA): detailed analysis of contributors to major unwanted events, using quantitative methods
vi. Failure modes, effects and criticality analysis (FMECA): general to detailed analysis of hardware components reliability risks

The risk assessment application is used for systematic accident investigation. This practice started since early 1990s (Joy 2004). One of the widely used accident analysis methods is the modified human factors analysis and classification system (HFACS) framework. It is an adaptation of Reason's Swiss cheese model of accident causation (Verma and Chaudhari 2017). To counter the data uncertainty about safety and accidents, fuzzy-reason based approaches are gaining popularity (Verma and Chaudhari 2017). Some of these methods are fuzzy analytic hierarchy process (FAHP) (Baker et al. 2007), fuzzy technique for order of preference by similarity to the ideal situation (Grassi et al. 2009). In India, Verma and Chaudhari (Verma and Chaudhari 2017, 2014) proposed fuzzy-reasoning application-based models for risk assessment in metal mines (2014) and manganese mines (2017). However, such risk assessment models needed to be developed for all the other minerals and non-mineral mines (Table 1).

3.2 Emerging Technologies and Associated Challenges in Mining

The fourth industrial revolution or Industry 4.0 is the direct benefit of digital or virtual technology, based on the internet of things (IoT). Like the other portions of the economy and industries, mining is also evolving with Industry 4.0. (Bertayeva et al. 2019; Loow et al. 2019). There are several encouraging possibilities attached with it. However, the proper application requires some important considerations to optimise the effect (Bertayeva et al. 2019; Loow et al. 2019). Among these one of the important considerations is assessing the innovation from the point of view of human capability and limitation. In other words, ergonomics and human factor analysis of any new technology should be provided (Dempsey et al. 2018).

3.2.1 Automation in Mining Industry

The most critical topic related to Industry 4.0 and ergonomics is the case of automation or semi-automation. The first priority of studies of ergonomics and human factors in automated systems is the allocation of functions among human and machines. The allocation is based on relative advantages. It was observed that speed, power and repetition are the advantages of machines; whereas human intelligence, fine manipulation and adaptability to a situation are essential human qualities (Dempsey et al. 2018). However, this topic is still under debate. The increasing capability of automation may soon lead to rather unidirectional advantages (Parasuraman et al. 2000).

Table 1 Scopes of ergonomic studies and interventions in mining sectors

Area	Examples	Scopes of ergonomics
Physical hazards	Noise, vibration, heat, humidity, radiations, barometric pressure etc	Hazard identification Design of engineering controls (e.g., barriers etc.) Design of administrative controls (e.g., shift design, working hours) Personal protective equipment (PPE) design
Chemical and biological hazards	Crystalline silica, coal dust, asbestos, diesel particulates, lead, cadmium, cobalt, aluminium, mercury etc Malaria, dengue etc	
Biomechanical hazards	Repetitive movement, posture, vibration, force, cumulative trauma, fatigue	Study of WMSDs (such as of neck, back, hand and wrist etc.) Identification and quantification of risk Design of interfaces, equipment, tools, workstation etc Task design, work-rest cycle etc
Cognitive ergonomics	Information processing, mental workload, vigilance and attention, decision making, human error and reliability etc	Identification and quantification of the risks Design of perceptual environment Task design Protocol design Training design Human-automation resource allocation etc
Organizational ergonomics	Work environment, work-related stress, reward system etc	Design of organizational management Proactive measures etc
Safety and wellbeing	Accident, injuries, work-related disorders and diseases	Safety analysis Accident prevention and investigation System design Perceptual and physical environment design and control etc

However, automation is not without any limitations. Many assumed automation might create more problems than solved (Dempsey et al. 2018; Parasuraman et al. 2000; Brainbridge 1982). Also, the effect of automation on mental stress, perception, attention, learning, human errors and overall safety and accidents are needed to be investigated properly. A newer approach to tackle this issue has been developed with the integration of neurobiology in ergonomics. This area, known as neuroergonomics employs the help of objective neurological techniques such as functional magnetic resonance imaging (fMRI) to understand the human brain's interaction with an automated system. This will help to the development of more efficient adaptive automated systems (Mehta and Parasuraman 2013; Parasuraman 2011).

In the mining industry, automation is there from quite some time. Processing plants are mostly equipped with automated systems (Dempsey et al. 2018). Recent advancements include extraction of ores using automated longwalls in underground coal mines (Ralston et al. 2017), the loading of materials using automated draglines and shovels (Marshall et al. 2016) and transport of materials by automated haul and dump trucks (Marshall et al. 2016). Autonomous haul trucks are gaining popularity and the manufacturers of these trucks are in the process of developing some levels of automation in the system (Dempsey et al. 2018). This initiative will help to reduce the effect of whole-body vibration on human operators (Mayton et al. 2014) and accidents caused by haulage equipment (Zhang et al. 2014).

Although at a glance, automated systems seem to be only beneficial for productivity and occupational health and safety, risks such as those associated with maintenance work are still there (Dempsey et al. 2018).

3.2.2 Teleportation in Mining Industry

One of the major benefits of the new technologies is the teleportation of mining equipment. This will increase the safety and health perspective. The miner can operate the equipment a safe distance away from the hazardous environment. It can also be used in rescue operations if the environment is too hostile for rescue teams also (James et al. 2011). The main interfaces for this system will be the control and feedback mechanisms.

Thus, there are several scopes for ergonomics practices in this area. One major factor will be the design of the workplaces for the operators (Dempsey et al. 2018). If the equipment and workstations are designed following ergonomics principles, the whole system will be benefited (Horberry et al. 2016).

However, the teleportation technique may lead to more sedentary work. Extensive research is on the health effects of this technology is needed (Dempsey et al. 2018). Different interventions such as alternate work in sitting and standing positions, designing workplaces that enable more movement (Pronk 2015). Extensive research in this area can be very beneficial for mining industries.

3.2.3 Wearable Sensors in Mining Industry

To ensure the safety of the mines, collecting performance data from workers in real-time is important. However, it is a big challenge that remains in case of the mining industry (Dempsey et al. 2018). Body-worn technology evolution plays an essential role in this regard. Existing technologies such as externally worn goniometers, in-shoe pressure sensors are limited in use. The unfavourable environment inside the mines ensures early damage to these devices. This forces researchers to adopt different indirect methods such as video-based methods or laboratory simulations

(Nasarwanji et al. 2016; Pollard et al. 2015; Heberger et al. 2012). The evolution of body-worn technologies can provide solution to these challenges by shrinking their size and being more accurate (Dempsey et al. 2018).

One such evolved product is wearable sensors. The real-time information about miners' safety and health can be obtained easily as these sensors can be worn continuously (Patel et al. 2012). The main structure of wearable sensors consists of three main parts: sensing block, communication block and signal converter (Patel et al. 2012). Some commonly applied sensors in the mining industry are environmental sensors, physiological and biochemical sensors and motion sensors (Dempsey et al. 2018). Temperature, humidity and presence of gases can be measured by environmental sensors (Kassal et al. 2018). Different physiological parameters of miners such as pulse rate, blood pressure, respiratory rate and body temperature can be measured by physiological and biochemical sensors (Kaur et al. 2018; Qian and Long 2018). There are several types of motion sensors such as inertial measurement units (IMUs), smart textiles, a global positioning system (GPS). IMUs are used to measure gait stability and estimate fall risk (Jebelli et al. 2016). Respiratory rate and joint angles can be measured by smart textiles (Totaro et al. 2017; Atalay et al. 2017). To warn a worker about perilous environment GPS are used (Choi et al. 2017).

However, wearable sensors also have limitations. Study emphasising those shortcomings will yield a better result. IMU like sensors are prone to get disrupted by magnetic fields and drifts (Robert-Lachaine et al. 2017; Guow et al. 2018). Thus, the accuracy and validity of these devices are one of the emerging challenges. Durability in mine settings is also required to be investigated (Dempsey et al. 2018).

Data fusion and algorithms can provide a mostly accurate scenario of activities and environments of the mines (Dempsey et al. 2018). The development of complex algorithms can lead to an accurate estimation of risks in the mines. For example, complex algorithms can do a real-time assessment of workers' whole-body fatigue, heat stress, fall risk and risky postures (Dempsey et al. 2018; Jebelli et al. 2016; Bullar et al. 2018). This area also provides an interesting research lacuna to pursue in future (Dempsey et al. 2018).

Arguably, the most important challenge in this context is addressing the perception of wearable sensors among the miners. It was observed that subject's willingness to adopt wearables such as GPS vests or wrist bands is influenced by three factors. These are perceived usefulness of the sensors, social influence and perceived privacy risks (Choi et al. 2017). These issues are needed to be discussed and resolved before wearable sensors can truly be a part of industries and increase the safety and health perspective.

3.2.4 Exoskeletons in Mining Industry

Other than wearable sensors, a new aspect of technology is exoskeletons. The main purpose of an exoskeleton is to augment human capability by reducing biomechanical loads. This in turn reduces the risk of work-related musculoskeletal disorders. Two types of exoskeletons are there. Active exoskeletons augment human power using

actuators. Passive exoskeletons store and release energy during movement. These are used in rehabilitation (Huysemen et al. 2018).

However, despite the benefits of active exoskeletons, some issues are there to be worked upon before their widespread and more effective use:

i. It was observed that some designs increase tension in the back extensors while providing upper body support. Otherwise, these increase lower body stress while providing back support (Berret and Fathalla 2001).
ii. The design of attachments may lead to contact pressure discomfort (Berret and Fathalla 2001).
iii. From a safety context, the effect of exoskeletons during emergencies needed to be evaluated (Dempsey et al. 2018).
iv. The rest and recovery time is important, as other muscle groups may be at risk due to redistribution of loads (Weston et al. 2018).
v. Workers' perception and willingness is a major point to consider.
vi. The effect of long-term use on overall fitness, strength and production capability is needed to be investigated (Dempsey et al. 2018).
vii. Less force required for a task may make it repetitive leading to overuse injuries (Dempsey et al. 2018).
viii. The adjustability of design might lead to worker selection criteria (Dempsey et al. 2018).
ix. The overall space dimension and clearance may require unusual postures to be adapted (Dempsey et al. 2018).

Although new technologies show promise for better productivity and safety in different aspects of mining, the adaptation in the Indian context should be done with careful considerations. For example, a large number of people in India are dependent on the mining industry for their livelihood. Automation without consideration may create more problems than solutions. Proper treatment of human resources is necessary for reaping the benefits of Industry 4.0. Thus some considerations should be involved (Loow et al. 2019) (Table 2):

i. Ensure the profit and competence of the mines;
ii. Utilise the human resources instead of discarding them;
iii. Develop flat organisations based on a socio-technical system that encourages creativity and empowerment;
iv. Handle privacy and integrity issues;
v. Follow social responsibility.

3.3 Ergonomic Challenges in Indian Mining Context- a Special Consideration

The Indian mining industry, like the country itself, is huge and diverse. The geography, environment, population, culture and social structure of India produce some of the unique characteristics of this industry. To optimise productivity and workers'

Table 2 Emerging mining technologies and scope of Ergonomics

Area	Scope of ergonomics
Automation	Allocation of functions Effect on mental stress, perception, attention, learning, human errors and overall safety Maintenance work
Teleportation	Design of control and feedback mechanisms Effect on work pattern (sedentary work) Health effects Design of workstation and alternate work
Wearable sensors	Effect of unfavourable physical conditions Users' perception
Exoskeletons	Changes in the muscles other than those supported by it Discomfort and perception of the users Safety in emergency situations Redistribution of loads Effect of long term use

health and safety in this sector, ergonomics researchers and practitioners should take care of these special challenges. Several steps were already taken officially in that direction (Sishodiya and Guha 2013). However, a major part of the necessary approach is still remaining undone. Mining is arguably the most dangerous profession in India (Rajashekar and Sharma 2017). To tackle this stigma, the associated unique sociotechnical system should be understood first.

Indian mining sector comprises big and small, manual and mechanised mines. Most large mines are fully or partially owned by the state or central government. However, a large number of small-scale mines are mostly owned by private entrepreneurs. These are generally operated manually (Sishodiya and Guha 2013). These also utilise a large number of unorganised workforces, which can be a major area of concern for occupational health and safety (Sishodiya and Guha 2013). Being one of the most populated countries, India is never short of skilled and unskilled labours. This results in a negative approach about occupational health and safety. This is especially true for this kind of privately owned, small scale industry with unorganised labours.

Outside the official data, analysing the news and non-government organisation reports, the plight of the miners and to that extent mining industry is evitable. Some of the infamous cases are:

i. Silicosis is a large part of India due to working in mines and quarries or living nearby; many of the affected are underage whose employment is illegal (https://www.nationalgeographic.com/culture/2019/01/silicosis-sick-indian-miners-sandstone/).
ii. The abandoned dumps of asbestos mines in Raro village of eastern India still cause a high prevalence of asbestosis among villagers (www.medicalexpress.com).

iii. Rathole coal mining in the Jaintia Hills of Meghalaya often leads to flooding and other accidents killing many workers; the unorganised labours there cannot access any benefits of safety acts (https://economictimes.indiatimes.com/industry/indl-goods/svs/metals-mining/sc-asks-meghalaya-to-deposit-rs-100-cr-fine-for-illegal-coal-mining/rticleshow/70053543.cms?from=mdr#:~:text=The%20National%20Green%20Tribunal%20had,to%20resume%20as%20per%20leases).

These cases clearly show that one of the major challenges is the implementation of an ergonomics intervention in small scale mines as they remain outside the radar of the legislatures. Thus, the main focus of ergonomic research in the Indian mining industry should be creating an environment that will ensure proper considerations of safety and health. The stakeholders should emphasise the specific needs for small- and large-scale industries, for both the owners and the workers.

From the framework of the Indian Mines act of 1952, some researchers have identified several future prospects that should be addressed (Sishodiya and Guha 2013):

i. Prevention and control of pneumoconiosis;
ii. Hazard monitoring at mines;
iii. Noise-induced hearing loss (NIHL);
iv. Risk from vibration;
v. Prevention of sudden deaths at work;
vi. Prevention of musculoskeletal disorders;
vii. Development of human resources;
viii. Accident prevention and safety.

To tackle NIHL, noise mapping is an effective measure. Noise maps provide a clear scenario about the propagation of noises in an area surrounding a source. Under the support of the Indian Ministry of Mines, several projects of noise mapping in mining areas has been undertaken. These projects are yielding effective results for battling NIHL (Manwar et al. 2016; Kulkarni and Mandal 2015). However, extensive studies like this, especially for small scale mines should be carried out.

Vibration related risks in Indian mines are often underestimated and remains unexplored. Indian mining legislatures do not cover vibration specifically. Thus, there is a lack of strategy about the risk of vibration in mines. Some researchers have prescribed mandatory vibration monitoring for all mechanised and semi-mechanised mines (Mandal and Srivastava 2006).

There is no database for musculoskeletal disorders in Indian mines. However, some primary studies showed that underground mine workers are particularly prone to develop WMSDs (Sishodiya and Guha 2013). In some other studies risk of WMSDs has also been found for surface mine workers. Operators of dumpers, dozers, graders, electricians are among the affected groups. Back, neck and hand injuries are common in these cases (Jeripotula et al. 2021). Extensive research for developing a database is needed.

Table 3 Few important scopes for ergonomics application in the Indian mining sector

Hazard identification and preventive measure design- especially for small scale mining sectors and hazard prevention for the settlements near mining areas
Development of an elaborate database of WMSDs in different mining industries- monitoring the dynamics over the year
Risk quantification and ergonomics intervention in designing a workplace, equipment, interfaces etc
Designing cost-effective and sustainable solutions for optimized safety, wellness and productivity
Participatory intervention design involving all the stakeholders
Application of cognitive ergonomics to understand and design the mining operations
Assessment of the effects of Industry 4.0 in Indian mining and sociotechnical context

There are different statistics of using PPEs in different mines (Rajashekar and Sharma 2017; Pandit and Tiwari 2008). The reasons for not using PPEs can be varied, ranging from inconvenience, hot and humid weather of the country to a perception of the workers. However, any comprehensive studies or reviews on PPE distribution and use in Indian mines were not found. To reduce the risk from exposure to chemical and biological hazards in mines, this area of research is exclusively important.

Finally, the recent developments of Industry 4.0 are changing the mining industry rapidly (Loow et al. 2019). The final challenge for the Indian mining industry will be to access the benefits of this advancement with careful considerations of the Indian context. Analysing these technologies from human factors point of view will help to reach that goal (Table 3).

4 Conclusion

Mining industry is a traditionally hazardous environment for occupational health and safety. This documentation provides an overview of traditional and new challenges of ergonomics in this context. The traditional challenges of hazard and risk assessment and control still remain. However, the methods to analyse these are improving to be more and more accurate with time. A substantial amount of research is still being undertaken. The control and prevention measures also require a lot of attention in this regard. The ideas of industry 4.0 is revolutionising the assessment, prevention and control measures, but also opening newer areas of ergonomic challenge.

The scenario in the Indian mining industry becomes more critical with the addition of more complex sociotechnical systems. Thus, with all the mentioned challenges, the Indian context should be adapted to get a more suitable result. One of the major challenges that need to be addressed is developing an awareness program to improve the perception of ergonomics among the stakeholders and also to understand the criticality of the individual stakeholder's needs.

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Disasters in Mine: Strategies for Prevention, Management and Control

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1 Introduction

The mining sector contributes significantly to national development. The earth crust has innumerable minerals and the development of recent technologies for its extraction demands strategies for the prevention, management and control of possible hazards that may arise during these activities. India stands second in the world, in terms of coal production and is the fifth largest country in terms of coal deposits. India has rich deposits of many metallic and non-metallic minerals. There are around 1531 mines currently operational which contributes significantly to the economic growth of India and provides employment to around 7,00,000 individuals (Randive and Jawadand 2020).

According to the Directorate General of Mines Safety (DGMS), India, an agency, functions under the Ministry of Labour and Employment, a *mining disaster* can be defined as an accident where ten or more fatalities have occurred however, in the US, a *mining disaster* is when five or more fatalities at any given point occur at any mine. In India, during 1901 to 2007, 55 mining disasters have been recorded accounting for 2200 deaths. The mines in China are far more unsafe. In the year

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_12

2004, around 6300 miners died due to flooding, gas explosion, and fires in China's mines. In contrast, in the year 2007, only 65 deaths were recorded in the mines in the United States (Kumar 2010). Figure 1a shows comparative year-wise fatality data from 2015–2020 of the United States (US), South Africa and India. From the figure, it is clear that the fatality rate was higher in Indian mines compared to the other two countries; however, South Africa had an increased fatality rate in 2020 compared to

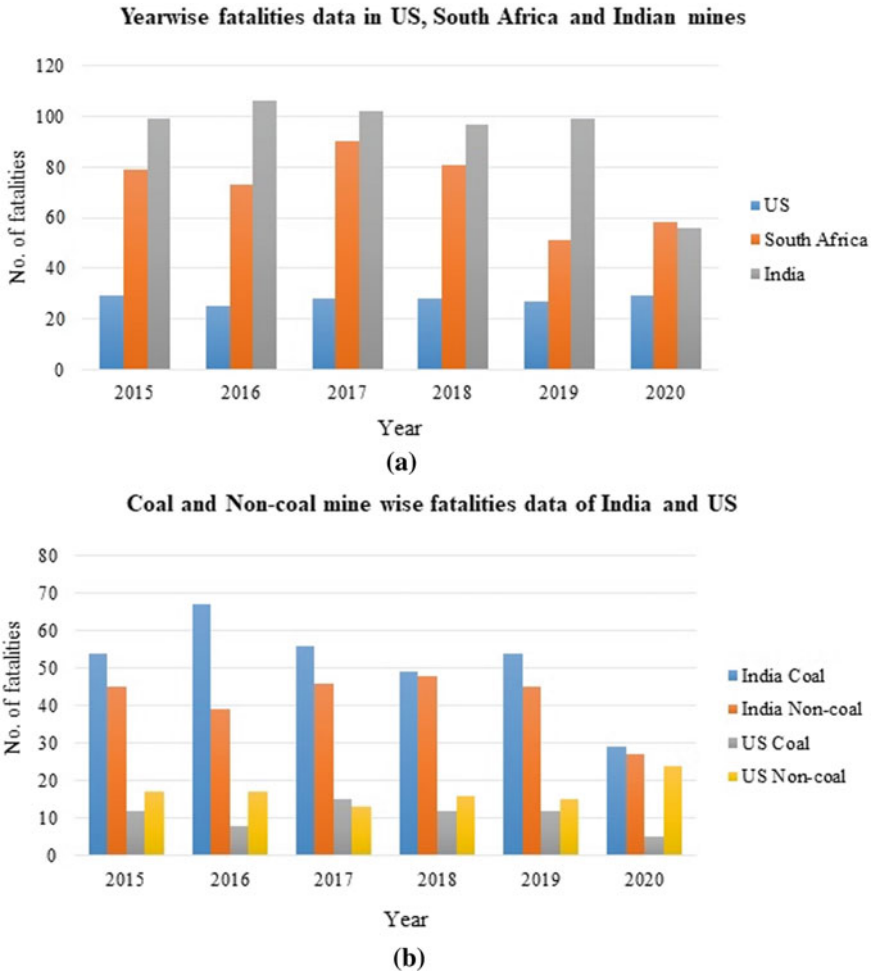

Fig. 1 **a** Year-wise fatalities data in US, South Africa and Indian mines (The data for 2020 in case of Indian mines was collected till October month). **b** Coal and Non-coal mine wise fatalities data of Indian and US (The data for 2020 in case of Indian mines was collected till October month). [*Source* for Fig. 1a, b: Fatality Reports. Mines Safety and Health Administration. Virginia; Annual reports, Department of Mineral Resources, Arcadia; Annual Report 2019–20. Ministry of Labour and Employment]

the other two countries. For the year 2020, the Indian mining data was included till October month only, hence it is slightly close to South Africa. Similarly, the fatality statistics of coal and non-coal mines of India and the US, indicates higher fatality in Indian mines (Fig. 1b). The fatality rate was higher in coal mines than non-coal mines in India while the reverse was observed in US mines, which might be due to vehicle accidents and non-transport machinery apart from other causes (Fig. 2a, b) (Fatality Reports 2021; Annual reports nd; Annual Report nd).

The mining and allied activities are vulnerable to a variety of hazards for the workers and the community at large. Therefore, it is essential to consider this issue in order to establish precautionary measures to minimize the occurrence of hazards. *Hazard* can be defined as a source or condition that can cause harm or adverse events to human beings by means of injury or ill health or may damage to the property or the environment or collectively all of these (Rout and Sikdar 2017). A safe and healthy

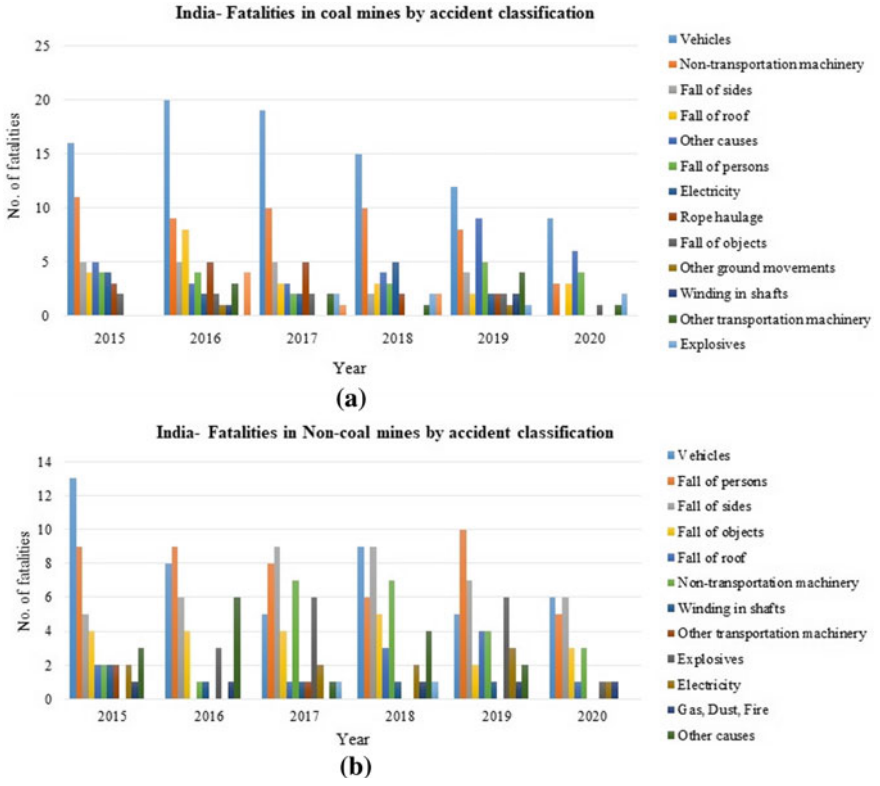

Fig. 2 **a** Fatalities in coal mines by accident classification of Indian mines [*Source* Annual Report 2019–20. Ministry of Labour and Employment]. **b** Fatalities in Non-coal mines by accident classification of Indian mines [*Source* Annual Report 2019–20. Ministry of Labour and Employment]. **c** Trends of serious accidents in Indian coal mines [*Source* Annual Report 2019–20. Ministry of Labour and Employment]. **d** Trends of serious accidents in Indian Non-coal mines [*Source* Annual Report 2019–20. Ministry of Labour and Employment]

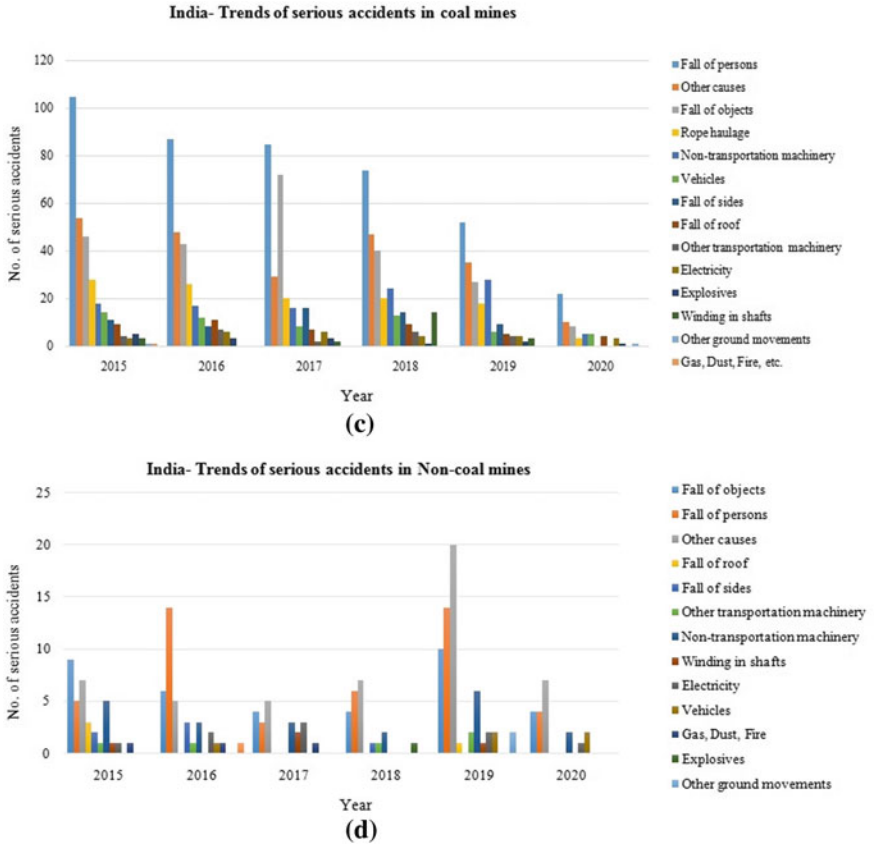

Fig. 2 (continued)

working condition should be there, for a worker in the mining settings. Moreover, the environmental settings should be ergonomically suitable and installed in such a way that doesn't cause any harm to their working efficiency (Tripathy and Ala 2018).

To minimize the occurrence of disasters in mining, risk evaluation and assessment is the first point one should consider. *Risk* can be defined as the probability of occurrence of hazardous events in future and their effects while risk assessment is the systematic approach of evaluation of risk factors associated with the hazardous events or actions (Shi 2019). Risk valuation, assessment and management deals with the prevention of mishaps and control the dangerous activities. It is a collective precautionary effort taken by qualified and experienced personnel after examining the possible risk by both qualitative and quantitative approaches. In different domains of life, such as stock market, or weather forecasting; the risk assessment is done by market survey or forecasting analysis based on historical data and by evaluating the possible outcomes of recent events. However, risk assessment for mining disasters is

totally different and demands individuals' planning before installation of equipment and initiation of mining (Kenzap and Kazakidis 2013).

2 Types of Disaster During the Mining Operation

According to Dash et al. (2017), inundation, roof fall, workplace accidents, fires are the major health and safety hazards in the mining industry (Dash et al. 2017). Manual operation and automatic operation of mining both are well connected with disasters. The disruption of the functioning of mines leads to widespread human, material or environmental losses, which can't be repaired by affected workers using their own resources. The mining disasters are classified into the following categories:

a. **Workplace accidents**

Accidents at the workplace can be disastrous for both employers and employees. Many factors such as chemicals, physical factors, ergonomic factors like poor workstation arrangement, biological hazards (bacteria or animal excrement), safety-related and emotional factors such as mistreatment or extreme stress can be responsible for workplace accidents. The most commonly reported accidents in the workplace include the following:

i. *Overexertion:* It is often observed that the mine workers excessively exert themselves either for self-benefits (over-time payment) or the employment compulsions (absence of one worker in a particular shift). Often to conquer a temporary challenge such as pulling a particular load, erecting a mast, carry a heavy load over their back, carry heavy equipment, or pulling or lifting boxes. Sprains and strains are majorly observed workplace injuries from overexertion.
ii. *Falling:* Accidental fall is a serious health risk in many work environments. Either falling down from stairs or tumbling off a roof, can cause fatal injuries.
iii. *Slips and trips:* Slip is the involuntary act of sliding for a short distance while walking. Slipping may occur due to mud or wet surface because of water accumulation in an area. The trip occurs when the foot gets obstructed by any object on the road surface. Slips and trips can cause muscle sprains, strains, and sometimes rupture of ligaments. The uneven ground surface created due to the movement of haul trucks, loaders, dozers; ruts, holes, hoses, rocks is responsible for most of the accidents due to slip and trips.
iv. *Falling objects:* The falling objects pose a risk of head, shoulder and neck injuries to the workers. Although, wearing a helmet is compulsory inside the mining area, sometimes it can be missed due to oversight.
v. *Repetitive motion:* It's a little less obvious, but repetitive motion injuries have an impact on many types of workers, from frequent computer users who struggle with *carpal tunnel syndrome* (numbness and tingling caused by a pinched nerve) to auto mechanics who develop chronic back pain (Slip, trip nd).

According to DGMS, India, in the year 2019, vehicle accidents contributed to 22% of fatal accidents and fall of persons contributed to 27% of serious accidents in coal mines while in case of non-coal mines, fall of persons and other causes (except to those included in graph) were responsible for fatal and serious accidents. However, in 2018, the fall of persons and fall of objects contributed to 33% and 17% of serious accidents in coal mines while it was 28% and 22% in the case of non-coal mines (Fig. 2a, d). While comparing the data from the last six years, fatalities due to vehicle accidents were highest in the year 2016, among coal miners while in the case of non-coal miners, 2015 was the year with the highest number of fatalities due to vehicle accidents. The overloading of materials, poor illumination, and poor maintenance might be the responsible factors for these accidents (Annual Report nd).

The recent data from Mine Safety and Health Administration (MSHA), an agency of the US Department of Labor, reported 14% fatalities due to slips and trips in US mines (Fig. 3) while according to the Department of Mineral Resources, the Republic of South Africa, 17% fatalities due to slips and trips were observed in the year 2017 (Fig. 4). Due to the non-availability of recent data according to accident classification in South Africa's mines, the 2017 data is presented here (Annual reports nd; Kuykendall 2020).

The comparative evaluation of data from mining areas of Canada suggests that exertion and excessive physical effort by the worker, stress or strain on the body remain the primary cause of the highest numbers of serious accidents from 2015–2019 (Fig. 5) (Annual reports nd).

b. **Subsidence, Caving, and Sinking of floors**

Subsidence is a time-dependent process in which sudden sinking or gradual downward movement of the earth surface occurs. It may result from natural or artificial causes. It occurs in the areas influenced by underground mining in which, the extraction of minerals leads to the creation of big voids. There are many factors that can

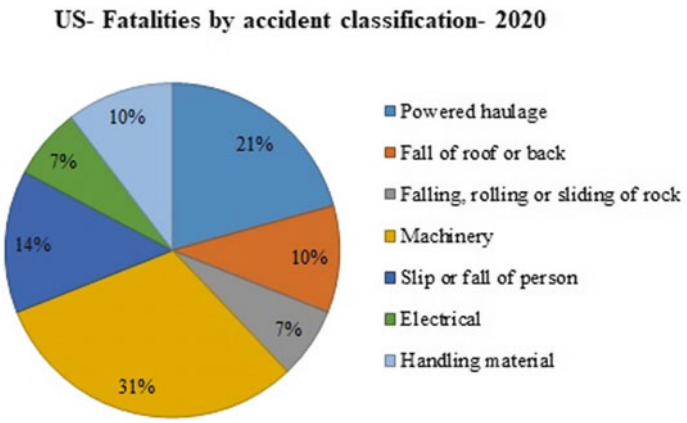

Fig. 3 Fatalities in mines by accident classification in US -2020 data [*after* Kuykendall (2020)]

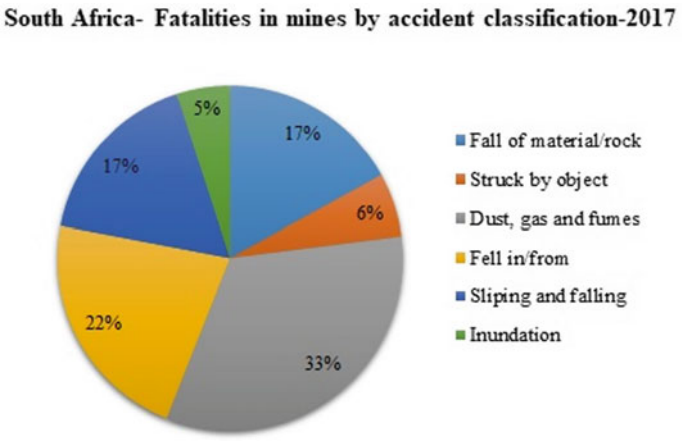

Fig. 4 Fatalities in mines by accident classification in South Africa -2017 [*Source* Annual reports, Department of Mineral Resources, Arcadia]

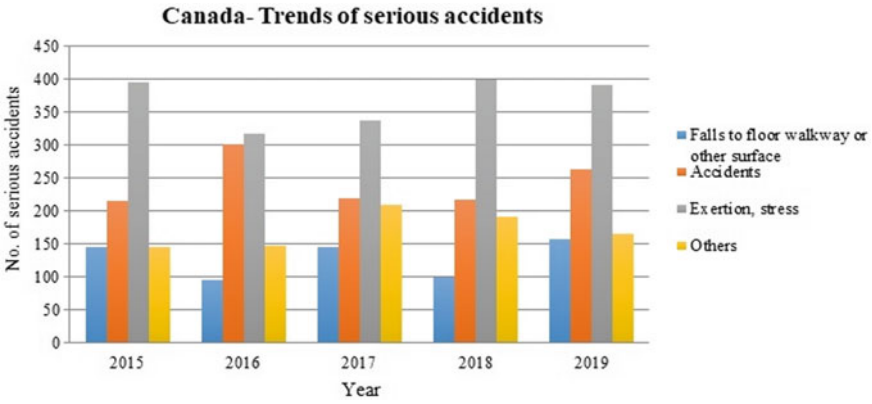

Fig. 5 Trends of serious accidents in mining areas of Canada [*Source* Workplace Safety North. Ontario]

determine the degree of subsidence for example the thickness of deposits, depth of extracted minerals, topography and other geological factors (Lee and Abel 1983).

Over the time, surface deformation (lowering) causes bending of the subsiding area. This bending motion will cause tensile strain in the surface strata that initiates caving/fractures. It increases with continuous extraction and leads to the collapse of the floor area and the void space is filled with overburdened materials. The cracks in mining area affect the ground water quality, which in turn influence the vegetation and animals. It has been reported that subsidence has caused approximately 50% of deaths in underground bituminous coal mines (Yu et al. 2018). An average of 51% of fatalities was caused due to mine collapse in coal mines in Pakistan between the years

2010–2018 as shown in Fig. 6 while in China's mines roof caving was responsible for 15% of fatalities in the year 2016 (Fig. 7) (Shahani et al. 2020; Wang and Fb 2016).

c. **Roof and rock fall**

Roof collapse is a major concern in underground mines, whereas, rock fall is a common concern in opencast mines. To prevent the roof fall, the roof bolting technique is used. During the early 1950s, the roof bolting technique in coal mines was preferred. During the course of time, the grout systems, design of bolts, accessories

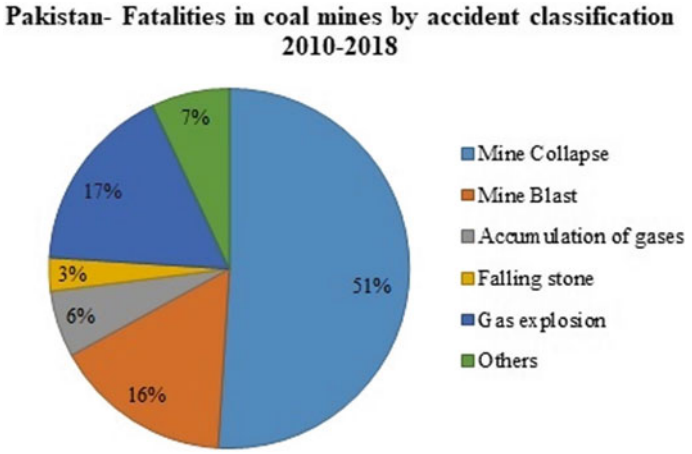

Fig. 6 Fatalities in coal mines by accident classification in Pakistan [Redrawn *after* Shahani et al. (2020)]

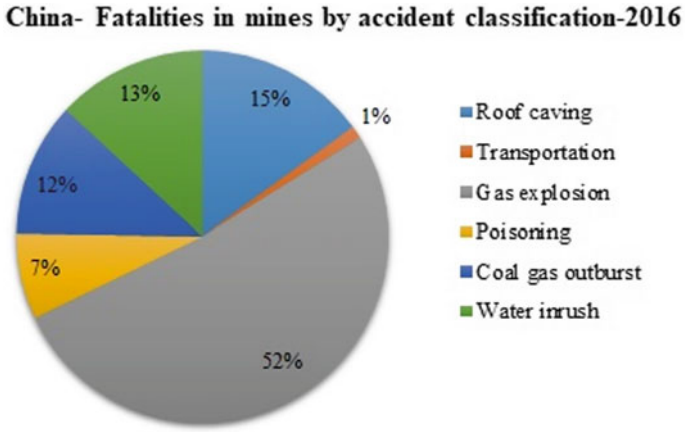

Fig. 7 Fatalities in mines by accident classification in China -2016 data [Redrawn *after* Wang and Fb (2018)]

and installation techniques have advanced considerably. However, in the case of bituminous coal mining, this technique is still used as a primary measure. To support the roof, ground-level stability is a must hence its maintenance with a proper supporting system needs to be done from time to time.

When a rock is detached due to mining activities like blasting or drilling in the high-altitude areas, it moves in the downward direction by rolling, free-falling, bouncing or sliding known as rock fall, which may cause personal and/or instrument loss or both. According to the National Institute of Occupational Safety and Health (NIOSH), the US, around 400–500 injuries are recorded in coal mines due to rock falling every year (Bajpayee et al. 2014; Mark et al. 2009). There were 17% fatalities in mines reported in the year 2017 due to rock fall in South Africa while in Indian coal and non-coal mines, fall of roof accounted for 7% and 2.17% fatalities in the same year (Figs. 2a, b and 4). In US mines, roof fall caused fatalities among 10% of miners in 2020, while in the same year, Indian coal and non-coal mines, recorded fatality rates of 10.34% and 3.70% due to fall of roof (Fig. 3) (Annual reports nd; Annual eport nd; Kuykendall 2020).

d. **Fires**

Fire in mines is another cause of fatalities in mines. This is most common in coal mines where flammable gases are abundant. Other reasons for fire in underground mines are commonly due to electrical damage, hot surfaces also led to fires in cases where flammable liquids are present, vehicles fires (including rubber tires). Fires in underground mine environments can spread in the entire mine depending on the airflow.

In order to make the evacuation strategies smooth or to prevent fires, various safety equipment or systems like fire-extinguisher equipment, ventilation systems or rescue chambers have to be placed at different locations in the mines apart from building an additional escape tunnel. These days, mining systems are becoming more complicated with increasing demands and proportionally the number of shafts, ramps, drifts and other equipment are also increasing in mines. In such cases, it is a tedious task to control fires in mines. Hence, the focus must be given to proper ventilation system (Hansen 2009).

In the case of fire, the following effects are important, namely, stratification, smoke rollback, and throttling. Stratification occurs in response to the differences in density between the warmer, lighter gases (heated by the fire) and the cooler, heavier ambient air. In areas of low-velocity flow, stratification may be evident and pronounced for quite some distance downstream of a fire. An increase in the average airflow velocity leads to turbulent mixing that will disperse the stratified layer into the main body of flow (Hansen 2020; Zhou and Smith 2012).

The smoke rollback also known as smoke reversal or back layering has enough velocity and energy to flow against the mainstream, causing a serious threat to miners. The dimension of the tunnel, the strength of fire and the air velocity are the factors that determine the influence of smoke rollback in any underground mines. Smoke rollback may be seen as an extreme form of stratification, in which the rising plume has enough energy and velocity to move against the main body flow, thus developing

a stratified layer flowing counter-current to the main airflow. There are three main stages of smoke rollback, a critical velocity stage, a partial smoke rollback stage, and a complete smoke rollback stage (Fig. 8). The heat generated may affect the flowing fresh air and the smoke, and the products of combustion may pollute the flowing fresh air in the direction where miners are evacuating (Zhou and Smith 2012).

The minimum airflow velocity which is required to prevent the smoke from rolling back is known as *critical ventilation velocity* (uin). Figure 8a shows the critical velocity stage in which the direction of smoke is in the upward direction of the source of the fire. Figure 8b shows the partial smoke rollback stage in which the highly buoyant heated air may take on upward flow, against the normal air movement and thus generating two layers of air flow, the lower layer of fresh air moving towards forward direction and upper layer of smoke rolling in backward direction. Figure 8c represents the complete smoke rollback stage in which hot air causes complete air flow reversal in cases where fires are growing rapidly. It is usually seen in underground mines (Zhou and Smith 2012).

e. **Inundation**

During heavy rains, the mines may get flooded with water that may cause closure of operation for few days, economical loss due to delay in operation, deaths of workers who are trapped while working in underground mines, are some of the major impacts of flooding. Usually, mining operations take several years to extract the ores and when it is done, the mine is closed. Such derelict mines do not have proper maintenance. Therefore, the dewatering systems which were usually operational during active mining also remain nonfunctional. It leads to inundation inside mines, which often mixes with the groundwater and contaminates it (Risk assessment disaster management plan 2020). In the year 2017, 5% of mine workers died due to inundation in South Africa while in 2016, inundation caused fatalities in 13% of miners in China as depicted in Figs. 4 and 7 respectively (Annual reports nd; Shahani et al. 2020).

To control water inundation following measures should be adapted: (i) The supervisor or manager should make a schedule for routine examination of accumulation of rain water or blockage in the drainage system, (ii) An emergency drainage system must be made which should be monitored from time to time, (iii) Drainage of mine water must be done by using a suitable capacity of pumps, (iv) In case of heavy rains, an inspection of vulnerable areas should be done and workers should be evacuated to a safer place, and (v) In case of the monsoon period, the working in deep mining areas should be avoided.

f. **Release of toxic gases**

Nature has made proper balance in the earth atmosphere and thus has the level of various gases in different layers of the atmosphere. The gases which are produced by mining activities are comparatively high in concentration (conc.) for example methane gas concentration is usually high in coal mines. Due to various mining activities, toxic forms of these gases are generated which are responsible for many mining accidents for example during 2010–2018, a gas explosion was majorly responsible for more than 50% of fatalities in coal mines in Pakistan (Fig. 6) while there were

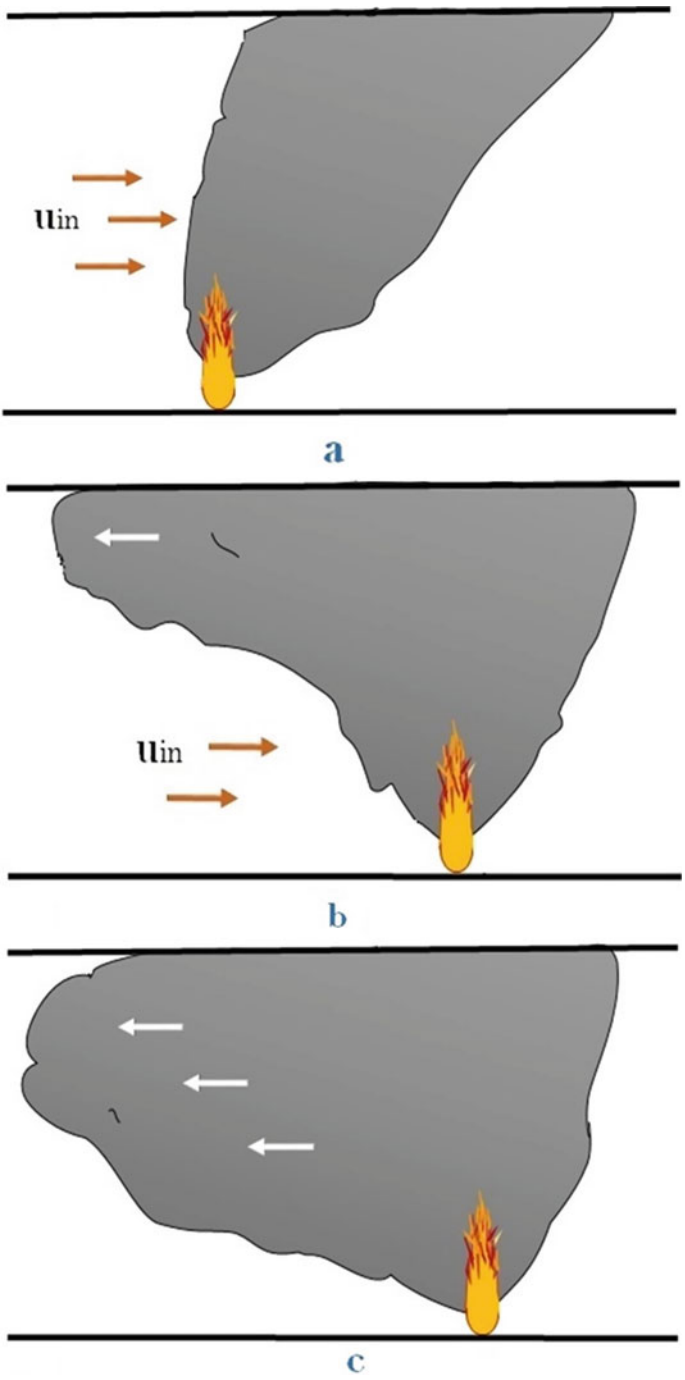

Fig. 8 Diagrammatic sketch showing three stages of smoke rollback [Redrawn after Zhou and Smith (2012)]

52% and 15% fatalities reported due to gas explosion and coal gas outburst in China in 2016 only (Fig. 7) (Shahani et al. 2020; Wang and Fb 2018). Common causes are overpressure of a particular gas, improper sealing of gas tank/valve, tank leakage due to collision with any object. The nature and possible health effects of toxic gases in mines are summarized in Table 1 (Mine Gases nd; Osunmakinde 2013).

g. **Suffocation due to oxygen paucity or improper ventilation**

Ventilation in underground mines is crucial for the safety of miners. The depth of mine lacks oxygen and an increase in sweating is usually seen due to heat inside the mines. The worker may experience suffocation due to difficulty in breathing and may collapse. The quality mining ventilation procedure is a secure and efficient way for maintaining proper aeration in mines and avoids the accumulation of toxic gases. Although ventilation doesn't contribute directly to production the lack of proper ventilation often causes a reduction in workers' efficiency and decreased productivity, increased accident rates and absenteeism (Kursunoglu and Onder 2015; Howden Article 2021).

Exposure to an oxygen-deprived atmosphere causes asphyxiation, headache, nausea, mental confusion, dizziness or loss of life. Oxygen is the only component of the air capable of supporting life. However, the addition of any gas, other than oxygen to air reduces the oxygen concentration through displacement and dilution. Nitrogen and inert gases like Argon and Helium may lead to asphyxiation. Breathing as little as one or two breaths of air containing too little oxygen can have severe and immediate effects, including unconsciousness. Because there are no warning signs of reduced oxygen concentrations, these environments are extremely risky. Deterioration of wooden objects, mineral oxidation in mine, fire and explosion are other factors for increasing the concentration of toxic gases. It is well known that atmospheric air is composed of approximately 20.94% oxygen, 78% nitrogen and other trace components. When the level of oxygen reduces below 19%, difficulty in breathing is observed while when it reaches below 15% symptoms like dizziness, visual impairments are observed. However, when the concentration is less than 9%, unconsciousness and even death are seen (Özmen and Aksoy 2015). Due to dust, gas and fumes, 33% of fatalities were recorded in 2017 in South Africa's mines (Fig. 4) while in Pakistan from 2010 to 2018, the accumulation of gases caused 6% of fatalities in coal mines (Fig. 6) (Annual reports nd; Shahani et al. 2020).

h. **Accidents during transportation**

According to a recent report (2019–20) by DGMS, India, the rate of a fatal accident in both coal and non-coal mines have been reduced for the period 2011–2019 (up to Oct 2019) as compared to 2000–2010. The average fatal accidents and fatality rates per thousand workers for the period 2000–10 was 0.27 and 0.40 while it was 0.20 and 0.24 during 2011–19 (up to Oct 2019) for coal and non-coal mines respectively. Another analysis revealed that during 2018, in coal mines 30% of fatal accidents were only due to dumpers, trucks while there were 17% accidents in the case of non-coal mines. Reasons could be workload, fatigue, reduced alertness of drivers while driving or use of mobile phones, drivers' wish to keep working and earning.

Table 1 The nature and possible health effects of toxic gases in mines

Gases	Properties	Health effects	Concentration in atmosphere	Remarks
Carbon Dioxide (CO_2)	Colorless, odorless, heavier than air. At high concentrations, it has an acidic taste	At 5% conc., it stimulates respiration; at 7–10%, individuals experience unconsciousness after few minutes of exposure	0.03% approximately 280–390 ppm	It is the common gas in black damp produced as a result of biological oxidation and it replaces oxygen in case of enhanced conc. in mines thus forming a toxic environment
Carbon Monoxide (CO)	Colorless, odorless, tasteless and combustible in nature, lighter than air	In case of inhalation, the CO immediately binds with blood hemoglobin (Hb) thereby affecting the regular oxygen-carrying capacity of blood. At 200 ppm conc. slight headache, fatigue, vertigo, nausea. At 400 ppm conc. an individual may experience a headache on font head while it is lethal after 3 h of exposure. Lethal period reduces with increase in conc. Death may occur in 10–15 min when exposed to 6400 ppm conc	0-trace ppm	It is produced by detonated explosives and diesel engines and by partial combustion of organic carbon-based materials

(continued)

Table 1 (continued)

Gases	Properties	Health effects	Concentration in atmosphere	Remarks
Hydrogen (H_2)	Colorless, highly reactive, tasteless, odorless and combustible in nature, lighter than air	High concentration causes oxygen-deficient environment; headaches; ringing in ears; drowsiness; nausea; skin having blue colour. At higher concentrations, it can cause an oxygen-deficient environment, headache, lethargy, nausea	0.5 ppm	It is produced as a result of the partial combustion of explosions. It is released when water is showered over hot mine fires or when strong acids are added on iron or steel materials. It is a common gas in battery charging stations. Being highly explosive in nature, it needs only 5% of oxygen to ignite and in presence of heat or flame it explodes. The explosive range is between 4.1–74%. Conc. above 7–8% can result in an explosion
Methane (CH_4)	Colorless, odorless, tasteless, flammable; lighter than air, largest component of fire damp	At higher conc. it displaces oxygen and causes asphyxiation, vertigo, headache and nausea	1.79–2.0 ppm	Around 70–98% of methane is found in fire damp and is common toxic gas found in underground coal mines. The explosive range is 5–15% with 12.5% of oxygen
Nitrogen Dioxide (NO_2)	It has a bleach odor, nonflammable and reddish-brown colour in high conc. heavier than air	At 1–13 ppm conc. irritation of nose and throat, at 10–20 ppm conc. irritation of eyes, nose and in the upper respiratory tract. It produces nitric acids in the lungs at higher conc. i.e. 90 ppm that leads to pulmonary edema after 30 min of exposure	0.03 ppm	Extremely toxic

(continued)

Table 1 (continued)

Gases	Properties	Health effects	Concentration in atmosphere	Remarks
Sulfur Dioxide (SO_2)	Colorless, suffocating or choking odor, tasteless, acidic in nature, nonflammable and heavier than air	Irritation of eyes and coughing at 20 ppm conc. At 50 ppm, irritation of eyes, nose and throat, choking, cough, shortness of breath occurs. Conc. above 150 ppm is enormously displeasing while conc. above 400 ppm is lethal	1.0 ppm	It is produced during the blasting of sulfide ores. It is also present in diesel exhaust. When exposed at higher concentrations, it causes the same effects as of NO_2, except that sulfuric acid is produced inside the lungs

Apart from these, poor shift management, achievement of production target, lack of maintenance of vehicles could also be the cause of accidents due to vehicles (Bajpayee et al. 2014; Sudiyanto and Hendra 2017).

i. **Accidents during conveyor belt handling**

Belt conveyor is an important transport system in mining operation. Speed control is considered as the crucial factor in belt conveyers to reduce energy consumption. Belt breaking, motor overheating and spilling of loaded materials from the belt are some of the risks associated with belt conveyers. Figure 9 shows a conveyor belt transporting the iron ore. The image illustrates the functioning of a belt conveyor. Accidents may occur due to overloading, blockage during transport, rip or torn in a belt, using the too old belt for transport or materials being removed while the conveyer is functional (Hea et al. 2018).

Blockage detector, rip detector, rotation detector are the devices that detect blockage, rip or tear in conveyor belt and number of rotation respectively. For example, a rip detector is a sensor-based device that is installed after the material loading point below the carrying run of the belt. When a broken belt surface sweeps through the cable of rip detector, it is detected by the device. The rotation detector or speed controller gives an alarm signal or may shut down the system if the speed of belt conveyor deviates from the preset speed (Shah nd).

In case of electric drive motors, the system is protected by overload alarm signals. Handling metal ores may tear up the belt when used for a longer duration, hence routine check must be done and the belt should be changed whenever required. Suitable motor oil and grease should be applied for the proper functioning of the motor. According to operation and maintenance requirements, for conveyor belt, recommended illumination is 40 to 100 lx. For the control room, illumination must be 300 lx (Shah 2018).

Fig. 9 A conveyor belt in an iron ore mine

ii. **Road accidents**

Road accidents in mining is of great concern because road accidents affect mining activity in various ways like workers' injury, accident or death due to road accident, damage of the vehicle, traffic jam due to vehicle accidents which may lead to interruption in mining activity to some extent. The number of fatal accidents due to dumpers and trucks were highest in Indian coal mines during 2015–2020 as shown in Fig. 2a and is not at an acceptable level (Annual eport nd). In Canada, 27% of injuries were recorded due to accidents in the year 2019 (Fig. 5). The major causes of accidents are reversal run over, front-run over, overloading, lost control, collision (Annual reports nd). As per the report published in The Hindu newspaper, there were 377 workers in coal and other mines who died due to accidents between the years 2015 to 2017. Out of 377 cases, 129 workers died in 2017 alone, 145 in the year 2016 and 103 in 2015. Coal mines of Jharkhand state of India had the highest number of deaths i.e. 69 deaths in these three years. Telangana and Madhya Pradesh recorded 32 and 29 deaths respectively. Among the metal mines, 152 deaths were registered of which Rajasthan recorded 48 deaths (Singh 2019).

Accidents due to transport vehicles can be controlled by taking the following measures (Risk Assessment Disaster Management Plan 2020; Patrucco et al. 2021; Durga and Swetha 2015):

(i) Broad signs must be provided at each turning point in mines, (ii) While reversing the vehicle, care should be taken that it should be man free and alarm and light systems must be used while reversing, (iii) Routine checking and repairing should be done for all the transport vehicles, and (iv) It should be under the direct control of supervisors or managers and overloading must be avoided, (v) Proximity sensor device: There are chances of collision between machines and personnel in mines due to restricted access, small spaces, decreased visibility. To avoid collision NIOSH, US has made a proximity sensor device, Hazardous Area Signaling and Ranging Device (HASARD) system which is based on low-frequency magnetic fields and found successful in detection of a possible collision between mining equipment by giving audible, visual and vibratory signals. Similarly, devices based on an ultrasonic sensor, infrared light anti-collision sensor and radar sensor have been developed.

3 Prevention and Management Strategies for Control of Disasters

Over the last few decades, many mining industries around the globe including Canada, Australia, New Zealand, Britain, America, and South Africa has made certain regulations and adopted various risk management strategies for control of mining disasters. Risk assessment and management is a systematic approach applied to mitigate or eliminate risk by implementing preventive measures at the workplace.

Risk management strategy mainly involves context establishment, assessment of risk, and treatment strategies (Tripathy and Ala 2018).

(i) **Control of gas leakage**

The increase in the number of deaths in mining operations due to gas leakage is alarming. Leakage of gas is as such can't be detected by the human respiratory system. Thus, a monitoring device must be installed in the mining route which should be able to efficiently detect the gas leakage.

Coal mine gas drainage

To stop coal mine gas disaster, emptying of coal seam gas is a most acceptable method that also provides a secure environment, energy conservation and is also applicable in high gas mines i.e. degree of gassiness- II in which methane emission rate is 1–10 m^3/t. Though the concentration of gas drainage in coal seams is usually low, the gas can be collected by the use of pre and post-drainage devices. The selection of a suitable gas drainage method is also important to increase the purity of captured gas in coal seams and prevent methane to enter in the mine airways, and to reduce the low capture efficiency. By following proper installation and maintenance, routine monitoring, and appropriate drilling method, the methane gas drainage technique can be improved (Best Practice Guidance for Effective Methane Drainage and use in Coal Mines 2010; Ba 2020).

Detection device

The detection device or gas leakage usually has a sensor that detects the concentration of gas (for e.g. methane) and gives a signal according to the proportion of gas present in that area. It may be coupled with other devices that initiate ventilation in case of presence of toxic or combustible gas is observed, disconnects the power supply or may give an alarm signal. The popular sensors and their range of gas detection are mentioned below (Kumar et al. 2013; Liu et al. 2012; How does an oxygen sensor work 2020; Diamagnetism and Paramagnetism nd):

- Electrochemical method: Oxygen, CO, Nitrous oxide (N_2O), Nitrogen dioxide (NO_2), Nitric oxide (NO), Hydrogen sulphide (H_2S), Sulphur dioxide (SO_2)
- Paramagnetic: Oxygen
- Flame lamp method: Oxygen, CH_4
- Catalytic oxidation: CO, CH_4, Hydrogen
- Thermal conductivity: CH_4
- Infrared: CO_2, CO, SO_2
- Semiconductor: CO, H_2S
- Optical: CO_2.

Catalytic bead sensor

Catalytic combustion is a method by which the gas can be ignited at a lower temperature in the presence of some chemical media. In order to burn the combustible gas, mixtures have to attain an ignition temperature but by using chemical media, the

ignition temperature can be reduced. The wire coil is either coated by the glass or ceramic material with a catalyst. When electricity is applied, the coil is heated and the desired temperature attains, it allows burning of the combustible hydrocarbon (CHC) gas which is to be monitored. When the flammable gas is oxidized, a change in temperature is observed which can be detected by the coil.

Infrared Radiation (IR) detector

When the IR radiation passes through a volume of gas, the gas molecule absorbs a part of IR radiation and starts vibrating more vigorously due to the gain of energy resulting in a rise in the temperature of the gas molecules. The rise in temperature can be detected by the detector. The other signal could be the decrease in radiation energy caused due to a decrease in the wavelength of the gas molecule. It can be used for the detection of CO, CO_2, NH_3 (ammonia) gases.

Semiconductor

The metal oxide semiconductor sensors are based on the principle of redox reaction between the target gas and the oxide surface. To detect the combustible, reducing or oxidizing gases, metal oxides of SnO_2 (Tin (IV) oxide), CuO (Copper (II) oxide or cupric oxide), Cr_2O_3 (Chromium (III) oxide), V_2O_5 (Vanadium (V) oxide), WO_3 (Tungsten (VI) oxide) and TiO_2 (Titanium dioxide) can be used. The redox reaction initiated between the metal oxides and molecules of target gas leads to an electronic variation on the oxide surface which is transduced into an electric resistance variation of the sensor. By measuring the change of capacitance, mass, work function or reaction energy, the change in charge carrier concentration can be detected. The semiconductors are primarily used in toxic gas detection.

Electrochemical sensor

As the name suggests, the chemical reaction caused due to the presence of gas generates a current which is detected by the detector. The device contains an anode, cathode, and an electrolyte.

Flame Ionization Detector

The Flame Ionization Detector (FID) technique utilizes a hydrogen flame to burn organic molecules. In this way, ionized species generate current which is detected by the ion collector.

Fiber optic sensor

In this method, when the wavelength of the gas molecule overlaps with the absorption band wavelength of the analyte, the spectro-chemical changes are observed. Also, the optical signal can be obtained by converting the analyte concentration using the analyte-specific reagent transducer.

Paramagnetic sensor

The paramagnetic property of oxygen is used as the basis of the development of paramagnetic sensors while most other gases are diamagnetic in nature i.e. they are

repelled out in presence of a magnetic field. The reason is, the diamagnetic substance contains paired electrons and they don't have any unpaired electrons. According to *Pauli Exclusion principle,* 'the electron spins are oriented in the opposite direction and no two electrons can occupy the same orbital at the same moment,' this causes the cancellation of magnetic fields of the electrons and the atoms are no longer attracted into a magnetic field. In fact, a diamagnetic substance creates an induced magnetic field in the opposite direction of an externally applied magnetic field and thus they are repelled in presence of a magnetic field. The oxygen molecules get attracted towards strong magnetic fields, hence in this type of sensor, the sample gas is passed through the magnetic fields and the change in flow rate of the gas is directly proportional to the oxygen level in the gas. In another method, as paramagnetism is temperature dependent, the cold oxygen molecules get attracted towards magnetic fields while when the heat is applied, they leave the magnetic fields, leading to the generation of current that can give information about the oxygen level.

RFID (Radio Frequency Identification)

The RFID technology can be applicable even in deep underground mines to detect methane level efficiently. To detect methane gas and CO_2, a wireless device has been developed by US based Tunnel Radio. It contains a gas sensing module which can be easily installed and gives continuous gas level readings to the computer system. The methane monitoring tool has to ability to auto off once the methane level is 1.5% (Durga and Swetha 2015; Liu et al. 2012).

Remote monitoring gas sensing framework

The study done by Osunmakinde (2013) on remote monitoring of toxic gases targeting underground mines has analyzed various aspects of using a Wireless Sensor Networks (WSNs) and temporal statistical models in an attempt to effect autonomous decision making in real time. Mining and associated activities are linked with possible hazards to both the workers and the community at large. Therefore, it is essential to consider particular problem in order to find out solutions against the issues. The environmental settings should be such as not to harm the worker's efficiency (Osunmakinde 2013).

There are limitations of these devices for example; the thermal conductivity sensors are less selective and sensitive. Similarly, the semiconductor sensor takes more time to respond than electrochemical sensors. When the operational temperature limit exceeds, the IR detector fails to operate. While working in highly humid, dusty environments, the IR detectors demand high maintenance costs. Those gases that don't absorb IR energy, can't be detected by this detector. There are characteristics of an ideal sensor such as low detection limit, high sensitivity and selectivity, less response time and good linearity with a long life cycle. However, whether the above-mentioned sensors would be perfect in all these parameters can't be said thus a combination of the appropriate sensor with the sampling device would give reliable analysis (Kumar et al. 2013).

Fig. 10 A rock breaker operating in limestone mine. The dust generated by this process can be clearly seen

(ii) **Dust monitoring**

Mining areas are considered as the dustiest environmental areas where drilling, blasting, extraction, block lifting, loading of blasted material by excavators to tippers for transport, vehicle movement and other activities generate dust. Figure 10 depicts dust generated during the operation of a rock breaker in a limestone mine. Inhalation of airborne respirable dust generated at the workplace is associated with irreversible diseases including, asthma, silicosis, lung cancer, Coal Workers Pneumoconiosis (CWP), kidney disease and nonmalignant respiratory diseases. Noteworthy, India is the second major producer of cement in the world and the major ingredient in the production of cement is limestone. According to the Indian Bureau of Mines (IBM), limestone usually contains Magnesium Carbonate, either in the form of dolomite [CaMg $(CO_3)_2$] or magnesite ($MgCO_3$) mixed with Calcite ($CaCO_3$). In commercial terms, the rock having 40–45% of $MgCO_3$ is usually known as dolomite (Minor Minerals 2018). Similarly, quarry operations are dispersed all over India and many of these are unorganized operations. Exposure to respirable silica dust (<5μ in size) is associated with silicosis, lung disease, rheumatoid arthritis, small vessel vasculitis and other autoimmune diseases (Hazard prevention and control in the work environment nd; Bhagia 2012; Indian Bureau of Mines 2018; Gallagher et al. 2015). Hence, routine dust monitoring in mining operations would suggest to the mine operators whether the dust levels are under control or there is any need to follow additional preventive measures. Though it is not possible to completely reduce the dust generation few preventive measures can be followed in order to reduce the dust generation: (i) Wet drilling must be done by an inbuilt water injection system at proper intervals to reduce the dust emission from the drill machines, (ii) Regular water sprinkling should be done on blasted heaps and haul roads, (iii) Sharp drill bits must be used for drilling holes and arrangements should be made for bit regrinding, (iv) In order

to clear the accumulation of loose materials, regular grading of haul roads should be done, (v) Over filling of dumpers should be avoided, (vi) Routine maintenance of equipment and vehicles should be done, and (vii) Plantation around mining areas such as road side or in barrier zones should be promoted.

The dust monitoring studies in Indian mines are carried out as per the statutory regulation of DGMS. These studies can give us information like the gravimetric mass of total respirable dust, the chemical composition of dust and the free silica component of the respirable dust. The sampling device consists of a cassette filter of 37 mm size, coupler and aluminum cyclone. The cassette filter has polyvinyl chloride (PVC) filter paper of 5 μm pore size. The PVC filter is pre- and post-weighed on a digital pan microbalance and labelled. Pre and post-calibration of the dust sampler must be carried out for a flow rate of 2.2 L/min. At the site of dust generation, area dust monitoring can be carried out by keeping the sampler vertically at a distance of 5 to 15 m as shown in Fig. 11a. For personal dust monitoring, a sidekick 51 Ex pump is attached to the worker's belt in such a way that it doesn't interfere with the routine work (Fig. 11b). The cyclone and cassette are attached to the collar of the worker (near the breathing zone). The sampling should be done for 8 h shift or it is done from the time the worker enters the mine till he lefts the mine. The Time Weighted Average (TWA) can then be calculated for 8 h shift. According to DGMS, India, the Permissible Exposure Limit (PEL) for 8 h shift TWA should be 3 mg/m^3. The collected dust is used for mineral analysis like free silica content using the Fourier Transform Infra-Red Spectroscopy (FTIR) method by making digestion of the collected dust sample under muffle furnace at 600 °C. The resulting ash can then be mixed thoroughly with 0.2 mg of KBr (Potassium Bromide) (pre-dried overnight at 110 °C oven) using a mortar and pestle and converted into a 13 mm pellet die. The pellet can be analyzed qualitatively by FTIR at 798 cm^{-1} wavelengths (Mankar et al. 2019).

(iii) **Noise Monitoring**

Exposure to loud noise (>85 dBA) in the workplace environment leads to hearing loss. Duration of noise exposure and individual's susceptibility are primarily responsible for hearing loss. Apart from these; age is also a factor that causes hearing loss. It is believed that the noise causes disturbances in ongoing activities like poor work performance, anxiety, vertigo, and headache. in addition to the direct health impacts i.e. Noise-Induced Hearing Loss (NIHL). Noise is considered as a second most important occupational hazard in the mining industry according to NIOSH, US (Metidieri et al. 2013).

There are various sources of noise in mining areas such as drilling, blasting, vehicular movement etc. Though noise due to vehicular movement is discontinuous it will also add to the background noise level. Even the impulse noise can cause devastating changes in the hearing mechanism. For instance, blasting generates high-intensity noise for an extremely short duration (Imaizumi et al. 2003). Drilling also generates continuous noise. Studies suggest that minimum 10 years of exposure to noise can lead to the development of NIHL (Robinson et al. 2015). The higher noise level has been observed in mechanized mines and various reports mentioned about

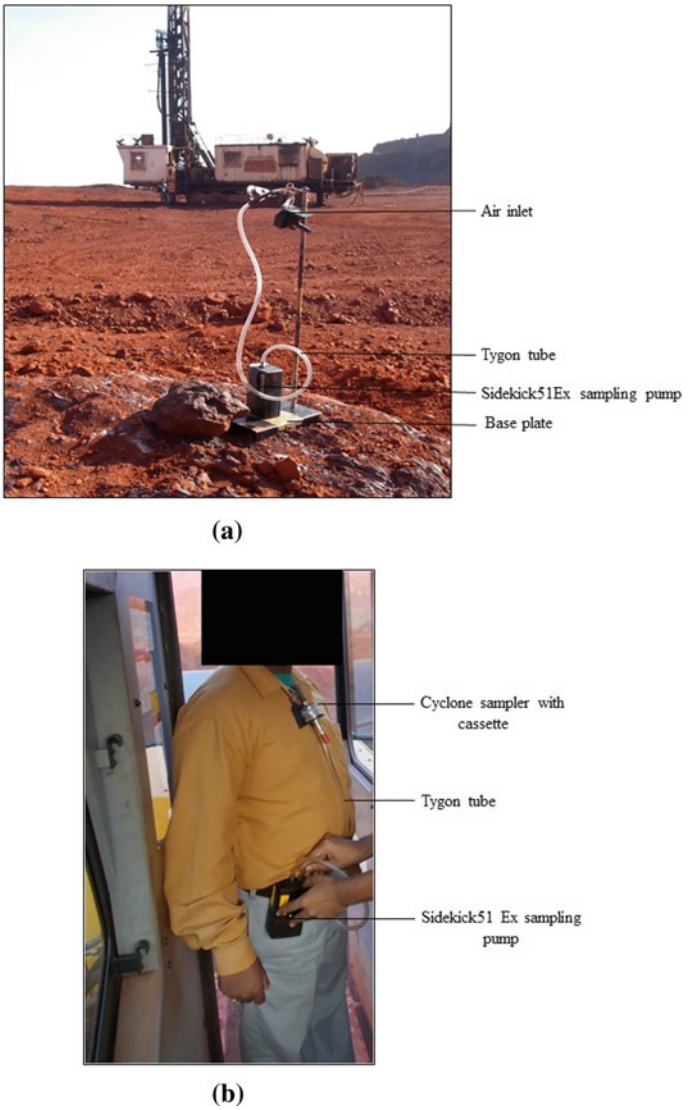

Fig. 11 **a** Dust sampler performing area dust monitoring. The DGMS approved sidekick 51Ex sampling pump is pre-calibrated for a flow rate of 2.2 L/min. The area sampling is usually done till the completion of the shift. **b** shows the personal dust monitoring. The cyclone samplers along with the PVC filter cassette are fitted into the collar of the worker at the breathing zone, to collect the respirable dust while the sidekick 51 Ex is attached with the belt

the occurrence of NIHL cases, thus controlling agencies made certain guidelines by which they can reduce the noise levels. The impact of noise on the surrounding habitat can be reduced by adopting certain precautionary measures while working in mines. Noise monitoring is therefore essential for monitoring the area where the worker is getting exposed. The equipment such as noise dosimeter and Sound Level Meter (SLM) are used for the measurement of noise levels while the audiometry technique is used to detect individuals hearing status and to detect NIHL. The noise dosimeter is a battery-based device that calculates the dose of noise exposure and gives a reading for 8 h TWA. Figure 12a shows a personal noise dosimeter. The microphone is attached to the collar of the worker while the dosimeter is attached to the waist in such a way that it doesn't hinder his movement while performing his normal duties. The logging interval of the noise dosimeter is set at 1 min with an Exchange rate of 3 dB and with the "Slow" response in "A" weighting.

The SLM meter is a device that can be used as a static noise measuring device as shown in Fig. 12b or can be used as a handheld personal device (Fig. 12c) to record the intensity of noise at the noise prone areas. In the first case, it is attached with the tripod stand around 1.5 m from the ground while the handheld device is kept at a distance of 100–200 m from the sound source. The logging interval of the noise dosimeter is set at 1 min with an Exchange rate of 3 dB and with the "Slow" response in "A" weighting. Noise levels at various places are recorded and tabulated to know the noise exposure in a particular area. The average 8 h TWA is calculated in LAeq (A). LAeq is the equivalent continuous sound level, used when the noise level is continuously changing and the sound level varies over time. According to DGMS, India, Circular No. 18 Tech. 75, the prescribed warning limit for eight-hour exposure is 85 dB(A) below which there is very little risk to an unprotected ear while 90 dB(A) is considered as danger limit above which hearing impairment and deafness may occur to an unprotected ear.

A study published in 2017 by the National Institute of Miners' Health (NIMH), Nagpur, Maharashtra, India in iron ore mines of Jharkhand found 23.8% of workers had NIHL out of total 92 male mine workers participated in the study while 9.7% of mine workers were having bilateral hearing loss and 10.8% were having unilateral hearing loss. Overall, around 45% of workers were having some form of hearing loss as shown in Table 2 (Dhatrak et al. 2017). Similarly, another study published in 2018, by NIMH, Nagpur documented higher noise levels in opencast iron ore mines of Dantewara district of Chhattisgarh, India. A personal noise monitoring study was conducted among 133 mine workers. From Table 3, it is evident that 46% of workers of HEMM were exposed to the warning limit of 85 dB(A) while 18% of worker of this group were working in the danger limit of 90 dB(A). However, only 9% i.e. one worker was exposed to the danger limit in the case of workers working in the Mines operation and workshop (Deshmukh et al. 2018).

The year-wise NIHL cases reported in mining areas in Canada is shown in Fig. 13. From 2015 to 2019, the highest number of cases (103 numbers) were found in 2017 while 2019 had the second-highest number of cases i.e. 96 (Annual reports nd).

The following standards were set by DGMS, India (vide circular no 18 of 1975) in the work environment:

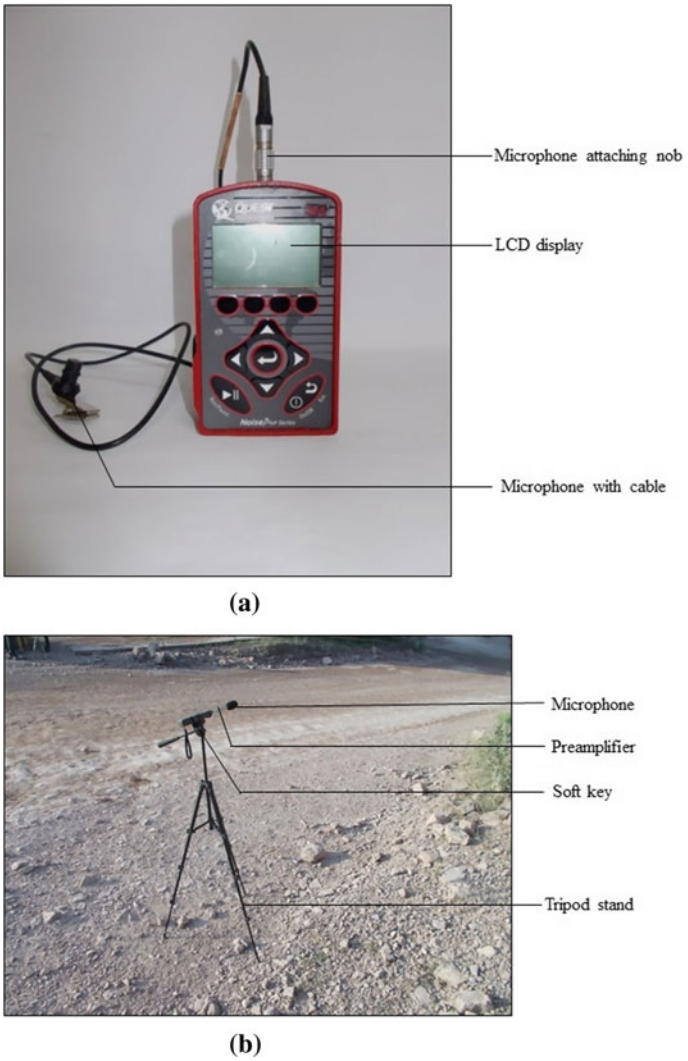

Fig. 12 **a** A Noise Pro DLX personal noise dosimeter. **b** A sound level meter set in the haul road for area noise monitoring. **c** A Sound level meter measuring noise level at conveyor belt transfer point

- A warning limit of 85 dB(A) is set below which there will be little risk to unprotected ear for an eight-hour shift.
- The danger limit value of 90 dB(A) is set, above which hearing impairment and deafness may occur to unprotected ear.
- In an area where the noise level is 115 dB(A) or more, a worker should not be permitted to enter without appropriate ear protection.

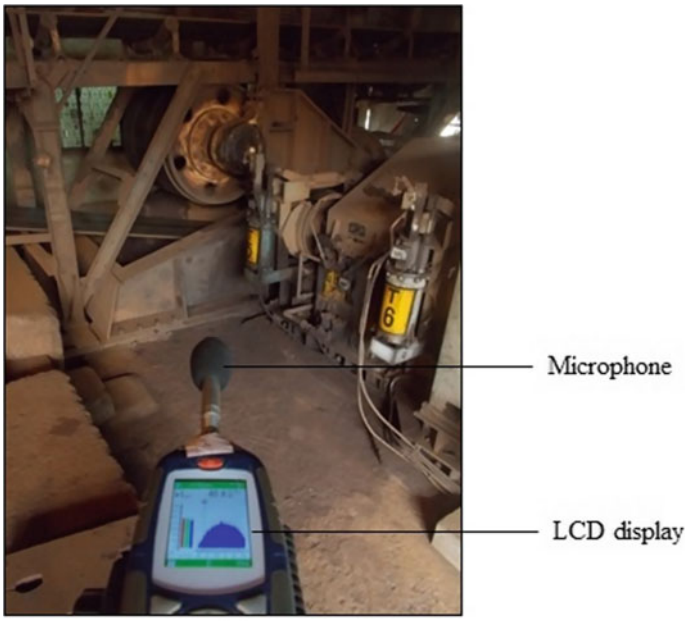

Fig. 12 (continued)

Table 2 Findings of audiometry evaluations among study groups [*after* Dhatrak et al. (2017)]

	Mine workers (n = 92)	General population (n = 119)
Normal	51 (55.4)	93 (78.1)
NIHL	22 (23.8)	0
Bilateral Hearing Loss	9 (9.7)	18 (15.1)
Unilateral Hearing Loss	10 (10.8)	8 (6.7)

Figures in parenthesis indicate the percentage

- In case of single isolated outbursts of noise which can go above 130 dB(A) "impulse" or 120 dB(A) "Fast", personal protective equipment is mandatory.
- Workers should refrain from visiting the sites where the noise level surpasses 140 dB(A).
- Only DGMS approved equipment should be used for noise monitoring

(iv) **Rock fall monitoring strategies**

Rock falls are major hazards in the underground as well as surface mines with consequences ranging from minor to severe. The risk to personnel and other damage associated with rock falls must therefore be managed. In the case of exposed areas,

Table 3 Percentage of SEGs exceed warning and danger limit [*after* Deshmukh et al. (2018)]

Workplace of SEGs[a]	Exceed warning limit 85 dB (A)	Exceed danger limit 90 dB (A)
HEMM (n = 55)[b]	25 (46%)	10 (18%)
Crushing plant (n = 28)	9(32%)	3 (11%)
Loading plant (n = 15)	9 (60%)	Nil
Screening plant (n = 23)	8 (35%)	7 (31%)
Mines operation and workshop (n = 12)	4 (34%)	1 (9%)

[a]HEMM: Heavy Earth Moving Machineries
[b]SEGs: Similar Exposure Group i.e. the category of workers who were directly exposed to iron ore mine and processing units. HEMM operators (dumper, dozer, shovel and drill), workers in the mining, and screening, crushing and workshops

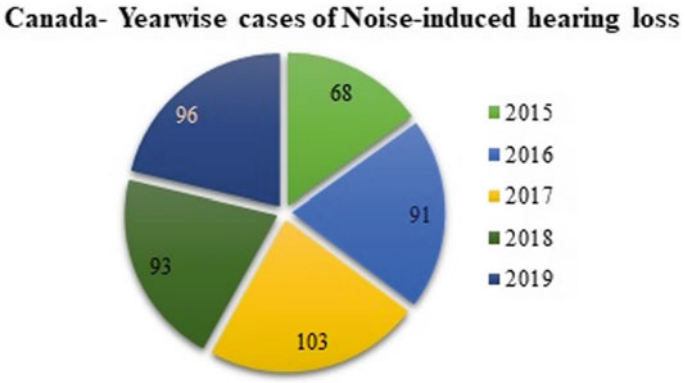

Fig. 13 Year wise cases of NIHL in mining areas of Canada [*Source* Workplace Safety North. Ontarios]

individuals' life and property are at risk due to rock fall. The mitigation approach for rock fall requires a cost-effective method for risk assessment and the design of a method to counter the rock fall like the creation of rough slope to reduce the speed of rock which could cause less damage. A rock fall hazard rating system must be followed which can give an idea about slope height, geographical structure, rock friction, block size, average vehicle risk and history of rock fall (Hoek 2015).

There are new technologies like Automated Temporary Roof Support (ATRS), automated roof bolting system ND Mobile Roof Support (MRS) are available in which self-drilling injectable rock bolts are done. It can protect the injuries that may results due to roof fall and rock fall during pillar recovery or rock bolting (Durga and Swetha 2015). Figure 14 depicts the roof bolting method to stop roof fall in an underground mine and Fig. 15 shows the ATRS system.

Fig. 14 The rock bolts along with W-straps support system

Fig. 15 ATRS system [*after* Durga and Swetha (2015)]

(v) **Role of remote sensing and Geographic Information Technology (GIS) in disaster management**

The development of advanced techniques has emerged as a strong supporting tool for mining engineers and mining supervisors to envisage the upcoming disaster by utilizing expertise from remote sensing and GIS technology. Though it is difficult to map the underground mines correctly because of the reduced way of viewpoints for clear imaging but one can definitely take help from geo-referenced digital pictures and available surface maps which can give an idea about the geospatial distribution and geometry of mineralized zones. However, this difficulty is not there in case of surface mining. The smart functions of GIS techniques such as spatial database, spatial mapping, watershed analysis and spatial modeling could be employed for mining disaster management. With this technique, a personal orientation system can be developed which can detect the exact location and status of a miner in an underground mine. A device has been developed with a wireless sensor network and GIS server, ZigBee nodes which can be installed in an underground mine to detect environmental attributes like humidity, temperature and even gas concentration. By using the Python Programming language (ArcPy), ZigBee could send an emergency message using a geo-processing model which could also be used to control ventilation fans (Choi et al. 2020).

The Light Detection and Ranging (LiDAR) is a remote sensing device that can detect the distance of an object by sending a laser pulse and receiving the reflected pulse and detecting the signal with a sensor. It can also be used to detect the topography, retrieve digital elevation data and as a dust monitoring tool. The instrument can be operated with an accuracy of measured coordinates in the range of 2–10 mm by a distance of up to 1 km. The horizontal resolution of LiDAR ranges from 0.5–2 m with having a stated vertical accuracy of 0.15 m (Griffin et al. 2015; Abzalov 2016).

The photogrammetry and laser mapping techniques are in high demand to collect information distantly which could produce digital 3-Dimensional surface models known as Digital Terrain Model (DTM). It can be used to characterize the geological features of rocks. The term Digital Elevation Model (DEM) is being used by many professionals for both DTM and DSM. DTM gives an idea about the elevation of the bare ground surface (the physical surface of the earth) while Digital Surface Model (DSM) refers to the upper surface of the landscape comprises a height of vegetation, structures created by human beings such as buildings and other surface features (Griffin et al. 2015; Abzalov 2016).

Prakash and Vekerdy (2004) has developed a GIS-based device named 'Coalman' which can detect fires in coal mines. It uses Integrated Land and Watershed Information Management System (ILWIS) software by which various operations like image registration, pre-processing, enhancement classification, can be performed. It can generate and display coal fire risk maps in complete 3D data models. It has the ability to detect and map coal fire areas by indirect or direct indicators (Prakash and Vekerdy 2004).

(vi) **Real-time location-based transportation surveillance in mines**

The advancement in technologies has empowered the mining operators to track the exact location and movement of transport vehicles, miners and each equipment which in turn has improved mine safety and productivity. In the past because of the lack of this system, many accidents happened and lots of miners were left untraced due to mining accidents. Now because of the creation of novel surveillance devices, the mine manager or supervisor can trace the exact location and guide and prevent if any vehicles are about to smash together. In this way, the remote surveillance system is protecting the resources and life of miners. A brief introduction to such devices is given below (Bandyopadhyay et al. 2010).

- *Dumper Shield*: It is a GPS and radio frequency-based alarming device that gives a secure virtual shield around the dumpers thus protecting dumper collision with other vehicles or human beings.
- *Dumper Trace*: Another smart automated system that can count the number of trips any dumper has made. It keeps an eye on the movement patterns and gives the exact location of the dumpers.
- *Wireless Underground System*: As the name suggests, it is a completely wireless automatic device to monitor the activities in underground mines. It provides real-time details of miners and mining equipment apart from monitoring the underground mining environmental conditions such as humidity, emission of toxic gases like methane and CO_2. It has audible warning signal systems which avoid collision between vehicles and miners. It is also enabled with emergency messaging services by which any mine worker can send messages to the control room in case of emergency.
- *Wireless Infrared Intrusion Detection System (WIID)*: This device is based on an Infrared wireless perimeter fencing system that monitors the physical intrusion inside mines and gives the information by sending SMS or buzzer to the control room with a location for immediate actions. Any violation in physical security, loss or theft of expensive equipment could cause risk not only to the mine operator but also to the fellow members of the mines. Hence, this device is developed with a similar concept to protect the mines from physical damage.

(Vii) **Role of National and International bodies in preventive measurement**

Many international and national regulatory agencies have made regulations and preventive measures to control mining disasters. Internationally, US agencies such as NIOSH, Occupational Safety and Health Administration (OSHA), MSHA. and in India, DGMS are responsible for regulating the mining activities and design regulatory guidelines to prevent, and mitigate the risk.

The Queensland Government in 2016 created a mining industry safety hazards database in Australia. In order to know the information related to hazard and risk control, online interactive software namely MIRMGATE and RISKGATE were launched by the Mineral Industry Safety and Health Centre at the University of Queensland (Tripathy and Ala 2018).

In India, the Disaster Management Act was enacted on 23rd Dec 2005 and established the National Disaster Management Authority (NDMA) which is an apex body for disaster management and of which the Prime Minister of India is the Chairperson. The Central Ministries like the Ministry of Mines and Coal Ministry, and agencies such as DGMS, India formulated certain guidelines, regulations for the proper functioning of mines. Apart from this, the state government is also responsible for disaster management. Section 14 of this act mandates the state to establish a State Disaster Management Authority (SDMA) of which the Chief Minister of that state will be the chairperson (Ministry of Labour and Employment 2020**).**

Role of DGMS, India includes, (a) Inspection of mines, (b) Investigate in case of mining accidents, dangerous response, emergency cases, and complaints, (c), Approval of mining safety appliances, equipment and materials, (d) Development of safety legislations and standards, (e) Encourage safe work practice, development of safety equipment, workshops for interaction, (f) Dissemination of safety information, (g) Organize conferences, National safety awards, safety week and campaigns for safety promotion, (h) Promote safety education and awareness programs, and (i) Grant statutory permissions, exemptions and relaxations.

The Government of India has made certain legislations which are described in the next section. Apart from this, the government has installed an anti-collision system for dumpers, electronic telemonitoring systems, gas monitoring systems and slope stability systems. Ministry of Petroleum and Natural gas, Government of India, has made a committee to investigate the cause of major accidents that occurred in the oil and natural gas industries. The lessons learnt from these accidents will be circulated among other similar industries.

The launch of the National Programme for Control and Treatment of Occupational Diseases in the year 1998–99 by the Ministry of Health and Family Welfare, Government of India with the National Institute of Occupational Health, Ahmadabad, as the nodal agency, accelerated the screening of the prevalent occupational illness and their control measures. Silicosis, CWP, Asbestosis are some occupational lung diseases caused due to exposure to mining dust (Saha 2018).

DGMS, India has made it mandatory to use only DGMS approved instruments in mines. In this way, the agency has tried to regulate mining accidents to some extent. In the month of December 2018, the government had created a task force of twenty-two states to search the illegal mining and take necessary action against them (Akanksha 2019). Some of the major initiatives taken by the government in this regard are:

(1) The government has tried to broaden livelihood opportunities by the implementation of schemes like Mahatma Gandhi Employment Guarantee (MGNREGA), Prime Minister's Employment Generation Program (PMEGP) etc. This helps the workers to engage in other types of work like road or building construction rather than opting for mining work. Further, due to the establishment of this initiative, the migration of workers has reduced.

(2) Recently, the government has announced a new scheme the 'Garib Kalyan Rozgar Abhiyaan' with an outlay of Rupees 50,000 Crores which will be implemented among 116 districts of six states namely Uttar Pradesh, Jharkhand, Rajasthan, Madhya Pradesh, Bihar and Odisha.

In the US, NIOSH is responsible for implementing rules and regulations for mining industries. It grants financial support for conducting research on mining activities, development of software and tools which could be helpful for the detection of risk while working in mines. Also, it approves the Personal Protective Equipment (PPE) kits and other instruments for use in mines (NIOSH 2020). The NIOSH, US is responsible for:

(1) Granting approval for respiratory protective equipment
(2) For the Health Hazard Evaluation (HHE) program and for occupational safety and health research, conduct investigation at the employment site
(3) Implement the World Trade Center Health Program
(4) Routine X-ray analysis of coal workers to check for CWP
(5) Conduct research and training program for officers of mine workers

Following recommendations and regulations are made by NIOSH, US:

Recommendation to control fall of persons, slip trips, material collapse:

(a) As far as possible the mining company has to ensure that the surfaces are stable
(b) To access unstable work surfaces, bucket trucks can be used
(c) It should be ensured that workers must have PPE kits containing slip-resistant soles safety shoes, eye protections device, certified helmets and cut resistant gloves.

Recommendation to control hearing loss:

(a) The use of ear muff devices while working has been made mandatory for miners. The supervisor must check whether the worker has worn it or not.
(b) Reduce noise level by the instruments by routine maintenance of the system

Recommendation to control toxic dust inhalation:

(a) Use of goggles, protective eyewear with ANSI Z87 mark or face shield along with mask is a must
(b) Use of N95 or a better mask by the worker is a must
(c) In the case of the asbestos mining area, half-mask elastomeric respirator with N, R, or P-100 series filters should be used
(d) In cases where workers complain about eye irritation, full-face respirators with P-100 OV/AG (Organic Vapor/ Acid Gas) combination cartridges must be used
(e) Use of surgical masks should be avoided as they can't protect from dust inhalation
(f) The supervisor should ensure that the worker has properly worn the mask
(g) Routine dust monitoring of the mining area should be done. In case the dust level is higher than the recommended level, entry of workers should be restricted and only those having proper respiratory devices should be allowed

(h) Routine medical check-ups of the workers should be done. Those workers having symptoms like chest pain or chest tightness, breathing difficulty, medical attention must be sought for them
(i) Workers must know the risk of 'take-home toxic contaminants' and should follow the safety rules at the end of their shift
(j) Respirators should be maintained properly and damaged respirators should be replaced with the fresh ones

Recommendation to maintain ventilation

(a) Purging, Flushing or ventilation of the mining area should be done
(b) Self-Contained Breathing Apparatus (SCBA) should be used
(c) Lighting in the mine as much as possible should be done. NIOSH, US, has developed LED (*Light-emitting diode)* cap lamp which has better illumination in underground mines (Max Martell and Sammarco 2017)
(d) Good communication and alarm systems should be available nearby
(e) Safe entry and exit in the space must be there. A ladder can be used where ever possible
(f) Rescue equipment should be available nearby

Recommendation in case of fire or chemical exposure

(a) SCBA with full face piece in pressure-demand or other positive-pressure modes should be used
(b) In case of fumes present, the use of a gas mask front-mounted with an Organic Vapor Canister (OVC) or having any chemical cartridge respirator with an OPC is a recommendation. A dust mask or surgical mask is not going to protect from chemical vapors exposure
(c) A fire extinguisher must be available nearby
(d) Rescue equipment should be available nearby
(e) Alarm and communication tools should be available with the workers
(f) Gas detection monitoring must be done in routine intervals in the mines or gas detectors must be installed in the mines
(g) The engine should be immediately shut down in case of any sign of gas leakage
(h) Avoid the use of gasoline generators or portable fuel carriers in confined spaces or poor ventilation areas

Other recommendations:

(a) Workers must be educated for safe work procedures before beginning of their task
(b) Proper training of handling heavy equipment should be provided
(c) The operators should obey the speed limit in mines and follow traffic rules while moving in/out of the sites
(d) In case of confined space, the entry of persons should be limited
(e) In case of heat stress due to mining environment or wearing insulated bunker gear:
(f) Work schedules should be adjusted or workers should be rotated with others

(g) Sports drinks or drinking water (in every 20 min) and small meal should be provided to the workers
(h) The heartbeat of the worker should be monitored and in case it is increasing, the worker should be sent for a medical emergency
(i) Medical evaluation for excessive sweating, excessive fatigue and confusion should be performed
(j) A cooling station having ice pack, fans, water misting should be available

(viii) Legalities and the role of the legislature

The mining disaster management in India has the motto of prevention, preparation, and mitigation and thus there is a paradigm shift from the past where the actions were taken after the damage has been caused. The disaster management act has made certain policies by which they are continuously doing research to prevent the disaster. Public–private partnership and community disaster management is being encouraged by the government. Efforts are being taken to reduce the risk of disaster (Gupta 2017).

The Constitution of India has provided equal rights to every individual with equal protection of the law (Article 14). In case of mining and allied activities, Article 14 can be used to confront the government when there is a stake on human rights and environmental impact. Following are the brief overview of legislation related to mines safety in India: (Gupta and Nair 2012; Nanda 2020; Mines and Minerals 1957; The Coal Mines Regulations 1957; Mines Rescue Rules nd; The Gazette of India: Ministry of Labour and Employment nd).

- **Factories Act, 1948:** The factories Act 1948 is concerned for the health and safety of the workers and the environment. Apart from this it also cares about the employment benefits of the workers. A comprehensive list of 29 industries involved in the hazardous process is also mentioned in this act [Section 2C (b), Factories Act]. Appointment of inspectors, annual leave with wages, and employment of young person are also important provisions of this act.
- **Mines Act, 1952:** This act states the requirement of labor safety and protection of health and safety of workers in mines. It also defines the working conditions in mines, provisions for management and conduction of mining operations.
- **Mines and Minerals (Development and Regulation Act, 1957):** To maintain the mining sectors, this act was enacted by the Government of India. The detailed process of acquiring mines or seeking a license is documented in this act. Except for atomic minerals and small minerals, this act is applicable to all other minerals. It was amended twice in 2015 and 2016.
- **Coal Mines Regulations, 1957:** It is applicable to all coal mines in India. Under section 16 of this act, the owner, agent, or manager has to give notice to the Chief Inspector of Mines and to the Regional Inspector. The owner, agent, or manager has to inform the Regional Inspector about any accident that occurred in the mines within 24 h of any such accidents. The Board of Mining Examinations examines the competency and fitness of the mines according to the rules laid down in this

act. It has also details about the flammable materials, type of explosives to be used in mining.

- **Metalliferous Mines Regulations, 1961:** The provisions in this act are likewise as detailed in the Coal mines act 1957 with certain modifications according to working conditions of Metalliferous mines. The precautionary measures to be taken in case of danger are detailed in this act. Recently, with certain modifications, the Ministry of Labour and Employment has issued Metalliferous Mines (Amendment) Regulations, 2020 on December 15th, 2020.
- **Surface Mining Control and Reclamation Act, 1977**: States that the coal mining activity should be conducted with proper protection of the public and the environment. Coal mining should provide restoration for abandoned mining areas.
- **Mines Rescue Rules, 1985:** The coal mines rule was replaced by Mine Rescue Rule 1985, which was created with the purpose of providing rescue of the persons working in the mines in the event of explosions, fires, gas explosion, inundation, etc. It is applicable in both Coal and Metalliferous underground mines. The establishment of rescue stations and rescue work in the mines require professionally trained persons. The mine manager should be responsible for conducting all the rescue work.
- **Factories Amendment Act, 1987:** Another act that cares for the health and safety of the workers and the environment. Details about permissible limits of chemical and toxic substances exposure is described in section 41F. Chapter IV of this act also enunciates about reduction of risk through appropriate land-use planning and risk communication strategy.
- **Public Liability Insurance Act (PLIA Act), 1991:** As the name suggests, this act is for providing insurance for immediate relief of the affected individual.
    - *When the disaster has not occurred i.e. pre-disaster:* According to section 4 of this act, the owner is obliged to make an insurance policy of the worker (before handling any hazardous substance) which ensures the worker against any liabilities to provide relief under Section 3.
    - *In case of disaster has occurred i.e. post-disaster:* Section 3 of this act states that in case of handling any hazardous substance, any accident, injury or death occurred to any person or damage to any property has occurred, the owner shall be liable to give relief of such accident, injury, death or damage.
- **Oil Mines Regulations, 2017:** The oil mine regulation is applicable to all oil mining industries in India. The major points are:
    - In the event of commencement of any mining operation, the owner, agent, or manager has to give notice to the Chief Inspector of Mines, the Regional Inspector, and the District Magistrate in the Form under Section 16 of the act, for the purpose, geographical boundaries and safety management plan prepared for the mine.
    - Any material which is flammable shall not be stored within 30 m of any oil well except for fuel.

- Smoking should be prohibited within 30 m of any oil well. No smoking area should be demarcated in the mines.

- The emergency plan should be ready post risk assessment analysis with respect to:

  a. Fire
  b. Blowout, ignition, explosion, the influx of inflammable or noxious gas
  c. Breakage in a pipeline or petroleum leakage
  d. Failure of structures
  e. Chemical spillage
  f. Natural calamities
  g. Medical evacuation and
  h. Any other emergencies

The role of local bodies to control the disasters in mines is crucial as they are the first line of contact in case of an emergency. A brief description of the responsibilities of the local bodies is summarized below (Risk assessment disaster management plan 2020; Available from 2020b):

Role of the local authority: Among the local authorities, the Emergency Planning Officer (EPO) has to carry out his duties such as providing necessary equipment and manpower for cope up with the emergency situation in the mining area. The EPO may carry out rehearsals for off-site planning and keep the facility up to date.

Role of health authorities: Among the health authorities, doctors, surgeons, nurses, hospitals, and ambulance services, all these have crucial roles in case of emergency. The expert doctor needs to be available at the moment of emergency. The hospital must be well equipped with medical facilities.

Role of police: During an emergency situation, the role of the police is to protect life and property. Manage the traffic and evacuate the public from the danger zone. Deal with causalities and inform the family members about the death or injury of the individual.

Role of fire authorities: The supervisor in the fire brigade has the responsibility of dealing with fire and explosions in any mining area. They should be supplied with sufficient fire fighting equipment. The officer should know the location of water supply points in the nearby region. An emergency rehearsal should be performed to keep the unit up to date.

Role of government safety authority and mining personal: The factory inspector has to satisfy that the mining safety is not at the stake and he has to perform the routine analysis for mining inspection. The safety authority may check the documents related to safety protocol followed by the mining manager. The mining supervisor must ensure that the equipment is properly maintained and the detection devices are functional. The training should be given periodically for gas level detection, which should include the following:

- *Gas detection training programs:* Details should be given about the detection methods and how to operate the monitoring devices.
- The area where chances of accumulation of combustible or toxic gases are high should be identified and regularly monitored. Areas include: coal reclaim tunnels, dragline tubs, machine operator cabins, workshop pits, etc.

In order to prevent mining accidents, periodic gas monitoring and atmospheric gas evaluation must be done in and around the mining area. The need for a mask and other respirators is dependent on the amount of fresh air available. Following are the materials which should be available in the rescue vehicle inside the mine: First aid boxes, fireproof cloth, escape apparatus, Compressed Air Breathing Apparatus (CABA) (used in taking breathable air), gas detectors, stretchers, resuscitation device (used to inflate lungs of the unconscious person who is not breathing for proper oxygenation). Apart from the above-mentioned materials, the rescue vehicles outside the mine must contain, steel ropes, lighting devices, industrial gloves, PPE, hangers, ventilation fans, pneumatic lifting equipment (Özmen and Aksoy 2015).

(ix) **Compensation to workers and their families**

(A) **Compensation to the workers in foreign countries** (Alif et al. 2020; Office of Workers' Compensation Programs nd; CWCS 2020):

- According to the recent data by Alif et al. (2020), in Queensland, 186 claims for compensation were received till 31stJan 2020 from mid-September 2018. Out of 1017 workers, 199 were diagnosed with work-related respiratory disorders. Among these, 163 were having work-related silicosis, 26 with Progressive massive fibrosis, and 10 were having other respiratory issues. Among the 199 claims, 186 claims were accepted. The screening program was conducted among respirable crystalline silica dust exposed workers by the Office of Industrial Relations and Work Cover, Queensland (Alif et al. 2020).
- The Office of Workers' Compensation Programs (OWCP) was established in the year 1916 by the U.S. Department of Labor which provides compensation benefits for four major disabilities covering medical treatment, benefits of wage replacement, vocational rehabilitation, and other remuneration to workers or their kin who encountered with a work-related injury or occupational disease under the Federal Employees' Compensation Act. Around three million federal employees, members, and the Peace Corp can take the benefits of this program. Under the OWCP programs, one program is the *Black Lung Benefits Reform Act of 1977* also known as the *Coal Mine Workers' Compensation Program* in which the workers who got pneumoconiosis (black lung) attributed due to exposure to coal dust gets monthly payment and medical treatments. On the death of the worker, the act provides compensation benefits to the surviving dependents. IT also provides fast track process by which the image of the Black Lung case file can be uploaded to the web portal named Claimant Online Access Link (COAL).

- The other three programs are also there in OWCP. Briefly, the Energy Employees Occupational Illness Compensation program is for the workers working in the Division of the Energy, the Longshore and Harbor Workers' Compensation Program to provide compensation to the maritime workers who got injured or died upon the navigable waters of the US and the Federal Employees' Compensation Program is applicable to all civilian employee of the federal government, including employees of the legislative, executive and judicial branches. The federal government has all the data of workers' compensation and it maintains the same.
- There are other organizations which collect information related to claims made by the workers such as National Council on Compensation Insurance (NCCI) and the Workers Compensation Research Institute (WCRI). NCCI is a U.S. insurance and data collection organization that was founded in 1923 and has a mission to foster a healthy workers' compensation system. It's a non-profit organization that annually collects data of nearly four million workers' claims. Likewise, WCRI, a non-profit institute that was founded in 1983, has the main role to provide objective data and conduct scientific studies on a variety of workers' compensation issues that could serve the public in a better way.
- The NIOSH, US has cooperative agreements with five states of the US (California, Massachusetts, Ohio, Tennessee, and Michigan) for workers' compensation surveillance. The rationale is to prevent occupational injuries, diseases, mortality, and exposures to hazards within the states and throughout the nation by collecting, analyzing, distributing data related to workers' compensation claims. It is actively involved in conducting and funding research to reduce the disasters risk and improve the mining activities for the sake of miners' health.

(B) **Compensation to the workers in India:**

- The Workmen's Compensation Act, 1923 which is comprised of four chapters, enunciates the definition of workmen, details of injuries deemed to cause permanent disabilities or permanent partial disabilities, details of occupational diseases, and Employer's liability for compensation, etc. The compensation amount should follow the provisions of this Act i.e., in case of death occurred due to injury, fifty percent of the monthly wages of the deceased workman multiplied by relevant factor or rupees fifty thousand whichever is more should be paid. In case of permanent total disablement occurred due to injury, sixty percent of five monthly wages of the injured workman multiplied by the relevant factor; or rupees sixty thousand whichever is more should be paid (Saha 2018).
- Coal India Limited announced three times hike in Ex-gratia amount from Rupees. Five lakhs to Rupees. Fifteen lakhs in case of fatal mine accidents encountered by the worker. The family members of the worker may claim

compensation according to the Employee Compensation Act. It is applicable to both permanent and contractual workers (The Economic times 2019).

- According to the annual report by DGMS, India 2018, in the occupational health and safety survey carried out by the National Institutes of Miners' Health, Nagpur, 105 cases of Silicosis were found out of the 1566 workers around four states of India i.e., Telangana, Uttar Pradesh, Rajasthan, and Haryana. Among these, Rajasthan had the highest number of cases i.e. 83 in total. Silicosis is a compensable occupational injury according to the Employees' State Insurance Act (1948) and the Workmen's Compensation Act (1923) (Mines Rescue Rules nd; Sharma et al. 2016).
- The Rajasthan government has announced that a sum of Rupees. 1500 per month will be paid to workers diagnosed with silicosis. Additionally, Rupees. Three lakhs will be paid to workers post-diagnosis of silicosis and Rupees. Two lakhs will be paid to the family members of the deceased worker due to silicosis (Watts 2019).
- According to the judgment given by the Anand (Gujarat) Labour Court, a compensation of Rupees 5.7 lakhs should be provided by the employer to the surviving heir of the worker who was working in the agate industry for 19 years. The worker died due to silicosis in 2011 and the family member filed a case under the Employees Compensation Act for Silicosis (Gujarat 2019). The impact of this judgment may affect both, the worker and the mine management, for example, the patient who is suffering from silicosis will get compensation but may lose their employment. If the silicosis worker is found in the small mining industry, then the payment of the compensation amount would be a financial burden for the industry.

Although the government has made regulations for the compensation of workers in case of occupational injuries still the cases of getting occupational diseases in not reducing in Indian mines. Practically, all the mining disasters can't be excluded but a model for the same may be adopted. A brief overview of the model for disaster management is mentioned below.

4 A Model for Disaster Management in Mines

Mining disasters can be managed by proper strategic planning. Various scientists suggested models for mining disaster prevention and its management (Nojavan et al. 2018; Sohail et al. 2006). All these articles state clearly about the components required in order to prepare the strategic planning for disaster management. Figure 16 depicts the disaster management model with six components for disaster management which are:

i. Hazard Assessment
ii. Risk Management

Fig. 16 A disaster management model

iii. Prevention and Mitigation
iv. Preparedness
v. Response
vi. Rehabilitation

i. *Hazard Assessment*

The first step towards disaster management is hazard assessment. To understand the disaster management model, an example of a methane gas explosion can be considered. In case of a methane explosion in any underground mines, the first requisite is the *identification of hazard* which is responsible for the disaster. When the causing agent of hazard is identified, it can be *analyzed* for possible reasons of occurring the hazard i.e. methane gas explosion. This will help to check for whether any gas leakage device was defective or find out the way for management strategy.

ii. *Risk Management*

The *analysis* of hazards also helps in calculating the risk. How many individuals are going to be affected by the hazard? *Identification* of risk and *evaluation* of risk factors associated with the hazard, e.g. methane gas explosion should be done. It will help for the effective *treatment* of risk. The monitoring of risk factors will help in the preparation of strategies for its prevention.

iii. *Prevention and Mitigation*

The prevention and Mitigation approach is crucial for mining disaster management. The preparation of protocol and strategy for *control* of disaster will help to effectively regulate the hazard. It can also be useful for hazard prediction. The nature of a causative agent and how to reduce the risk, safety check in the mines, routine check for the entire instrument for proper functioning can be helpful for effective mitigation of disaster.

iv. *Preparedness*

Under this, all the mining staff must be ready to tackle the situation. Proper *training and education* to all the supervisors and workers should be given for possible hazard and its routine exercise should be done. This will help to their readiness to combat any situation in case of emergency. The mining management should also make sure about the *resources* available in the mining to control the disaster.

v. *Response*

The response is a post-disaster management strategy. An early alarm signal should be given during accidents in mines to evacuate the staff. The management should look for causality which happened during the accident and report the same to the nearby police station. Also, an emergency medical team should be ready for immediate treatment of affected individuals. A backup should be ready for the evacuation, emergency medical help. In case the in-charge doctor is not available, the information should be given to another doctor.

vi. *Rehabilitation*

Post-disaster, the mining management should calculate the loss, the mining area should be clear with debris (if present), reconstruct mining area with a modified plan to control the disaster or mitigate the risk with proper planning. How to cover up the loss and re-function the mining effectively should be considered during the rehabilitation of mines. The mine management may adopt the following strategies during rehabilitation, (a) Relocation: All the mining workers should be relocated to another mine for their living, (b) Medical support: The mine management should take care of the affected worker, they should be provided necessary medical support, (c) Compensation: The compensation to the family members of the deceased worker should be provided. Compensation to those who are severely affected and with minor injury should also be allotted, (d) In the case of underground mines, the accidental area should be restricted for entry and if there are chances of closing the mine, then closing guidelines should be followed, (e) In the modified plan, all the precautionary measures mentioned above for fire safety, inundation, noise, and dust monitoring, GIS tracking, gas detection, compulsion on wearing PPE kit should be adopted.

5 Summary

The mining sector contributes significantly to the growth of the nation and provides employment opportunities for many people. Disaster in mines has always been a matter of concern for policymakers. The proper workplace design, careful monitoring, and immediate medical response are crucial for the management of mining hazards. This chapter describes various types of disasters that happen during mining operations. This article represents the comparative statistics about injuries and fatalities caused by mining disasters in various countries. The nature and possible health effects of toxic gases in mines and smoke rollback in case of mining fires are explained in this chapter. The article demonstrates the prevention and management strategies for the control of mining disasters, for example, to detect gas leakage in mine, what are the available sensors and their principles? Moreover, this chapter highlights the importance of dust monitoring, noise monitoring, remote sensing and GIS-based tracking, management strategies for rockfall. Apart from these, the article draws attention towards the roles of national and international agencies, various mining laws, roles of local authorities, and compensation to the worker. This article also exemplifies the disaster management model system for strategic planning of disaster management.

Disaster management in mining demands strategic planning and involvement of various international and national regulatory agencies to set a method for the proper functioning of mines and to formulate guidelines for the control and prevention of mining disasters. NIOSH, US is giving opportunities to many scientific fraternities to conduct research in order to prevent mining disasters. DGMS, India has made it compulsory to use only DGMS approved instruments in the mining environment. The exposure limit for dust and noise exposure has been set by various international and national agencies. Additionally, the role of local authorities, police, fire authorities, health department, government safety authority and mining personal are crucial to control the disaster in mines. The compensation to the worker is important for the survival of family members in case of a mining disaster.

A typical model for disaster management and prevention strategy should have six components i.e. hazard assessment, risk management, prevention and mitigation, preparedness, response, and rehabilitation. Though controlling the disaster in mines is completely not achievable but the strategic planning could be helpful for effective prevention. Nevertheless, the role of government is vital for disaster control in mines.

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"We Did not Notice This Demon in Our Backyard!"—Introducing a New Source of Geogenic Health Hazard

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1 Introduction

The composition of rocks and minerals has significant impact on the air, water, and food. These media being capable of direct interaction with human body are more vulnerable sources of health hazard (Selinus Finkelman Centeno 2010; Selinus et al. 2011). Nevertheless, such transference of minerals and the trace elements they contain is a primary source of nutrients such as calcium, iron, magnesium, potassium, and about a dozen other elements, which are essential for a healthy life. However, sometimes the local geology may contain minerals that are enriched in certain elements which naturally dissolve under oxidizing or reducing conditions in groundwater. Excess of some of these elements, notably, arsenic, mercury, lead, fluorine, etc.; gases such as methane; abundance of dust-sized airborne particles of asbestos, quartz or pyrite, or certain naturally occurring organic compounds are major sources of geogenic health hazards (Selinus Alloway Centeno Finkelman et al. 2013; Centeno et al. 2016).

Among others, major areas of concern even in the developed countries include arsenic in drinking water in several countries e.g. USA; mercury emissions from coal combustion and its bioaccumulation in the environment; the impacts of mercury, arsenic, and lead mobilizations in surface and ground water in regions where artisanal gold mining is conducted (Centeno et al. 2016). Other geogenic sources of health hazards include impacts of geologic processes such as volcanic emissions, earthquakes, tsunamis, hurricanes, and geogenic dust; exposure to fibrous minerals

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_13

such as asbestos and erionite; and the health impacts of global climate change. Billions of people, most in developing countries, are afflicted by these and other environmental health issues that can be avoided, prevented, mitigated or minimized. However, detailed and comprehensive research and educational outreach programs have been conducted and solutions identified (Selinus Alloway Centeno Finkelman et al. 2013; Kirtikumar 2012).

The present study has attempted to portray peculiar condition in which contemporary soils show a remarkable presence of secondary silica equally enriched in all size fractions. This silica, or silicon dioxide (SiO_2) which is a group IV metal oxide naturally occurs in both crystalline and amorphous forms (i.e. polymorphic) (NIOSH 2002). Various forms of crystalline silica are termed as α-quartz, β-quartz, α-tridymite, β-tridymite, α-cristobalite, β-cristobalite, keatite, coesite, stishovite, and moganite (Davis et al. 1984). Crystallinity of the silica is a determinant as little damage is caused by amorphous silica. It only takes a very small amount of airborne silica dust to create a health hazard. A prolonged exposure to silica dust can cause a range of serious lung diseases including silicosis, chronic bronchitis, chronic obstructive pulmonary disease (COPD), lung cancer and autoimmune diseases, which profoundly affect the work productivity and the economic and social well-being.

Occupational exposure of silica dust in the mining area is prevalent; however, we observed its interaction in the civic area in the vicinity of Futala Lake. The concern regarding ambient exposure of silica dust has emerged making it important to gather information about the same on its non-occupational exposure including possibility of lung diseases in the affected civic areas. Several cases of non-occupational silicosis from non-industrial sources have recently been reported but there has been no attempt to measure silica dust (quartz) concentrations in the environment. Bhagia (Bhagia 2012) provides an overview of several non-occupational dust exposures. Franco and Massola (Franco and Massola 1992) found 6–9% quartz in sedimented dust from the Himalayan regions, whilst Norboo et al. (Norboo et al. 1991) reported the silicosis across Himalayan village residents. Saiyed et al. (Saiyed et al. 1991) investigated silica dust exposure in central Ladakh, India. Sepke (Sepke 1961), in 1961, reported silicosis from street dust. An unusual instance of silicosis caused by inhaling desert sand was reported by Farina and Gambini (1968), U.S. Environmental Protection Agency (1996) reported that average quartz levels in US metropolitan areas are in the range of 1.1–8.0 $\mu g/m^3$ with an average of 3.2 $\mu g/m^3$.

The percentage of quartz in total dichotomous mass (>15 μm aerodynamic equivalent diameter) ranges from 2.5 to 8.2 (Pande et al. 1969). It is commonly known that the atmospheric dust contains "environmental" level of mineral dust which is <50 $\mu g/m^3$; whereas in active mining areas, this level is of the order of ~10 mg/m^3 (Richards 2003; Berube et al. 2004). During the present study, alarmingly high levels of mineralized silica were recorded. This potentially exposed silica dust generates a great concern; for it can be a source of geogenic hazard. Thus, the present study is conducted to examine the abundance of secondary silica and its enrichment in all size fractions and to identify the influence of the remarkable quantity of silica on the soil, the ecosystem, health and environment.

2 Field Geology of the Area

The study area of Futala Lake and adjoining area falls near Vayusena Nagar within the jurisdiction of Nagpur city. The area is bounded by latitude and longitude 21° 8' to 21° 10' E and 79° 0' to 79° 3' N respectively. Geologically, the study area in regional set-up consists of Precambrian crystalline metamorphic rocks, Permo-Carboniferous Lower Gondwana sediments, Upper Cretaceous Lameta sediments, Cretaceous—Paleogene Deccan Trap basaltic lava flows separated by intertrappean beds and recent alluvium of Nag and Peoli rivers (Fig. 1). The geology of Nagpur city has been studied in detail by several authors (Subramanyanan et al. 1996; Deshpande 1998; Randive et al. 2019; GSI 2000), and more recently the geological information is compiled by GSI (GSI 2000) on a regional scale. Table 1 summarizes a detailed stratigraphy of the area.

The Archean metamorphics forming the base consist mainly of dolomitic marble and quartzites of the Sausar Supergroup over which the Gondwana Formations rest unconformably. They are exposed between Mahadula and Suradevi, and Khaperkheda and Koradi. These metamorphics are also exposed near Bardi, Itwari, Indora, Pardi and Kalamna (Fig. 1); however, due to thick population density, none of the outcrops was preserved (Rees and Murray 2007). The Gondwana succession is mainly represented by the Talchir, Barakar and Kamthi Groups, of which, the Barakar contains good deposits of coal. Their exposures are available near Jaripatka,

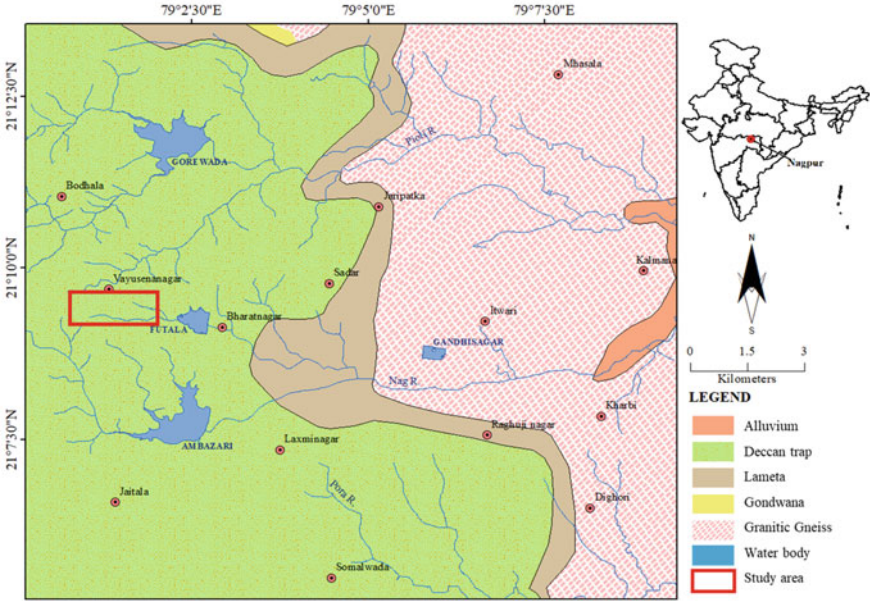

Fig. 1 Geological map of Nagpur city and surrounding areas (modified after Subramanyam et al. 1996)

Table 1 Various stratigraphic units occurring in the regional set-up of the study area (modified after Subramanian et al. 1996)

Geological Time Unit	Chronostratigraphic Unit		Approximate Maximum Thickness (in meters)	Description
Recent to quaternary	Alluvium and soil		10	Predominantly gravel, sand, silt and clay
Lower eocene to upper cretaceous	Deccan traps		45	Two basaltic lava flows separated by Intertrappean beds; compact to vesicular, amygdaloidal, at places highly weathered and jointed basalts
	Inter-trappean		3	Green earth, calcareous and fossiliferous clayey and marly sediments
Upper cretaceous	Lameta formation		15	Sandstones, earthy, red and white, silicified limestones
Upper permian	Gondwana	Kamthi group	168	Sandstones, shales, and ferruginous (ochre, reddish, brownish coloured) sandstones
Lower permian		Barakar group	140	Sandstones, shales and carbonaceous shales
Upper carboniferous		Talchir group	>20	Green shales, Bounder beds (Tillites)
Archaean	Sausar group		–	Mica-schists, quartzites, marbles, streaky- and ortho-gneisses

Bokhara, Nara and Kalamna (Fig. 1). Lametas are freshwater deposits that rest horizontally over the older Gondwana and Archaean rocks with an unconformity. These are exposed between NW of Nagpur and south of Umrer as disconnected patches and in turn, unconformably overlain by the Deccan trap basaltic lava flow which is the major rock type of the area. The Deccan Traps comprise a series of basaltic lava flows with each flow having a massive unit at the bottom and a vesicular unit at the top of the flow. To the west of Nagpur, layers of freshwater sedimentary rocks are interbedded with the Deccan basalt flows that are exposed near Dhapewada, between Bhokara and Mahurjhari, Takli, Telankhedi and Sitabuldi. A thin blanket of alluvial soil is spread over the Deccan trap including the study area; the thickness of which gradually increases as one approach this lake. There are two other prominent lakes, namely Gorewada towards the north and Ambazari towards the south of the area.

Also, a small lake is present inside the campus of the ordinance factory towards the southwest.

Deccan trap basalt form hard rock aquifers. In exposed lava flows, groundwater is phreatic, whereas in deeper subterranean flows, groundwater is semi-confined to confined. Groundwater is present in the pore spaces of each flow's vesicular unit, as well as the jointed and fractured sections of the massive unit (Pradeep et al. 2005). Secondary porosity and permeability caused by weathering, joints and fractures play an integral role in the storage and flow of groundwater. Weathering expands cracks, joints, and shear zones as well as produces granular materials. The study area consists of detrital soil, chiefly composed of sand, silt clay and kankar. The soils (the term 'soil' in the paper is used collectively for sediments of all sizes) spread over the catchment area of the Futala lake, are laden with innumerable, granule to pebble-sized clasts of crystalline, cryptocrystalline and amorphous silica. The density of silica pebbles varies considerably in the area. The flood plain has a higher density of silica nodules than the top of the basaltic hill. The adjacent area which is free from human activities has a reasonable population of silica nodules. Besides, it represents rain wash or sheet wash type deposits (Fig. 2) within an area comprising of an irregular network of ephemeral first-order streams. Towards the northernmost side of the ground (Katol-Amravati Road bypass) second-order stream flows. A gentle break in slope is observed; which drive the first-order streams to the second-order stream and represent the lowest elevation in the area. Considering the drainage system of the above-mentioned lakes, it appears that there is a domal structure near wadi which, by and large, acts as a water divide in the area.

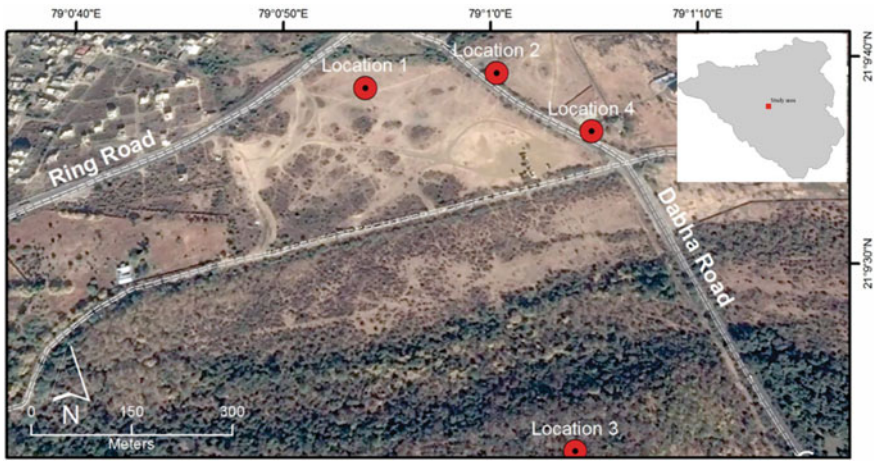

Fig. 2 Satellite Imagery using Google Earth showing the location of the study area and sampling sites

2.1 Distribution of Silica Pebbles

In the study area, debris with different forms and variations in silica morphology including crystalline, microcrystalline, cryptocrystalline and amorphous are distributed within the regolith and on the surface. It is observed that such debris is known hereafter as silica pebbles, dramatically reduce in number after a break in the slope. However, they follow certain patterns in their distribution. The scree of such pebbles is either randomly distributed or systematically follows linear tracks apparently with the direction of water drains (Fig. 3a and b). There are linear and arcuate tracks in the area wherein the transportation of pebbles takes place in two ways viz. (a) by the velocity of streams and (b) by creeping causing the removal of wet soil laden with the pebbles. These pebbles get concentrated near the hummocks or rock debris (typically country-rock basalt) (Fig. 3c and d), nevertheless, there is a reasonably good concentration of silica sand and pebbles within the regolith (Fig. 3e and f). The silica nodules generally occur as secondary cavity-filling mineralization within the Deccan trap basaltic lava flows and that these are detached from the host rock (basalt) by weathering of lava flows. Subsequently, these are carried away by water currents during rainy seasons or transported as overburden by gravity in the colluvial areas. The detritus along with separated silica pebbles form sheet wash deposits that are spread over the area and ultimately get deposited into the perennial lakes, in the present case Futala Lake. It was however observed that the overall density of pebbles significantly dwindles and fining trend of the sediments towards the lake. Therefore, there is an overall paucity of silica nodules around the fringe of the lake. Moreover, the pebbles are also exposed every year during the rainy season and get transported through either existing or newly made channel ways (Fig. 3g and h).

2.2 Vertical Distribution (Soil Profile)

In order to check the depth persistence of the silica pebbles within the soil, small pits were hand-dug. Two 15 cm profiles of the soil up to the persistence of silica pebbles about 100 m apart were taken and measured at two sampling locations, namely Location 1 and Location 2. At location 1, the density of the silica pebbles was much higher compared to location 2 (Fig. 2).

Section 1 (Sample Location 1) has been divided into four zones (Fig. 4a) in which the topmost part is comprised of grass, humus, roots, soil attached to the root and silica pebbles. The subsequent zone is dominated by silica pebbles embedded within the soil. The next zone consists of soil with fragments of bedrock basalt and the bottom-most zone consists of bedrock basalt showing spheroidal weathering. In this zone, silica pebbles were not seen. In Sect. 2 (Sample Location 2), the topmost soil horizon is composed of grass, grassroots, humus with minor silica sand. The next zone has few silica pebbles, silica sand, plant debris and humus. The last zone which is below 10 cm is comprised of the bedrock basalt showing spheroidal weathering (Fig. 4b.).

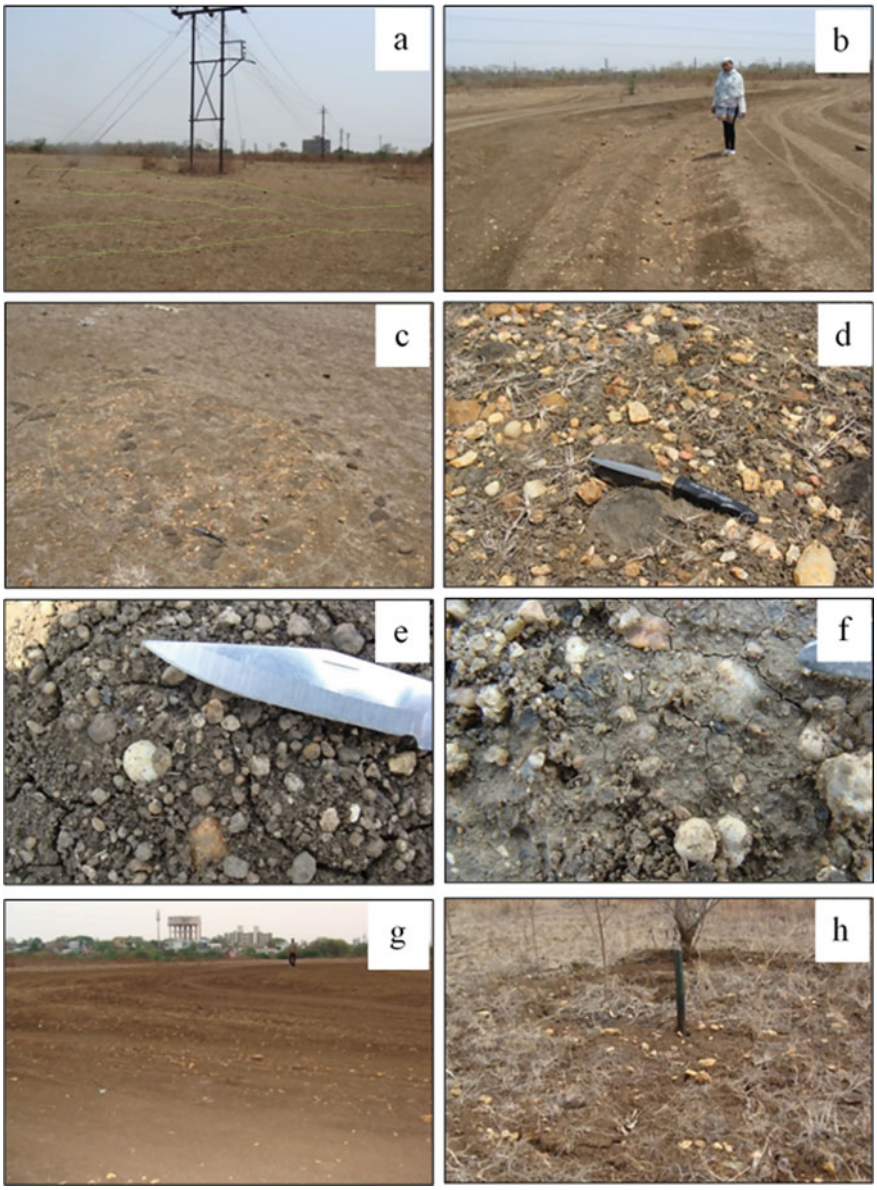

Fig. 3 **a** Silica pebbles are concentrated along the course of small first and second-order streams. The dashed line indicates the rough boundary of streams in which pebbles were concentrated, **b** Large concentration of silica pebbles along the road, **c** Dotted circle shows the maximum concentration of silica pebbles, **d** Thick populations of silica pebbles were exhibiting variation in their shape and sizes, **e** A closer view of the detritus showing the presence of rounded silica pebbles (knife-edge around 5 cm), **f** Another view showing silica pebbles mix with soil, **g** A view of playground showing the profuse presence of silica pebbles on the surface and also buried soil, **h** A view of non-littered forest soil showing the abundance of silica pebbles

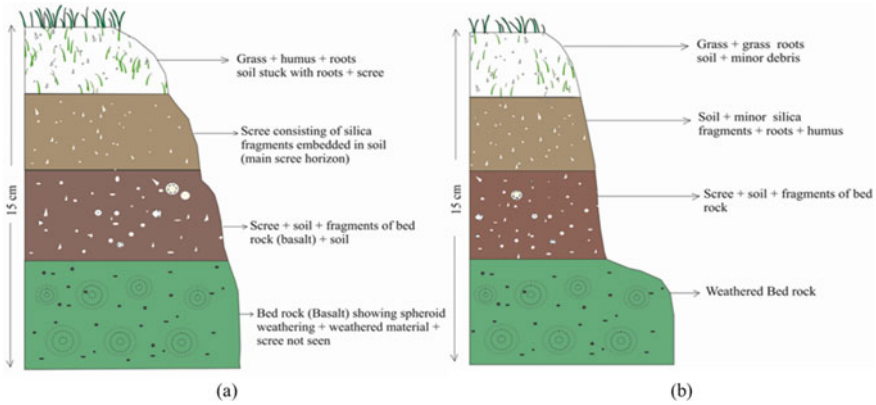

Fig. 4 **a** Soil profile at Location 1 **b** Soil profile at Location 2

3 Sampling and Analytical Techniques

3.1 Sampling

Ensuring a representative soil sample, composite surface soil samples were collected from different parts of the area. Samples were collected from (a) flood plain area having a high density of silica nodules, (b) flood plain area having the low density of silica nodules, (c) the adjacent area (at the foothill) which is free from human activities and has a reasonable population of silica nodules and (d) the top of the basaltic hill.

Total four samples, one each from the above-mentioned areas were collected from shallow pits which were hand-dug with hammer and chisel (Table 2). Pits were 60 cm wide, 60 cm broad and 10 cm deep (Fig. 5a–d). The depth was intentionally kept low because the silica pebbles occur at a very shallow depth. Moreover, there is no depth persistence of the silica nodules although the thickness of the soil column increases towards the lake. The collected samples have the following components:

1. Detritus, which is dominantly composed of soil with silt and clay,
2. Suspended silica nodules,
3. Fragments of country rocks, in this case, basalt, and
4. Biomass, which is composed mostly of roots, leaves, and smaller stems of plants.

3.2 Sample Processing

The collected sample from each pit was weighed accurately and afterwards, the fragments of country rocks (rounded basaltic nodules) were separated. The silica nodules and biomass were also separated; however, the biomass was not stored,

Table 2 Composition of collected samples. The remaining fraction of soil is calculated separately

Sr. no	Sample number	Weight of original sample collected (kg)	Total weight of silica fragments	Total weight of country rock (Basalt)	Weight of remaining sediments	Sample selected after coning quartering		Sample location
						Sample A	Sample B	
1	KR/486	44.48	0.371 kg	3.109 kg	41.00	0.553	0.626	Flood plain area with low density of silica pebbles
			0.83%	7.00%	92.17%			
2	KR/487	46.96	2.607 kg	0.052 kg	44.301	0.790	0.525	Flood plain area with low density of silica pebbles
			5.55%	0.11%	94.34%			
3	KR/488	42.30	0.120 kg	0.180 kg	42.00	0.505	0.840	Top of the hill
			0.35%	0.53%	99.30%			
4	KR/489	41.00	3.29 kg	2.68 kg	35.03	0.642	0.621	At the foothill
			8.02%	6.54%	85.44%			

since its weight was negligible. Then the weight of separated fragments of country rock and silica nodules were accurately measured. After weighing, the country-rock fragments were not attended further and discarded. The silica pebbles were cleaned and washed with tap water, dried, and kept for further study. From the remaining detritus, the soil was processed further. The desired quantity of soil sample was obtained by coning and quartering method (Fig. 5e and f; Table 2).

3.3 Grain Size Separation

The present samples being weakly consolidated contemporary sediments, no diminution or pulverization by percussion was necessary. Therefore, the samples were separated by sieving. The distribution of grain sizes in soil samples by sieve analysis is primarily applied to soil particles with sizes varying from 3.35 mm to 0.063 microns. Size separation can be achieved through dry sieving and wet sieving. Dry sieving is a sieving process that is used for soil with relatively coarser fragments (above 75 microns and below 4.75 mm) (Analysis and by Wet and Dry Sieve Analysis—IRICEN 2021). On the other hand, wet sieving is used only for the soil fraction with considerable plastic fines.

Fig.5 Sampling methodology and location of samples: **a**–**d** are sample locations as per samples KR/486 to KR/489 consecutively. Figure 5 **e** and **f** show coning and quartering of collected samples (see text for discussion)

3.3.1 Dry Sieving

For dry sieving, the weight of the dry soil sample retained on the 75-micron I.S sieve was weighed and recorded. The sieves were arranged in a sequence of decreasing mesh sizes from top to bottom Then the soil sample was poured into the top sieve and the sieve stack was shaken for 10 min to separate the particles from coarser to finer. Finally, it was observed that the particles having sizes larger than the sieve opening retained on it and those having smaller sizes were able to pass through. A pan was

used to collect those particles that pass through the last sieve. Then the cumulative % finer corresponding to each sieve size or grain size has been computed and plotted to obtain the grain size distribution curve from which the uniformity coefficient and coefficient of curvature were determined.

3.3.2 Wet Sieving

Prior to chemical analysis, the grain size separation for particle sizes finer than 75 μm was achieved through the wet separation method at the National Bureau of Soil Survey and land Use Planning, Nagpur (Table 3).

4 Data Analysis and Interpretation

The analytical data were generated and estimated from processed samples to study the abundance of secondary silica and its mode of enrichment in all size fractions, to recognize the influence of the unusual quantity of silica in the flood plains on soil and environment of deposition and to determine the presence of free silica that can affect lake water ecosystem and human health. For this purpose, the following analytical and modal computing approaches were adopted.

1. Modal analysis of silica pebbles using image analysis techniques
2. Grain size distribution
3. X-ray diffraction analysis.

4.1 Modal Analysis of Silica Pebbles Using Image Analysis Technique

Image analysis of the photographs showing an abundance of silica pebbles was carried out using the black-white threshold to estimate the population density of silica pebbles. However, it is also known that the distribution of these pebbles is not even and therefore would not be a true representative of their overall abundance in the soil. Nevertheless, silica pebbles are fairly abundant in the studied area so that an average of high population density and low population density can still provide a useful estimation of the overall distribution of silica within the soil. Therefore, in order to attempt the model analysis, five different images were chosen. Each image has been processed through IMAGE-J software.

Image-J software analyzes various objects showing contrast in tone, texture, hue, saturation, etc. Each object with a particular feature is identified as a polygon. The

Table 3 Procedure adopted for wet separation of soil

Separation methods	Reagent	Procedure
Removal of soluble salt and carbonates	Sodium acetate (NaOAc), 1 N, 136 g per litre, adjusted to pH 5 with acetic acid	Place 10 g air-dry soil containing no particles larger than 2 mm in a polythene bottle. Add 50 ml NaOAc solution, warm on water bath, then centrifuge and decant and supernatant. After removal of excess salt and $CaCO_3$, follow the treatment of H_2O_2 for removal of organic matter
Removal of organic matter	Hydrogen peroxide (H_2O_2), 30%	Add 5 ml of H_2O_2 in a sample previously to treat the removal of carbonates and soluble salt. Add H_2O_2 in increments of 5 to 10 ml or less. Stir the suspension and allow time for any strong effervescence or frothing to subside. Place it on a water bath to warm. Remove the centrifuge bottle from the water bath to warm
Removal of free iron oxide	Na-citrate dithyrite 0.3 M, 88 g, per litre sodium bicarbonate ($NaHCO_3$), 1 N, 84 g per litre and sodium dithionite ($Na_2S_2O_4$)	Add 40 ml of 0.3 M Na-citrate solution and 5 ml of 1 N, $NaHCO_3$ solution to the sample that has been treated to remove soluble salts, carbonate and organic matter. Warm the suspension to 75–80 in a water bath and then add 1 g of solid $Na_2S_2O_4$, stir the suspension constantly for one minute and occasionally for a total of 15 min, centrifuge and decant the supernatant. Repeat the treatment twice or thrice for a sample each originally contain more than 5% extra Fe_2O_3, then wash the sample with distilled water and make it free from Fe2O3. The sample freed from salt/ carbonates and organic matter and free iron oxide not dried at any time during the procedure. The sample is now ready for further processing

(continued)

Table 3 (continued)

Separation methods	Reagent	Procedure
Separating sand silt and clay (dispersion and wet)	–	The sample is in the centrifuge bottle (pre-treated to remove soluble salt, carbonate, organic matter and free iron oxide) is now ready for wet sieving to separate the sand. Use a 53-micron sieve to separate the sand particles. Tilt the centrifuge bottle neck downward over the sieve. Direct a jet of water up-ward into the bottle, sweeping the soil particles downward into the sieve by the force of the effluent stream. Do not rub the screen any time. When the transfer has been completed, agitate the residue on the sieve with a jet of water (cautiously, to avoid damage to the screen), and obtain as possible. Collect the coarser and fine fraction (sand) into a weighed beaker and place it in the oven at 110ºc for drying and weigh the contents. Transfer the fine fractions on the screen of the sieve into a 1-L polypropylene bottle. Add distilled water to make up the volume of the suspension Add 2% sodium carbonate (dispersing agent) in the suspension and raise the pH of the suspension to 9.5. Place it in a water bath for ½ an hour heating. Cool and transfer the suspension into the 1-L cylinder. Record the temperature of the suspension. Insert the plunger in the suspension, and move it up and down to mix the content thoroughly. Use a strong upward stroke of the plunger near the bottom to lift into suspension any particles that may have lodged there. Dislodge any sediment that remains in the lower corners by inclining the rod slightly and rotating it to impart a spinning motion to the plunger disk. Finish with two or three slow, smooth strokes and remove the plunger, tipping it slightly to remove the adhering drops. Record the time immediately. Note the temperature of suspension and see the sedimentation time for different particles settling through the water to a depth of 10 cm. Move the pipette towards the cylinder containing suspension and make the adjustment required to immerse the pipette 10 cm in the suspension. When the proper time is arrived then collect the volume of the suspension through a pipette and transfer to the weighed beaker and place it in the oven at 110ºc for drying. Similarly, the falling time for fine, medium and coarse clay fractions may be followed to determine the sub-fractions of clay

(continued)

Table 3 (continued)

Separation methods	Reagent	Procedure
Washing the sample	–	It takes three or four days to wash the sample. The washing of the sample is depending on the timing and centrifuge machine *a. Washing for total clay (T.C)* For the separation of the total clay, the sample is taken in the centrifuge machine each for 30 min. After 30 min, half of the sample's water remove and the remaining water is taken as it is. This process repeats till the sample water remove the turbidity and show clear water *b. Washing for fine clay (F.C)* For the separation of the fine clay, the sample is taken in the centrifuge machine for 45 min or 1 h. And repeat the same procedure as mention in the above process *c. Washing for silt + clay (S.C)* For the separation of the silt + clay, the sample is taken in the centrifuge machine for 30 min. And for the sand separation, it takes 5 to 10 min only

area under each polygon is automatically calculated and each polygon is automatically numbered. The complete data for every polygon is generated and finally, the total area is estimated by summing up the area under each polygon. However, rectification is necessary to delete the polygon of undesired material; in this case, the boulders of basaltic country rock and penknife (scale factor) were removed after rectification. Finally, the remaining polygon represents the actual population of silica pebbles.

4.1.1 Criteria and Purpose for Selecting Images

(1) Figure 6-1 represents the image of an area that has a reasonably high population density along with boulders of country rock, which is basalt.
(2) Figure 6-2 represents the higher population density of the silica pebbles which were arrested by a hummock.
(3) Figure 6-3 represents a high population of silica pebbles from a longer distance (comparison can be made with previous images by a penknife in the photograph)
(4) Figure 6-4 represents an image from high population density soil from a short distance (see penknife in a photograph for comparison)
(5) Figure 6-5 represents the area with a relatively lower population density.

4.1.2 Key Inference of Modal Analysis

Summary of modal analysis calculated from each image is given in Table 4. It has been observed that the percentage area occupied by high population density of silica pebbles (Fig. 6-1 and 6-2) is about 10% (8.878% and 9.436% respectively) whereas that occupied by a low density of pebbles is less than 5% (4.715%). However, the area covered by the photograph potentially influences the population density of silica pebbles. Therefore, Fig. 6-3 although appears to have large population density, actually has only about 5% area covered by silica pebbles (Table 4). On the contrary, the smaller area covered by a photograph (Fig. 6-4) shows a descent population of silica sand, but the silica pebbles seen under this image shows a surprisingly high population density of more than 10% (10.901%).

Obviously, the lower focal length (i.e. zoomed) images are worthless for estimating the population density of silica pebbles. Same is the case with an image having a higher focal length (long-distance). Therefore, the estimates here are based on the average focal length covering an area of about 1×1 m size. Such estimation has shown that the population of silica pebbles is up to 10% of the total area in the small channel ways. However, the rain wash channels are randomly distributed, which significantly reduces the reliability of the above data. Nevertheless, the modal analysis paves a way for visualizing the concentration of pebbles in the study area.

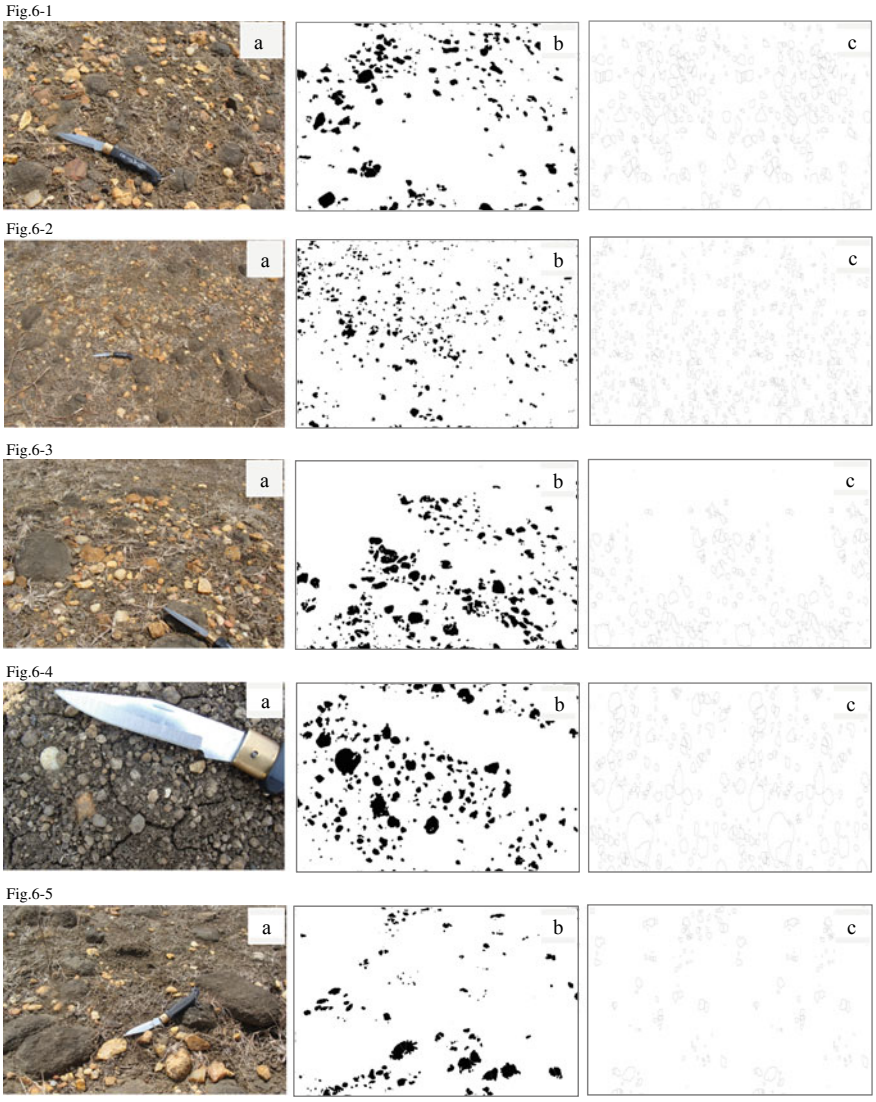

Fig. 6 Figures 6-1–6-5 modal analysis using the image capture technique. **a** Actual image from which calculations were made, **b** polygons identified and rectified, and **c** Final polygons that were used for calculating modal proportion of silica pebbles

4.2 Grain-Size Analysis

In medical geology, silica usually refers to respirable crystalline silica dust. Dust that is inhaled may consist of fine particles, invisible to the naked eye and mostly smaller than 7 microns in diameter (Berube et al. 2004). So, it is necessary to accurately

Table 4 Table showing the population density of silica pebbles within the soil in the Futala rain wash deposit. Emboldened figures indicate the total area occupied by silica pebbles at different places as mentioned in the remark's column

Image	Slice	Count	Total area	Av. Size	% area	Major	Minor	Angle	Remarks
Figure 6-1	DSC08634.tif	441	13,132.5	29.779	**8.878**	5.792	3.995	94.258	General view of the ground containing silica pebbles in the area
Figure 6-2	DSC08652.tif	497	11,376.65	22.891	**9.436**	5.002	3.645	97.243	Silica pebbles accumulated in a hummock, therefore the density (pebble-occupied area/total area) is more
Figure 6-3	DSC08631.tif	646	54,461.95	84.306	**5.086**	10.095	7.41	88.979	Little far-off view of the ground having a reasonably large population of silica pebbles
Figure 6-4	DSC08659.tif	380	1003.363	2.64	**10.902**	1.648	1.245	89.377	A nearer view of the ground showing a reasonable population of silica is present in the soil
Figure 6-5	DSC08646.tif	237	9864.102	41.621	**4.715**	6.674	4.711	82.086	An area containing a lesser population of silica pebbles. Although bigger ones are seen

measure individual particle sizes. The size and distribution of the sand, silt and clay fractions were determined by sieve analyses and wet separation method.

4.2.1 Primary Analysis

Table 2 gives an idea of various materials presents in the sample. It can be seen that a major portion is occupied by soil which ranges between 85 to 99% whereas the silica pebbles weigh between 0.3 to 8% which is a considerable range and show the influence of distribution pattern. The country-rock boulders that are mixed with soil and got collected in the samples vary between 0.1 to 7%. The reason for the observed variation in weighed percentage is discussed below.

Variation in soil percentage

The sample that was collected at the hilltop is almost entirely composed of soil (99.30%); surprisingly at these locations thickness of the soil bed was more compared to other locations. However, towards the foot hillside, the soil percentage is the lowest among the samples studied (85.44%). At other locations on the ground, soils percentage is 92.17% and 94.34% respectively. This distribution indicates that (i) the soil is very abundant in the rain-wash deposit of Futala lake, (ii) High percentage of the soil at the hillocks indicates in-situ weathering and incipient lateritization, which facilitated soil formation, (iii) Lower percentage of the soil at the foothill indicates that colluvial deposits have more percentage of dislodged fragments (scree and talus), and (iv) The sample collected on the otherwise plain ground comprises 90–95% soil by weight.

Variation in silica pebbles

Weight of the silica pebbles is usually lower compared to the fragments of bedrock basalt and basaltic soil which is rich in ferromagnesium-rich clay minerals. Therefore, the weight percentage of silica pebbles could be significantly different from its volume percentage, which was discussed in the previous section. Notwithstanding above, the weight percentage of silica pebbles provides useful clues about overall distribution. The most striking feature is the paucity of pebbles on the hilltop soil (0.35%) and its high abundance in the colluvial sample (8.02%). Another significant observation is the high abundance of pebbles at some places on the ground (5.55%) as compared to other (0.83%). Such difference may be attributed to the local influence of ephemerals channels carrying rainwater with the suspended load during the rainy season or flooding of the ground from the hilltop over the surface.

Variation of basaltic boulders

Boulders of the country-rock are separated due to spheroidal weathering. In this process, the unaltered core is separated as a spheroidal nodule whereas the remaining altered material which is not converted to clay also occupy the soil. The place where the bedrock is shallow, their percentage is higher (7%) and also in the colluvial area,

it is more abundant (6.54%). At other places, its concentration is very low (0.052%) and similarly, at the hilltop, it is lower (0.53%).

4.2.2 Analysis by Dry Sieving and Wet-Separation

The procedure for dry and wet sieving is described in Sect. 3.3. The mass of soil retained on each sieve was obtained by subtracting the weight of the empty sieve from the mass of the sieve + retained soil. The percent retained on each sieve was calculated by dividing the weight retained on each sieve by the original sample mass. Then, as a cumulative procedure, the percent passing was calculated by starting with 100 percent and subtracting the percent retained on each sieve. The final results of sieve analysis (dry sieving) are described in Table 5. However, sand, silt and clay fractions were accurately determined using the wet separation method.

The procedure for grain size distribution by wet sieving has been elaborated in Table 2. Accordingly, the cumulative results of the analysis are described in Table 6. Tables 5 and 6 give an outcome of this analysis, which is graphically represented in Fig. 8. The cursory inspection indicates that silt is the most abundant fraction (35–50%) among all sizes whereas fine clay is much lower (<0.45%). The overall proportion of clay varies marginally between 28.94 and 36.14%; whereas that of silt shows greater variation between 36.73 and 49.21%. The distribution of sand fraction in the samples is clearly bi-modal where two samples show a range of 16.21–16.47% and the other two samples having 30.39–33.96%. The fine clay varies from 0.3 to 0.43%; this variation though appears relatively lesser; this size fraction can greatly influence trace element concentration and a variety of biochemical processes. Figure 7 shows the grain size distribution curve; D_{10} indicates the grain diameter at which 10% of particles are finer and 90% of the particles are coarser; whereas D_{30} indicates the grain diameter at which 30% of particles are finer and 70% of the particles are coarser. The textural class was determined using the U.S. Department of Agriculture (USDA) textural triangle as given in Soil Survey Manual (Soil Survey Division Staff 1993). Accordingly, the present area soil would be classified as clay loam.

4.3 X-Ray Diffraction Analysis

X-Ray Diffraction Analysis is used here for the identification and quantification of mineral phases in clay and silt samples. Before the samples were analyzed, they were treated with calcium and potassium using the standard procedure (e.g. Soukup et al. 2008; Srivastav et al. 2011, 2013). The potash treated samples were analyzed at 25, 110, 300 and 550 °C temperature. Such different treatments allow seeing phase transition occurring in the samples. It is commonly observed that there is a marked shift in intensities as well as 2 theta (2θ) values.

Table 5 Distribution of sample weights as per size fractions. However, sand, silt and clay fractions are accurately determined using the wet separation method

Sr. no	Sample no	Weight of sediment	Sieve #	30	50	80	120	200	Pan	Total weight (kg)
			Diameter (mm)	0.600	0.300	0.180	0.125	0.075		
1	KR/486	Actual weight (Kg)		0.309	0.069	0.058	0.025	0.031	0.061	0.553
		Percent weight (%)		55.87	12.48	10.49	4.52	5.61	11.03	
		Cumulative weight (%)		55.87	68.35	78.74	83.36	88.97	100	
		Percent passing (%)		44.13	31.65	21.16	16.64	11.03	0	
2	KR/487	Actual weight (Kg)		0.475	0.119	0.084	0.03	0.036	0.048	0.79
		Percent weight (%)		60.42	15.11	10.13	3.61	4.56	6.17	
		Cumulative weight (%)		60.42	75.53	85.66	89.27	93.83	100	
		Percent passing (%)		39.58	24.47	14.34	10.73	6.17	0	
3	KR/488	Actual weight (Kg)		0.35	0.063	0.036	0.014	0.017	0.023	0.505
		Percent weight (%)		69.41	12.58	7.22	2.77	3.47	4.55	
		Cumulative weight (%)		69.41	81.99	89.21	91.98	95.45	100	

(continued)

Table 5 (continued)

Sr. no	Sample no	Weight of sediment	Sieve #	30	50	80	120	200	Pan	Total weight (kg)
			Diameter (mm)	0.600	0.300	0.180	0.125	0.075		
		Percent passing (%)		30.59	18.01	10.79	8.02	4.55	0	
4	KR/489	Actual weight (Kg)		0.323	0.113	0.087	0.033	0.034	0.051	0.642
		Percent weight (%)		50.31	17.6	13.55	5.24	5.4	7.9	
		Cumulative weight (%)		50.31	67.91	81.46	86.7	92.1	100	
		Percent passing (%)		49.69	32.09	18.54	13.3	7.9	0	
				Coarse Sand	Medium Sand	Fine Sand	Very Fine Sand	Medium Silt	Medium-Fine Silt	

Table 6 Distribution of sample weight percentage as per size fractions

Sr. No	Sample Number	Sand%	Silt%	Total Clay%	Fine Clay%
1	KR/486-1/B	16.21	49.21	34.16	0.43
2	KR/487-2/B	33.96	36.73	28.94	0.39
3	KR/488-3/B	30.39	38.2	31.13	0.3
4	KR/489-4/B	16.47	47.04	36.14	0.37

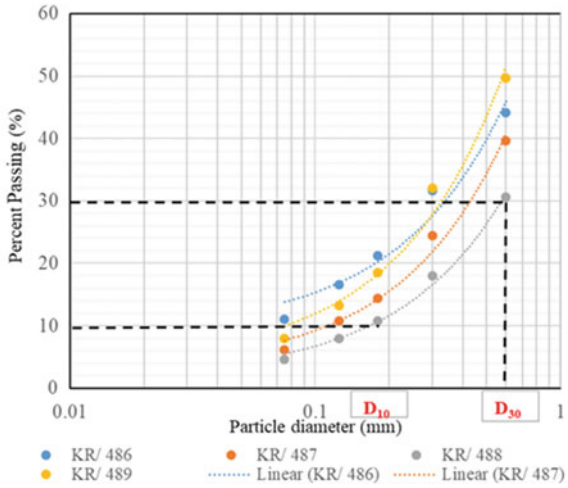

Fig. 7 Plot of percent passing versus particle diameter

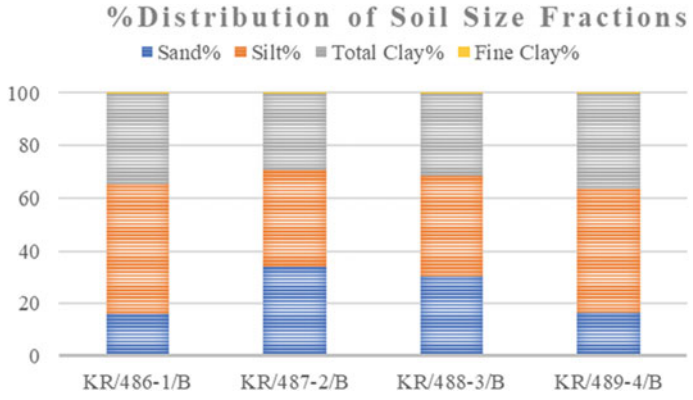

Fig. 8 Histogram showing percent distribution of sand, silt, total clay and fine clayin the studied samples from the Futala catchment area

The X-ray diffraction (XRD) analysis was performed on a Panalytical X'Pert Pro diffractometer with CuKa radiation generated at a voltage of 40 kV and a current of 40 mA. The diffractograms of 486 Silt, 486 Fine clay, 489 Silt, 489 Fine clay and 489 Total clay are shown in Fig. 9a–e. In the XRD graph, the narrow peaks represent non-clay minerals whereas the broader one represents clay minerals (Chacha 2014). Silt fraction shows characteristic peaks at d-spacing of 4.26, 3.35, 3.21, 3.18 indicating the presence of quartz, potash feldspar, plagioclase feldspar and pyroxene in soil samples (Fig. 9a, c). While in total clay fraction, the d-spacing corresponding to 2 theta values are located at 4.26, 7.15, 10.01, 14.45, 17.59 indicating the presence

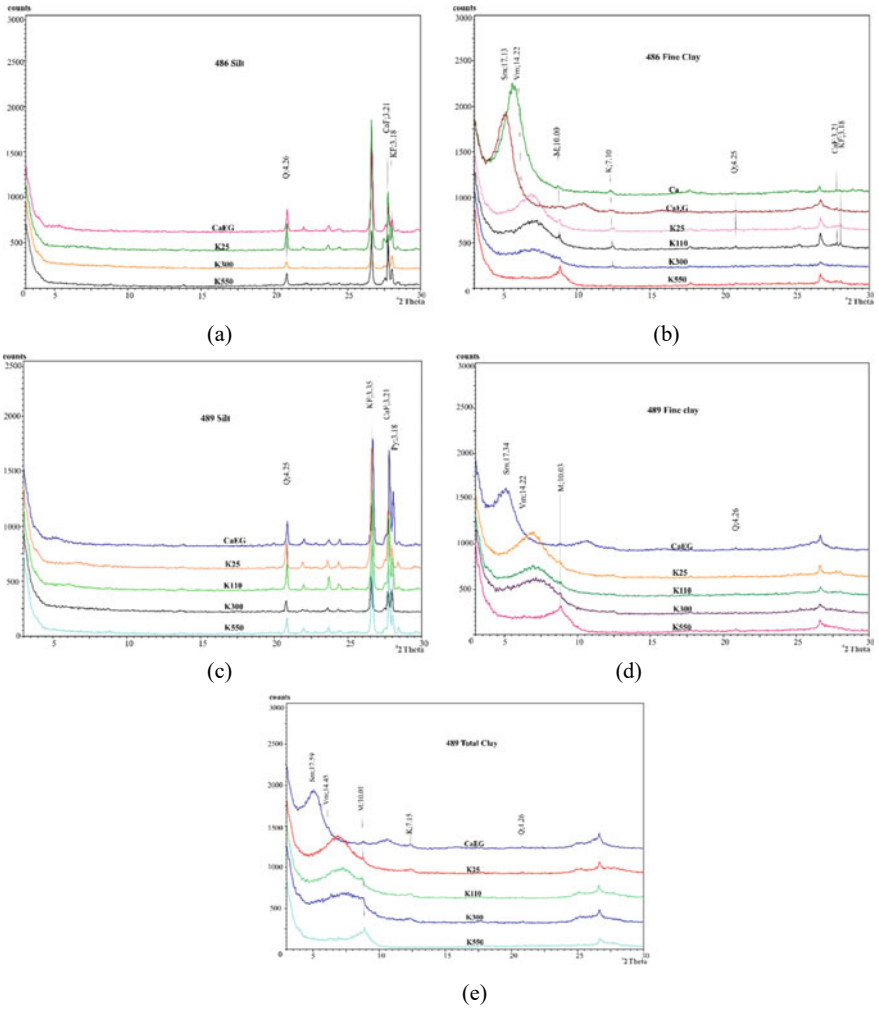

Fig. 9 Diffractograms of **a** 486 Silt, **b** 486 Fine clay, **c** 489 Silt, **d** 489 Fine clay and **e** 489 Total clay

of quartz, kaolinite, mica, vermiculite and smectite (Fig. 9e). Mineralogy of Ca-saturated 486-fine clay fraction of the representative soil sample indicates peaks at 3.18, 3.21, 425, 7.10, 10.00, 14.22 and 17.13 d-spacing regions (Fig. 9b, d) In the same diffractogram, the 14.22 peak shifts to 17.13 region on glycolation, indicating the presence of smectite. The conspicuous absence of 5° peak (17.34) in the silt sample is observed even at 550 °C, indicating the absence of smectite. In clay fractions, the 9° peak of mica is reinforced when K-saturated samples were heated from 25° to 300 °C, indicating the presence of mineral vermiculite at 14.45 d-spacing in a very small quantity. The peak of kaolinite at 7.15 d-spacing is broad at its base with narrowing towards the low-angle side indicating that this mineral is interstratified probably with expanding type mineral.

4.4 Rare Earth Elements (REE) Analysis

Rare earth elements (REEs) are thirteen in number (except Pr) which are named lanthanides. These are lanthanum (La) to lutetium (Lu) with mass number 57 to 71 and yttrium (Y^{3+}; mass number 39) although not falling under REEs, possess similar chemical attributes such as ionic radius and charge as lanthanides (radius almost equal to Ho) and hence yttrium is placed in between Dy and Ho (Rabha et al. 2018). Hence, in the present study, rare earth elements and yttrium (REE + Y = REY) characteristics and their ratios, upper continental crust (UCC) normalized distribution patterns are studied, as these are used as natural/environmental tracers for plants, soil, and aquatic-marine, geological systems (Welch et al. 2009; Han et al. 2017). The quartz concentration of soil influences the distribution patterns of many other elements. It crystallizes over a wide dynamic range—from low-temperature α-quartz (e.g., veins) to the high-temperature and pressure α-quartz and β-quartz stability limits in igneous and metamorphic regimes. Rare earth elements (REE) analyses of soils in the study area were performed using inductively coupled plasma mass spectrometry (ICPMS).

The soil samples under present study are in-situ surface soil samples and slightly influenced by sheet-wash activity as well as they suffered down the slope migration which are derived from a basaltic parent and as the bedrocks basalts are present in the study area; it is imperative that the study area is not under agriculture or influenced by industrial activity. The REY are fractioned, mobile during weathering and pedogenesis processes. The degree of fractionation and mobility depend on the physicochemical conditions that prevailed over the geological past. Their enrichment due to anthropogenic activity is also recorded from specific locales due to prolonged activities such as agriculture, mining, industrial etc., and REEs are highly sensitive to redox potential, soil pH, and adsorption/desorption reactions related to organic matter (OM) and iron-manganese oxides (Wenxiang et al. 2020).

The upper continental crust (UCC) normalized rare earth element distribution patterns (Cédric and Sophie 2009) of studied soil samples are highly coherent, less fractionated (La/Yb_N = 0.39–0.68) and show relative depletion of light REES

(LREE-Lu to Eu) over heavy (HREE-Gd to Lu) with positive Eu and negative Y anomalies (Fig. 10). The Ce, Y and Eu anomalies in the soils are attributed to the parent rock mineralogy, oxidation/reduction characteristics, leaching and other pedogenetic processes are observed in order Ce > Y > Nd > La > Gd > Dy > Sm > Er > Yb > Ho (Fig. 11). The REY distribution pattern in soils follows the geological parents in the Earth's crust, which is the original source of these elements in soils (Markert 1987). The dominance of quartz pebbles admixed in the soil horizon influence dilution of REE in the form of depletion of LREE of a flat, unfractionated basaltic REE distribution pattern (Alfaro et al. 2018). This is further substantiated by the observation of Chen and Yang (Jiyan and Ruidong 2010) and Alfaro et al. (2018); wherein the authors reported that the enrichment in HREE in some basaltic weathered soils may be due to the stability of the complexes formed by the HREE and other complex anions is higher than that of the LREE.

The ∑REY of the studied soil samples is in the range of 163–212 ppm with an average of 188.2 ppm, which is higher than the crustal average and upper continental crust (UCC) abundances which are 142.2 and 167.37 ppm respectively (Taylor and McLennan 1985), but the REY distribution patterns of the studied samples mimic European Shale (∑REY = 230 ppm) patterns (Haskin and Haskin 1966), except for a slight hump in the HREE when normalized with C1 Chondrites. The similarities in REY distribution patterns of studied soils indicate their parent from which the soils are derived with moderate modification in LREE. The Y, Ho and Dy are trivalent and exhibit similar geochemical behavior (Jahn et al. 2001). The Y/Ho and Y/Dy ratios of basalts (N-MORB) (Sun and McDonough 1989) are 27.7 and 6.2 respectively. The soil samples under the present study record fairly less ratios 21.7 and 5.6 respectively indicating significant mobility of yttrium from the soil samples thus dry and hot weather is responsible during the pedogenesis process (Liankai et al. 2020).

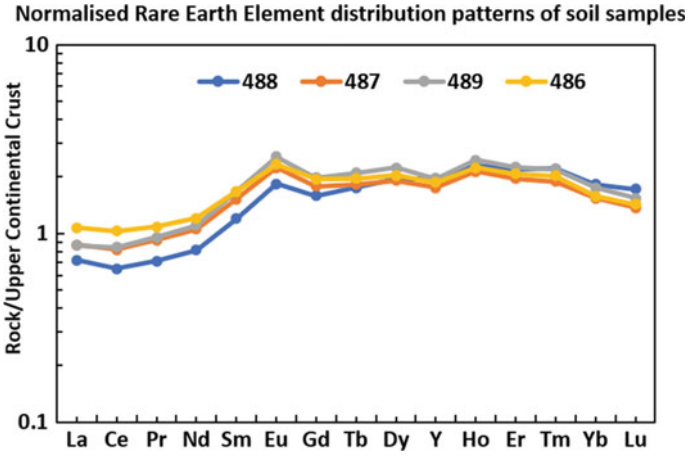

Fig. 10 Upper continental crust normalized rare earth element and yttrium distribution patterns of the studied soil samples

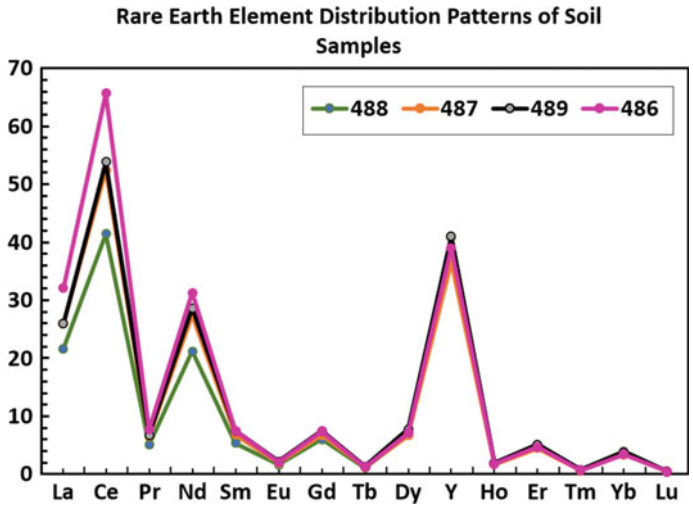

Fig. 11 Comparative distribution of REY of the soil samples

Thompson et al. (Thompson et al. 2013) studied the fractionation of yttrium and holmium using experimental studies on the Hawaiian basalts and derived basaltic soils. According to them, the $(Y/Ho)_{CN}$ of Hawaiian basalts is 0.994 and that of resultant surface soils is 0.99 ± 0.07. Fractionation of Y and Ho during weathering process of the surface soils resulted in decreased ratio to 0.76 ± 0.05 at 150 ky and then remained unchanged in the deep soil profile. If the same model is implemented for the soil samples of the present study, the $(Y/Ho)_{CN}$ range from 0.75–0.79 with an average of 0.77 which is in good agreement with the Hawaiian soils. Thus, it is can be speculated that the pedogenesis processes in the study area might be initiated before 150ky from the present. The above observations imply that; (1) the quartz pebbles are in situ, (2) formed by normal pedogenetic processes, (3) free of influences by the industrial or agricultural activities, and (4) formed within the past 1,50,000 years.

5 Discussion

The catchment of Futala lake and surrounding areas has a special geological cause for an anomalous concentration of mineralized silica, which is one of the most dangerous agents causing lung diseases such as silicosis and COPD. Therefore, evaluation of the hazard potential of this dust, which is unknowingly inhaled by the residents and regular visitors in the surrounding localities, is necessary. The measurement of dust by dust samplers would have been one direct method of estimation, however, during the present study such a sampler was not available. Therefore, we adopted an alternate method of estimation in which, sampling and analysis of soils were done

for characterizing the geogenic source of mineralized silica and estimating its hazard potential. Accordingly, the results of the present study are discussed below.

Presence of silica in different size fractions: In the study area, the secondary silica is equally enriched in all size fractions and distributed within the regolith and on the surface. There are linear and arcuate tracks in the area wherein the transportation of pebbles takes place by the velocity of streams, and the removal of wet soil laden with pebbles by creep. However, this distribution of pebbles does not remain systematic and it shows fining trend of sediments as they approach the lake.

Soil Profile: The vertical section of soil shows four distinct zones: top zone dominated by grass, humus, roots, soil attached to the root and silica pebbles; followed by zone consisting of silica pebbles embedded within the soil. The next zone consists of soil with fragments of bedrock basalt and the underlying zone of bedrock basalt showing spheroidal weathering.

Granulometric Analysis: The granulometric findings show that silt is the most abundant fraction (35–50%) among all sizes, whilst fine clay is significantly less abundant (<0.45%). The amount of total clay varies somewhat between 28.94 and 36.14%, but the fraction of sand varies significantly from 16.21 to 33.96%. The fine clay varies from 0.3 to 0.43%; nevertheless, this variation is minor. It is commonly known that respirable fractions are typically less than 5 μm in size. In the studied samples, the percentage of particles with a geometrical diameter less than 2 μm approximately ranged from 29 to 37%.

Modal Analysis using Image capture technique: The population density of silica pebbles is calculated using an average focus length encompassing an area of 1×1 m in size. Overall, the population of silica pebbles in small channel ways is estimated to be up to 10% of the entire area.

XRD studies: XRD study has been done to find the mineral phases in the soil sample. The XRD results indicate the presence of quartz, potash feldspar, plagioclase feldspar and pyroxene as main constituents in the silt fraction of soil samples. While in total clay fraction, the presence of quartz, kaolin, mica, vermiculite and smectite is significant. Fine clay has an overwhelming abundance of smectite, vermiculite along with mica and kaolinite whereas quartz plagioclase and potash feldspar occur in minor quantities. Strong peaks for quartz are present in the silt; however, it is also noticed in total clay and fine clay fractions. This implies that the soil of rain wash deposits is enriched in quartz in all size fractions. The presence of crystalline quartz in the overall clay fractions with other deleterious constituents (smectite, kaolinite, vermiculite) has a further implication that it will be present in the dust and can be inhaled and therefore may aggravate lung diseases.

Trace elements geochemistry: The overall REE distribution pattern of the studied soil samples indicate that the quartz pebbles are in situ, formed by normal pedogenetic processes, free of influences by the industrial or agricultural activities, and formed within the past 1,50,000 years.

6 Conclusion

Mineralized silica is a deleterious environmental constituent that forms a part of respirable dust in mining areas. However, it is seldom reported outside the active silica mines. The detailed study presented here is of the quartz and cryptocrystalline silica-laden soil within the municipal limits of Nagpur city. It has been demonstrated that the respirable dust emerging out of this soil has over 28–37 percent of the mineralized silica-rich clay fraction. Such highly mineralized silica-rich respirable dust, which can potentially cause severe lung infection, were not reported earlier from the urban areas. This study, therefore, presents a new source of geogenic health hazards.

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Toxicity and Occupational Health Hazards of Coal Fly Ash

Rajani Tumane, Shubhangi Pingle, Aruna Jawade, and Kirtikumar Randive

1 Introduction

In the world, Coal is mainly responsible for generating 38% of power. India generated 217.04 million tons of coal fly ashes (CFA), in 2018–19, of which only 168 million tones (77.5%) was utilized, according to the Central Electricity Authority. Coal combustion and precipitation technique; generate a waste product which consists of CFA, bottom ash, boiler slag, and flue gas desulfurization material with spherical in shape, either solid or hollow, and mostly glossy (amorphous) in nature that range from 0.1 μm to >100 μm in diameter (Pandey and Singh 2010; Zhou et al. 2020; Yao et al. 2015). India has to strictly regulate the disposal of toxic fly ash from coal-fired power plants to minimize environmental and health risks to local communities. Power utilities usually store the coal ash in landfills or unlined ponds close to water bodies and rivers. Breaches in the landfills and ash ponds frequently lead to environmental contamination, damaging local ecosystems and harming the health of local communities. CFA, fugitive dust emissions and leaching of metals into groundwater from landfills and surface impoundments may put people at risk for exposure (Zierold and Odoh 2020; Yashwant 2021). Toxic constituentsmainly occurred in CFA are aluminum, iron, calcium, oxygen, arsenic and lead, polycyclic aromatic hydrocarbons and silica (Zierold and Odoh 2020; Paul 1997). Short and Long-term CFA exposure leads to cause irritation of the nose and throat, dizziness, nausea, vomiting, and shortness of breath, liver damage, kidney damage, cardiac arrhythmia, and a variety of cancers. Lots of attention was reported on mining and burning of coal which leads to huge carbon emissions, the dangers of fly ash, the

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K. Randive et al. (eds.), *Medical Geology in Mining*, Springer Geology,
https://doi.org/10.1007/978-3-030-99495-2_14

residue left after coal is burnt in thermal power plants, have received less public attention, despite the risks to our health and to the environment. A new report released on "Coal Ash in India that a compendium of disasters, environmental and health risks seeks to remedy. It shines a spotlight on 76 major coal ash pond accidents between 2010 and June 2020 those has caused deaths and loss of property and have resulted in extensive pollution of nearby water sources, air and soil. Incidents of fly ash spills go unreported, though they were occurred on a regular basis had reported by healthy energy initiative India and community environmental monitoring, Chennai. Despite several policy and regulatory interventions, coal ash management in India remains a challenge.

Epidemiological studies in CFA exposed working populations have found no evidence for effects commonly seen in coal workers (pneumoconiosis, emphysema) with the exception of airway obstruction at high exposure. Most of the studies on CFA toxicity were not designed to elucidate the effect of its silica-content nor did they include coal mine dust as a reference (Yashwant 2021).

Taking this into account, available new technologies have not been implemented in India owing to variety of problems for human health hazards including inflammatory potential and fibrogenicity of CFA compared to silica and coal mine dust, environmental rehabilitation, treatment of CFA at vicinity of people living nearer to mine, and strategies for its management. On this backdrop, present chapter is aimed at shedding some light on the effects of CFA, environmental health hazards with special emphasis on the sustainability and Management of industrial mining CFA.

2 Sources of Fly Ash

India is the third largest electricity producer and consumer in the world. Coal based thermal power plants contribute about 70% of the total installed capacity of India. Coal combustion in thermal power plants is generating ~196 million-ton coal fly ash (CFA) annually. Coal is the major source of fossil fuel available all over the world in billions of tons and around 38% of the energy generated by coal. India's coal consumption will increase at an average of about 2.6% next 20 years. CFA is a byproduct of the combustion of coal and results in solid residue (Gollakota et al. 2019). Processes like thermal power generation plants (TPGP), steam generation plants, industrial boilers etc. will result in the formation of coal fly ash (Whiteside and Marvin Herndon 2018). 29% of coal supplies utilized worldwide for energy generation in 2015 (Bhatt et al. 2019). A TPGP of 1000 MW with 6600 equivalent working hours annually generates 377 kilo tons of fly ash partials (Eliche-Quesada et al. 2018). Coal is also the source of inorganic pollution (Ahmaruzzaman 2010). CFA are complex particles of a variable composition, which is mainly dependent on the combustion process, the source of coal, and the precipitation technique (Carlson and Adriano 1993).

3 Coal Fly Ash and Health Hazards

The health hazards of fly ash depend on the composition and concentration of elements found in the fly ash. When CFA is inhaled, this induces the leaching of genotoxic compounds to epithelial and alveolar cells and alters immunological functions. The accumulation of CFA in the lungs induced to release reactive oxygen species (ROS), enzymes (elastase, proteases, collagenase), cytokines (TNFα, MIP-1), growth factors (TGFb) stimulate fibrosis (Schins and Borm 1999). Studies also show that nanoparticles found in CFA can induce many toxic effects in the lungs including decreased host defenses, tissue inflammation, altered cellular redox balance toward oxidation, and genotoxicity. Oxidative stress and chronic inflammation can predispose to fibrosis and chronic lung disease (Whiteside and Marvin Herndon 2018).

Silicosis and coal workers' pneumoconiosis (CWP) has long been recognized as significant occupational lung diseases. The lung toxicity of coal dust varies from simple pneumoconiosis, characterized by the presence of small opacities (<10 mm) on the chest X-ray to complicated progressive massive fibrosis, pleural abnormalities, emphysema, chronic bronchitis, accelerated lung function loss, lung and stomach cancer have been reported in coal miners (Laney et al. 2010). The consequence of CFA on lung function is proportional to the cumulative dust exposure, the carbon content of the coal, and the amount of dust accumulated in the lungs after long-term clearance (Lighty et al. 2000). Coal contains a variable proportion of quartz, it has often been difficult to separate the pulmonary effects of coal dust from those of silica. Chronic obstructive pulmonary disorders and emphysema (shortness of breath) also noticed in coal workers studies at energy-generating industry including power plants and thermoelectric power stations, 10% of the free crystalline silica content was observed in the samples encountered at 14 work spots (Wojtczak et al. 1989).

The report shows presence of alpha-quartz, mullite, kaolinite and orthoclase in the ash samples. As compared to mining dust the concentration of the silica content is less in ash samples. With reference to diseases, the studies in the fly ash were limited to compare with mining data due to legal complications. An effect of silica toxicity and particles that incorporate silica as particle, needs to be monitored closely in general for future risk assessment as amatrix to generate data in comparison with mining population and those who are working near the ash disposal management.

The studies by Wozniak H pointed out occupational risk of power engineering workers, fly ash generated mainly contains coal fly ashes (CFA), possess quartz, orthoclase and mullite (fibrous in nature) with 31.6% silica content. He observed the occurrence of potentially fibrogenic and cancerogenic agents in ash.

The mineral components of CFA contain aluminum, silicon, and iron, which are known to induce pathogenesis of Alzheimer's and Parkinson's disease in humans and animal models. The development of neurodegeneration in CFA exposure is the consequence of susceptibility of the brain to oxidative stress due to high rates of metabolism, low antioxidant activity, and high cellular content of lipids and proteins (Whiteside and Marvin Herndon 2018).

The heavy metal content of coal ash can induce various disorders from respiratory and gastrointestinal tracts irritation, vomiting/nausea, stomach cramps, diarrhea, kidney damage, liver injury (jaundice), fragile bones, allergic skin reactions, hypertension, fatigue, hemolytic anemia, abdominal pain, nausea, arthralgias, headache, weakness, convulsions, irritability, constipation, weight loss, peripheral neuropathy, cognitive dysfunction, impotence, loss of libido, depression, depression of thyroid and adrenal function, chronic renal failure, and gout (Jaishankar et al. 2014; Rehman et al. 2018).

The children are more susceptible to CFA. Exposure to CFA induces symptoms of attention-deficit hyperactivity disorder, gastrointestinal problems, difficulty falling asleep, frequent night awakenings, teeth grinding, and complaint of leg cramps. The impairments in sleeping habits might be attributed to heavy metals, which are known to interfere with circadian rhythms of sleep and awake (Sears and Zierold 2017). Evidence indicates that short-term CFA exposure can change the skin bacterial community from adults of spring peepers (Pseudacris crucifer) and potentially alter the baseline function (diversity of metabolite production) of the bacteria (Hughey et al. 2016). The outcome from the study clearly shows that CFA can also alter the skin bacterial community and it may interfere with skin protection and functions.

4 Global View on CFA Related Health Impacts

The concentration of metals can be two times greater in CFA than coal and some of them are neurotoxins (Spencer and Drake 1987; Kim and Lynch 2002; Froehlich et al. 2011; Bouchard et al. 2006; Rodriguez-Barranco et al. 2013). Deposition of CFA dust at coal-fired power generating plants which is suitable for workers whom they were not directly exposed hazardous content of the CFA. But there are chances of exposure to the high concentrations of this dust during different tasks or activities like maintenance on electrostatic precipitators, baghouses, hoppers, and conveyors (ESKOM 1996). The main components of CFA are silicon, aluminum, and calcium showed on elemental analysis, and additional metal oxides like MgO, K_2O, TiO_2, and Pb_2O_5 also present at 1–3% and Pb_2O_5 at 0.3–3% (EURELECTRIC 2000). The dominated mass concentration of CFA is silica and aluminum oxide, while iron and calcium oxides present in significant amounts along with a variety of trace elements. CFA is a particle of fine spherical powdery with either solid or hollow in nature (Ahmaruzzaman 2010) and most CFA disposed of in landfills, widely used in concrete manufacturing processes or other industries (Alvarez-Ayuso et al. 2006).

The toxicological observations of CFA in experimental studies used higher concentration than environmental concentration and it might limit in mimicking natural condition (Mauderly et al. 2011). Borm reported (1997), that there is a lacuna in the design of toxicity studies in relation to silica-content of CFA and no inclusion

of coal mine dust as a reference and as well no suggestive data available that indicates CFA is solely an addition of (crystalline) silica and other components (Borm 1997). An obligatory step of closer investigation of matrix effects on silica toxicity is suggested in future risk assessment, where silica is used as a component of CFA and other particles.

The short-term exposure to CFA at occupationally relevant levels can induce mild neutrophilic inflammation in the lung and blood. However, the study reported that CFA does not have greater potency to cause pulmonary alterations when compared with concentrated ambient particles (Smith et al. 2006). The toxic metal analysis revealed its concentration far below the occupational exposure level while awareness about health effects and respiratory zones reported among workers (Engelbrecht et al. 2012). The author studied two case studies on coal combustion products (CCPs) and no adverse health effects of doses from both case study scenarios reported while, a mixture of multiple component effects remains uncertain (Liberda and Chen 2013).

5 Fly Ash Remediation

CFA management in India is a complex task as a huge quantity of CFA being produced in thermal power plants. An efficient utilization (100%) of FA in a timely manner is targeted by the Ministry of Environment, Forest and Climate Change (MOEF & Cc) (Government of India, Ministry of Environment and Forests. Fly Ash Notification (2009). CFA management has taken considerable strides over the last few decades. Researchers are trying to convert this coal waste into energy by exploring viable prospects for CFA management. The inappropriate discharge and management of CFA may create adverse environmental impacts (Markandeya and Mohan 2020). According to the CEA annual report (2014) on CFA generation-utilization, the cement sector has found maximum utilization of CFA (44.76%), followed by reclamation (Fig. 1). Though the CFA utilized in these sectors, about 55.79% FA is utilized of the total CFA generated. Therefore, proper attention must be required for CFA deposition, utilization, management and to preventive strategies for negative consequence on the environment and health impact on human being (Yao et al. 2015; CEA 2014).

Various approaches were attempted for the effective remediation of CFA, although it contains inherent toxic contaminants. In the view of toxic components of fly ash, the remediation involves combined approaches, viz; bioremediation, phytoremediation, vermicomposting, mycoremediation in agricultural land to reduce heavy metal loads (Fig. 2) (Roy et al. 2015).

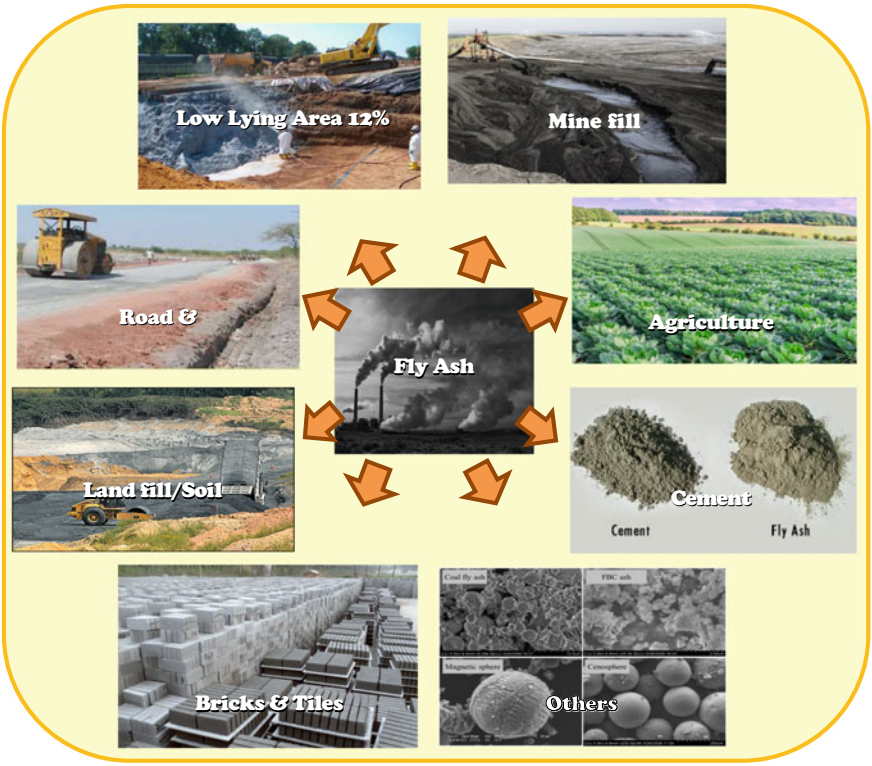

Fig. 1 Illustration of fly ash application in various fields (Rao et al. 2019)

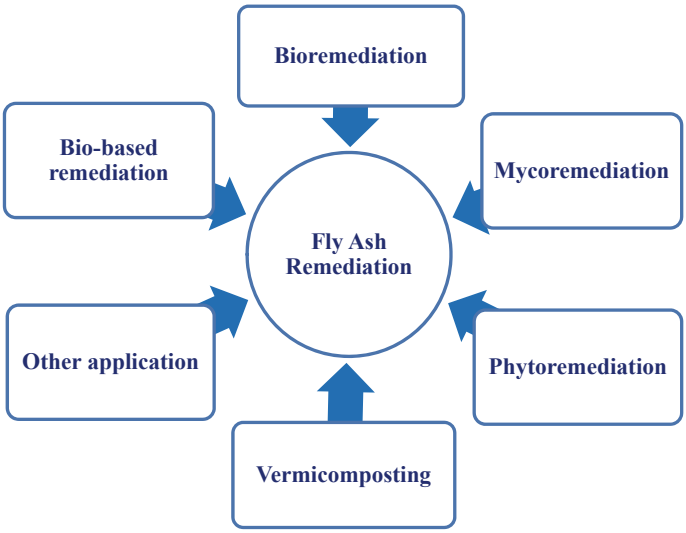

Fig. 2 Fly ash remediation through various approaches

5.1 Bio-Based Remediation

Combined applications of CFA and organic matter have the advantages of reduced heavy metal concentration in soil, elimination of soil pathogens, enhanced soil nutrients, enhanced soil texture, enhanced granule content, enhanced porosity, water content, the enhanced biological activity of the soil, and reduced leaching of major nutrients. The beneficial effects on soil pH and Ca, Mg, and P contents were observed and reduced translocation of heavy metals and enhanced growth, yields of crops were demonstrated in a pot assay (Sheoran et al. 2014). CFA has been extensively used as a stimulant in agricultural soils to accelerate the growth and yield of many crops. Furthermore, nitrogen cycling processes such as nitrification and N mineralization were inhibited while mixing of CFA with soil. Consequence of CFA to soil may also cause to reduce K availability in plants, due to low K concentrations in CFA, interaction of Mg, and Ca, with K during plant ion uptake and a possible biological dilution effect (Hughey et al. 2016).

Coal Fly Ash and Polyacrylamide Influence Transport and Redistribution of Soil Nitrogen in a Sandy Sloping Land studies were observed that simultaneous use of CFA and PAM, the reducing effect of PAM on NO_3--N and NH_4+-N concentrations in the runoff was noted in a lower CFA dosage of 10% and 0.01–0.02% PAM treatments. CFA had a greater effect on increasing the concentrations of NO_3--N and NH_4+-N retained in the sandy soil layer compared with PAM.

5.2 Bioremediation

Bioaccumulation in the food chain stars with single cell microorganism and end with human. Heavy metals were bind to the surface of the organism sometimes enter into the cell. Once they enter the cell, metals may react with chemicals released by organisms to digest food and they will undergo for chemical transformations. The high level of metals into food chain is called biomagnifications. The application of microbes at the site, viz; *Staphylococcus spp, Bacillus spp, Pseudomonas spp, Citrobacter spp, Klebsiella spp, Escherichia spp, and Rhodococcusspp* for the effective removal of heavy metals from CFA was successfully achieved (Roychowdhury et al. 2016; Mukherjee et al. 2017).

5.3 Mycoremediation

Mycoremediation, i.e., bioremediation involved in the application of fungi or root-colonizing mycorrhiza in decontamination of dioxins present in CFA. Ferns such as *Pteris vittata, Ampelopterisprolifera, Thelypteris dentata, and Diplaziumesculentum* adapt to Fly Ash by resisting Heavy Metals present in CFA (Kumari et al. 2013).

Zollacaroliniana, well recognized as mosquito fern has potential high efficiency in eliminating heavy metals from Fly Ash ponds with a high concentration (Pandey and Singh 2011).

5.4 Phytoremediation

Phytoremediation involved a photo-based approach, which involved vegetative cover on the concerned field. The land can be used for land reclamation and rehabilitation to stabilize Fly Ash and the toxicity of the heavy metals was reduced presence in CFA (Pandey et al. 2017). Together, phytoremediation dealt the environmental pollution issues by various types of plants and associated microbiota by either biotransformation, degradation, and elimination contaminants found in air, soil, and groundwater Phytoextraction is the most important strategy for the removal of heavy metals from CFA. In phytoextraction, plants uptake heavy metals through their roots and accumulate or hyperaccumulating them in the roots, stems, or leaves (Tangahu et al. 2011). Bioenergy crop production through integrated photo management can generate proficient capital from waste and provides a sustainable solution for fly ash management, with environmental, economic, and social benefits (Roy et al. 2015).

5.5 CFA Remediation Through Vermicomposting

CFA contains the basic mineral nutrients, which are necessary for plant growth. It demonstrated that vermicomposting is an effective technique for reducing the metal content in CFA substrates as well as in enriching the Nitrogen (N), Potash (P), Sodium (K) content of substrates. Thus the conversion of CFA into potential organic fertilizers is efficient in enhancing soil fertility. Therefore, FA utilization in the agricultural sector should be enhanced in order to reduce the trouble of its disposal (Swati Pattnaik and Reddy 2010).

6 CFA Utilization in Wastewater Treatment

CFA is utilized in the form of adsorbents in wastewater treatment plants. The modified cenospheres transfigured from CFA, that adsorbs disperse blue and disperse orange dyes from the industrial effluents of textiles, electroplating, plastics, paper industries, tanneries, cosmetics, pulp industries, paints, distilleries, and food processing industries. The used adsorbents can be used in landfilling, concrete work, and brick-making (Markandeya and Mohan 2020).

7 Electrodialytic and Mortar Approach

CFA form MSW (Municipal solid waste), CW (Co-combustion of wood), and straw (ST) subjected to electro dialytic and mortar bar experiments. CW ashes show the potential substitution of cement fraction in concrete in mortar experiment. MSW fly ashes are hazardous for soil application and ST ashes found to be low chances of reuse (Lima et al. 2012).

8 Conclusion

CFA related issues are underreported due to legislative complications. The health hazards effects of CFA generated disease is not compared with mining health related issues. Though references were available for different concentration of silica, quartz and mullet in the fly ash the complications reported with the dust is inadequate. The population nearby vicinity is always vulnerable due to fly ash emission. Which needs to be emphasized and matrices should be prepared on hazardous and heavy metals effect on the population. Ecosystem and economic sustainability should be addressed to prevent the impacts on the environment and health. CFA can be beneficial resources if it is efficiently utilized. Technology development and alternate resources can furnish ecological suitability.

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