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Correlation of cadmium and aluminum in blood samples of kidney disorder patients with drinking water and tobacco smoking: related health risk

Abdul Haleem Panhwar · Tasneem Gul Kazi · Hassan Imran Afridi ·
Salma Aslam Arain · Mariam Shahzadi Arain · Kapil Dev Brahaman ·
Naeemullah · Sadaf Sadia Arain

Abstract The combined exposure to aluminum (Al) and cadmium (Cd) causes more pronounced adverse health effects on humans. The kidneys are the main organs affected by internal exposure to Cd and Al via food and non-food items. The objective of present study was to measure the Al and Cd concentrations in cigarettes tobacco (branded and non-branded) and drinking water (domestic treated, ground and lake water) samples in southern part of Pakistan, to assess the risk due to ingestion of water and inhalation of cigarettes smoke containing high concentrations of both elements. The study population (kidney disorder and healthy) divided into two group based on consuming lake and ground water, while smoking non-branded cigarette as exposed, while drinking domestic treated water and smoking branded cigarette as non-exposed. Electrothermal atomic absorption spectrometry was used to determined Cd and Al concentrations in tobacco, drinking water and blood samples. The resulted data indicated that the levels of Al and Cd in lake and underground water were higher than the permissible limit in drinking water recommended by the World Health Organization. The biochemical parameters of exposed and referent patients, especially urinary N-acetyl-h-glucosaminidase, were used as a biomarkers of kidney disorder. Exposed kidney disorder patients have higher levels of Cd and Al than the exposed referents subjects, while difference was significant when compared to resulted data of non-exposed patients and referents ($p = 0.01$–0.001). The pearson correlation showed positive correlation between both toxic element concentrations in water, cigarettes versus blood samples of exposed subjects ($r = 0.20$–0.67 and 0.71–0.82), while lower values were observed for non-exposed subjects ($r = 0.123$–0.423 and 0.331–0.425), respectively.

Keywords Cadmium · Aluminum · Kidney disorders · Drinking water · Tobacco smoking · Blood

A. H. Panhwar (✉) · T. G. Kazi · H. I. Afridi ·
S. A. Arain · M. S. Arain · K. D. Brahaman ·
Naeemullah · S. S. Arain
National Centre of Excellence in Analytical Chemistry,
University of Sindh, Jamshoro 76080, Pakistan
e-mail: haleem_analyst@yahoo.com

T. G. Kazi
e-mail: tgkazi@yahoo.com

H. I. Afridi
e-mail: hassanimranafridi@yahoo.com

S. A. Arain
e-mail: salma_arain67@yahoo.com

M. S. Arain
e-mail: mshahzadi71@yahoo.com

K. D. Brahaman
e-mail: kr_brahman@yahoo.com

Naeemullah
e-mail: naeemullah433@yahoo.com

S. S. Arain
e-mail: ssadiashafi@gmail.com

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Introduction

Quality of drinking water concern is increasing worldwide. Epidemiological studies in recent years have indicated a strong association between the incidence of several diseases in humans with the exposure of toxic metals such as cadmium (Cd) and aluminum (Al) in water (Reddy and Gunasekar 2013; Flaten 2001). The high exposure of Cd produces a wide variety of toxic effects on internal organs of human (Järup and Åkesson 2009; Satarug et al. 2011). One of the major problems in ecology is linked to the path of toxic metals that consist in all matrices that involved in foods and food chain (Locatelli 2004; Cui et al. 2005). Cd is present in tobacco smoke and contributes significantly to cancer risk (Fowles and Dybing 2003). Cd has been found in several studies consistently to transfer into the smoke phase (Wu et al. 1995; Layten Davis and Nielsen 1999; Shaikh et al. 2002), which coupled with the fact that the tobacco plant is particularly efficient in accumulating Cd from the soil and translocating most of the metal to the leaves, making this element the prime focus for particular investigation for any potential toxic effects. The Cd accumulates in the human body especially in kidneys which lead to its dysfunction (Wang et al. 2010). Therefore, accurate determination of Cd has become increasingly necessary to study the problems connected with environmental water pollution (Shrivas and Patel 2010; Panhwar et al. 2015a).

The Al is a nonessential, toxic metal to which humans are frequently exposed. Normally it is very insoluble, and in most neutral natural waters, its concentration is very low (Panhwar et al. 2014). In recent years, however, a large amount of Al has been released into the environment through water acidification, waste discharge, and soils extract due to acidic rain. The maximum permissible content of Al in drinking water is 200 μg L^{-1} (World Health Organization 2004). Nowadays, much interest has been raised about the toxicity and adverse biological effect of Al (Venturini-Soriano and Berthon 1998). Some studies suggest that Al may be accumulated in the brain via different routes (drinking waters, food, and medicines) and interfere with the normal activities of nervous system (Flaten 2001; Sińczuk-Walczak et al. 2004). This metal ion has been considered as a possible cause of renal osteodystrophy, Parkinson's and Alzheimer's diseases (Flaten 2001). The determination of very low

levels of Al has become increasingly very important in environmental and clinical chemistry due to its negative role in the human life (Bishop et al. 1997). Al is present abundantly in tobacco (Bagchi 1997). At high exposure, the Al competes with and alters calcium metabolism in several organs of human including brain (Klaassen 2001). Al poisoning in chronic kidney failure patients who were in long-term maintenance hemodialysis is now recognized as contributing to encephalopathy syndrome, osteomalacia and anemia (Jeffery et al. 1996). It is accepted that long-term consumption of Al-containing agents can be potentially harmful to human (Jeffery et al. 1996). Therefore, there is a strong need for Al monitoring in natural water resources (Becaria et al. 2006).

The aim of this work was to investigate correlation of Al and Cd concentrations with tobacco sample (branded and non-branded cigarettes) and different drinking water (domestic treated, ground and lake water), blood samples of kidney disorder and referents in population of southern part of Pakistan. Furthermore, the study aimed to ascertain potential health risk of toxic metals concentrations to local population. The Cd and Al concentrations were determined in underground and lake water samples as well as in blood samples of male subjects have or have not kidney disorders, smoking locally made non-branded cigarette. For comparative purposes, the blood samples of referent male subjects (patients and referents) were also analyzed consuming domestic treated water and smoking branded cigarette. We also compared our results based on this study with the literature-reported data.

Materials and methods

Study population

One hundred and seventy-five persons aged 30–60 years, living in Hyderabad city, termed as non-exposed population. Furthermore, these individuals are again divided into two categories, i.e., non-exposed referents and patients (NER and NEP) who consume domestic treated water and branded cigarettes as shown in Table 1. One hundred and forty-five persons have same age group residing in rural areas, consuming contaminated Manchar Lake and groundwater, while smoking non-branded locally made cigarette, termed as exposed population.

Table 1 Demographics of male subjects under study ($n = 320$)

Non-exposed subjects ($n = 175$)		Exposed subjects ($n = 145$)	
NER	NEP	ER	EP
$n = 130$	$n = 45$	$n = 55$	$n = 90$

Values in parenthesis () are total subjects

Furthermore, exposed population divided into two groups, i.e., exposed referents and patients (ER and EP) as shown in Table 1. The all study subjects are living in their respective areas for more than 30 years, which suggests that they have been only exposed to toxic elements via drinking water and cigarette. Information about Al and Cd toxic effects and the screening program was disseminated to the villagers through loudspeakers and leaflets about 2 weeks in advance of the survey. The village health volunteers and the local health center workers were requested to deliver health message and the screening program to those persons who might not have received information. The villagers used mostly underground and lake water for drinking and other activities, because in these areas, no well-developed municipal treated water supply system is present. The exposed severe patients attended the OPD (Out-Patient Department) of health center and the urology ward of Liaquat Medical University Hospital, Jamshoro, Pakistan, from 2012 to 2013. The exposed referents were relative of the exposed patients. The study subjects had different occupation, most of the patients were labor (70 % of total), and others were farmers and shopkeeper. Each participant was interviewed about demographic characteristics, tobacco smoking and number per day and medical history of kidney disorder by trained health workers. The persons who gave their consent were recruited for biological samples collection. The study protocol was approved by higher education commission of Pakistan.

Instrumentation

The analysis of elements was carried out by means of a double-beam PerkinElmer atomic absorption spectrometer model 700 (Norwalk, Connecticut, USA) equipped with a graphite furnace HGA-400, pyrocoated graphite tube with integrated platform, an autosampler AS-800, and deuterium lamp as background correction system. The working parameters for the determination of analytes were followed recommended by the manufacturer. A domestic microwave oven (Pel, PMO23, Japan) programmable for time and with a microwave power of 100–900 W was used for digestion of the samples. Acid-washed plastic (polypropylene) vessels were used for preparing and storing solutions.

Reagents and glassware

Analytical-grade chemicals and ultrapure water obtained from ELGA Labwater System (Bucks, UK) were used throughout the experiment. Nitric acid and hydrogen peroxide were analytical reagent-grade from Merck (Darmstadt, Germany). Standard solutions of Cd and Al were prepared by the dilution of certified standard solutions (1000 ppm) of Fluka Kamica (Buchs, Switzerland) corresponding elemental ions. Moreover, matrix modifiers were employed to analyze Al (0.2 mg of $Mg(NO_3)_2$ and Cd (0.001 mg Pd + 0.0015 mg $Mg(NO_3)_2$) which were prepared from $NH_4H_2PO_4$ and $Mg(NO_3)_2$ obtained from Sigma-Aldrich (Milwaukee, Wisconsin, USA). All glassware and plastic material used were previously treated for a 24 h in 5 M nitric acid and rinsed with double-distilled water and then with ultrapure water. For accuracy of the analytical technique, Clincheck control-lyophilized human whole blood (Recipe, Munich Germany) were used as certified reference materials.

Sampling and pretreatment

Water samples

The lake water samples were collected on monthly basis, during 2012–2013, by using Van Dorn (polyethylene) plastic bottles (1.5 L capacity) from 5 to 7 spots of Manchar Lake. The water samples were collected from the surface of the lake because people drink mostly surface water. All groundwater samples were collected from >12 m depth. The groundwater

samples were collected from hand pumps and motor pumps directly into the polyethylene plastic bottles. The domestic treated tap water samples were collected from Hyderabad city. The tap water was allowed to run for 10 min, and approximately 1000 mL of water was collected ($n = 100$) in a beaker. All water samples were filtered through a 0.45-µm pore-size membrane filter (Millipore Corporation, Bedford, MA, USA) immediately after sampling to remove suspended particulate matter. The pH of all water samples was checked with a pH meter, then acidified to pH 2 with concentrated HNO_3 and subjected to analysis as described in previous work (Kazi et al. 2009a).

Tobacco samples

Nicotiana tabacum samples were collected from the agricultural lands irrigated with polluted lake during 2012–2013, fifty samples per year ($n = 100$). The non-branded cigarette ($n = 100$), made from the same raw tobacco leaves, was collected. The branded cigarettes were collected from Hyderabad city. The raw and cigarette tobacco (branded and non-branded) were ground in vibrational agate ball mill for 5 min using a power of 60 %. The powdered samples were sieved through nylon sieve to obtain particle size [ø] 30–65 µm and were stored in closed polyethylene bottles and kept in a refrigerator at 4 °C until analysis.

Blood and urine sampling

From each studied subject, 10 mL of venous blood was sampled by using metal-free safety Vacutainer blood-collecting tubes (Becton–Dickinson, Rutherford, USA) containing >1. 5 mg K2EDTA/mL blood. About 5 mL of blood samples of each patient and

referents was stored at −4 °C to detect Al and Cd contents, while 5 mL was sent for biochemical test to pathological laboratory. Morning urine samples (only for biochemical test) were collected in an acid-washed, decontaminated polyethylene tubes (Kartell1, Milan, Italy) and sent to pathological laboratory. All biochemical parameters were obtained from pathological laboratory.

Microwave-assisted acid digestion

Duplicate blood samples of each patients and referents (0.5 mL), tobacco of non-branded and branded cigarettes (0.2 g), while six replicate samples of each certified material (water, blood and tobacco), were directly taken into Teflon PTFE flasks. Three milliliters of a freshly prepared mixture of concentrated HNO_3–H_2O_2 (2:1, v/v) was added to each flask and kept for 10 min at room temperature, and then flasks were placed in covered PTFE container. This was then heated following a one-stage digestion program at 80 % of total power (900 W), and 5–8 min was required for complete oxidation of sample matrix. After cooling, the digestion flasks were cooled and resulting solution was evaporated to semidried mass to remove excess acid and then diluted to 10.0 mL in volumetric flasks with 0.1 M nitric acid; this mixture was filtered through a Whatman filter paper no. 42 into a 10-mL volumetric flask, and with the help of micropipette, samples were directly injected into ETAAS (Kazi et al. 2009a, b; Panhwar et al. 2015b). Results were validated by the analysis of certified reference materials as shown in Table 2.

Statistical analysis

All mathematical and statistical computations were made using Statistica v5.5, XLSTAT-Pro v7.5.2 and

Table 2 Determination of Al and Cd in certified samples ($n = 6$)	Certified samples	Certified values	Found values	$t_{Critical} = t_{Experimental}$
	Al			
	Water (SRM 1643e)[a]	141.8 ± 8.6	139.2 ± 7.2	0.942
	Whole blood (SRM 3101a)[b]	9.2 ± 6.4	9.1 ± 1.25	0.343
	Virginia tobacco leaves[b]	1680 ± 120	1660 ± 125	0.186
	Cd			
	Water (SRM 1643e)[a]	6.568 ± 0.073	6.53 ± 0.5	0.31
	Whole blood (Clincheck)[b]	1.2 ± 0.4	1.18 ± 0.15	0.437
[a] µg/L [b] µg/g	Virginia tobacco leaves[b]	1.52 ± 0.17	1.51 ± 0.11	0.13

Table 3 Biochemical parameters of referents and exposed subjects

Parameters	Normal range	Non-exposed subjects ($n = 175$)		Exposed subjects ($n = 145$)	
		Referents (NER)	Kidney patients (NEP)	Referents (ER)	Kidney patients (EP)
Hemoglobin (g/dL)	12–18	14.6 ± 0.85	10.15 ± 0.75	11.8 ± 1.24	7.46 ± 0.33
Creatinine mg/dL	0.6–1.3	0.91 ± 0.15	3. 61 ± 0.45	1.27 ± 0.23	6.76 ± 1.12
Blood urea nitrogen (mg/dL)	7–18	12.6 ± 0.95	31.5 ± 2.15	16.7 ± 1.18	41.2 ± 4.28
Total cholesterol (mg/dL)	140–310	203 ± 16.7	325 ± 27.5	275 ± 24.6	345 ± 31.6
Triglyceride (mg/dL)	35–106	82.3 ± 5.32	248 ± 30.3	101 ± 9.6	367 ± 41.8
High-density lipoprotein (mg/dL)	27–89	65.2 ± 7.31	73.6 ± 7.29	65.2 ± 5.38	94.7 ± 6.79
Creatinine clearance (mL/min)	88–137	123 ± 9.68	73.5 ± 10.1	103 ± 6.63	65.8 ± 3.67
Urinary *N*-acetyl-beta-glucosaminidase (NAG) (IU/L)		6.3 ± 1.06	17 ± 1.74	15.6 ± 1.56	21.8 ± 2.72

Minitab 2002 v13.2 software. Basic statistics and correlation calculations were carried out in order to give initial information about the elements in blood of kidney disorder patients and referents (Brahman et al. 2013).

Results

Biochemical parameters

Biochemical data concerning the patients who have kidney disorders, non-exposed and exposed control groups, obtained from the pathology laboratories of hospital, are shown in Table 3. The mean creatinine clearance in urine samples was significantly lower in exposed and non-exposed kidney patients as compared to both referent groups ($p < 0.01$). Blood urea nitrogen in exposed and non-exposed patients was significantly higher than in referents ($p > 0.01$).

Urinary (*N*-acetyl-beta-glucosaminidase) NAG concentrations in exposed subjects with or without kidney disorders were higher than in the corresponding groups from the non-exposed area (Table 3). The urinary NAG concentrations were significantly higher in exposed and non-exposed patients than in those without the symptoms of kidney disorders ($p > 0.01$), while the mean value of urinary NAG in exposed referents exceeded the normal range of 0.3–12 IU/L. In unexposed referents, the NAG levels were within normal range (Table 3). Elevated urinary NAG levels are indicative of kidney disorder. Increased NAG levels in the urine are an early indication of renal

disease and can serve as a valuable renal function test in disorders such as nephritis syndrome and other diseases associated with nephropathy (Liangos et al. 2007; Wang et al. 2009).

Cd and Al concentrations in different samples

The mean and standard deviation of Cd and Al concentrations in different drinking water, tobacco and blood samples are shown in Table 4. The range of total Cd concentration in the underground, lake and domestic treated water was observed at 95 % confidence interval (CI) [CI 4.85, 6.57], [CI 6.37, 8.58] and [CI 1.89, 2.36] µg/L, respectively. Al concentrations in underground, lake and domestic treated water were found [CI 391, 497], [CI 1010, 1210] and [CI 116, 146] µg/L, respectively. Concentration of both toxic metals in different drinking water found in the

Table 4 Al and Cd in water and cigarette tobacco (branded and non-branded) samples

Samples	Al	Cd
Lake water	1113 ± 239[a]	8.5 ± 2.1[a]
Ground water	444 ± 65.2[a]	5.71 ± 1.2[a]
Domestic treated water	131 ± 15.2[a]	2.12 ± 0.57[a]
Nicotiana tabacum L[c]	387 ± 5.62[b]	5.89 ± 1.53[b]
Non-branded cigarettes	355 ± 4.25[b]	5.39 ± 1.12[b]
Branded cigarettes	315 ± 15.2[b]	2.6 ± 0.95[b]

[a] µg/L

[b] µg/g

[c] Tobacco grown in agricultural land irrigated with lake water

Table 5 Comparison of Al and Cd (μg/L) in whole blood samples of exposed subjects vs. referents subjects

Elements	Non-exposed subjects		Exposed subjects	
	NER	NEP	ER	EP
Blood				
Al (Mean ± SD)	198 ± 11.5	485 ± 14.2	870 ± 142.2	1116.6 ± 258
Cd (Mean ± SD)	2.47 ± 0.45	4.14 ± 0.79	4.72 ± 0.35	6.84 ± 1.24

decreasing order as follows: lake > underground > domestic treated water.

Concentration of Al in tobacco samples of raw, non-branded and branded cigarettes samples was observed at 95 % [CI 455, 510], [CI 384, 390] and [CI 307, 312] μg/g, respectively. The concentration of Cd in raw tobacco, non-branded and branded cigarettes samples was observed at 95 % [CI 5.50, 7.00], [CI 5.00, 6.63] and [CI 2.30, 3.50] μg/g, respectively.

The mean and standard deviation of Cd and Al concentrations in blood samples of referents and kidney patients are shown in Table 5. In whole blood samples of EP, Cd concentration was observed at 95 % confidence interval [CI 4.96, 6.73] μg/L, while ER have lower concentrations [CI 3. 50, 3.90] μg/L. Concentration of NER and NEP observed at 95 % confidence interval [CI 3.95, 4.25] and [CI 1.67, 2.21] μg/L, respectively. We observed a significantly higher ($p = 0.008$) concentration of Cd in whole blood samples of EP as compared to NEP's. Resulted data indicated that level of Cd in blood samples of ER have twofold higher than NER's, whereas EP have 1.6-fold higher Cd levels than NEP ($p < 0.001$).

In whole blood samples of ER and EP, Al concentration was observed at 95 % interval [CI 745, 890] and [CI 1010, 1220] μg/L, respectively. Moreover Al concentrations in blood samples of NEP have significantly higher levels than in NER's [CI 470, 490] and [CI 193, 202] μg/L ($p < 0.01$). Resulted data indicated that level of Al in blood samples of ER value is about 4.4-fold higher than that in NER, while the EP value is about 2.3 times higher than NEP ($p < 0.001$). Pearson's correlation showed Al and Cd concentrations in tobacco samples and different drinking water (underground, lake and domestic treated) versus concentration of both metals in blood of patients and referents as shown in Table 6. The strong correlation between Al and Cd concentrations in blood samples of

exposed subjects (patients and referents) was observed, indicating higher exposure of both toxic metals via drinking water and smoking non-branded cigarette. In non-exposed subjects, lower r-values were obtained between toxic metals and blood samples (referents and patients), due to drinking domestic treated water, have low levels of these elements that are within the permissible limits (World Health Organization 2004). It was also observed that in exposed population, correlation of Al and Cd with tobacco samples was higher in blood samples than in drinking water. Therefore the increasing order of correlation was observed between blood samples of EP and two sources of exposure, i.e., drinking water < smoking.

Odds ratio and relative risk

The logistic regression analysis indicates the higher relative risk for incidence of kidney disorders in those people who drink non-treated contaminated water (lake and underground water) and smoking non-branded cigarette as compared to those who drink domestic treated water and smoking branded cigarette. The odds ratio showed 4.73-fold higher incidence at 95 % confidence intervals (2.93–7.62), $p < 0.001$, of kidney disorders as compared to those who drink treated water and smoking branded cigarette. The relative risk and prevalence of kidney disorders was 2.41 [CI 1.82–3.20] and [CI 1.43–2.42], ($p < 0.001$) in exposed group (exposed Patients and referents) as compared to non-exposed patients and referents

Discussion

The present study revealed that the consumption of non-treated drinking water (ground and lake water)

Table 6 Pearson correlation of cadmium and aluminum in drinking water and tobacco samples with their levels in blood of referents and kidney patients

Samples	Sample size	Referents		Impaired kidney functions	
	n	r	p	r	p
Al					
Water					
Ground water	30	0.364	0.085	0.59	<0.001
Lake water	30	0.423	0.067	0.67	<0.001
Municipal treated water	100	0.125	0.865	0.25	0.665
Tobacco					
Branded tobacco	20	0.425	0.021	0.75	<0.001
Non-branded tobacco	100	0.472	0.019	0.79	<0.001
Cd					
Water					
Ground water	30	0.264	0.24	0.55	<0.001
Lake water	30	0.423	0.067	0.63	<0.001
Municipal treated water	100	0.123	0.882	0.20	0.678
Tobacco					
Branded tobacco	20	0.321	0.025	0.71	<0.001
Non-branded tobacco	100	0.358	0.021	0.82	<0.001

and smoking non-branded cigarette cause high levels of both toxic elements by study population, providing evidence that in addition to different physiological disorders, kidney malfunctioning is also induced in humans (Kazi et al. 2009a, c; Afridi et al. 2008; Arain et al. 2008). The both sources of water (ground and lake) contained high concentrations of Cd and Al, exceeding the guideline level for drinking water 3 and 200 µg/L, respectively (World Health Organization 2004) as compared to domestic treated water supply in city. It was observed that the prevalence of kidney disorders was found to be higher in exposed population. It was reported in previous study that in some areas of Pakistan, the underground water has relatively high levels of Cd (Azizullah et al. 2011). Due to very high temperature in summer (40–50 °C) for southern part of Pakistan, the population mostly drink 3–4 L water/day (Muhammad et al. 2011). Therefore the exposure of Cd and Al from drinking water to population of southern part of Pakistan possesses greater possibility to develop the kidney-related disorders.

Contamination sources of drinking water obtained from underground and surface water with both toxicants are may due to release from phosphate fertilizers and sewage sludge used in agricultural land. The surface runoff may contaminate the surface and groundwater reservoirs for Cd, Al and other toxicants (Buschmann et al. 2008; Hussain et al. 2010). The high intake of Cd can cause health problems such as nausea, vomiting, diarrhea, muscle cramps, salvation, sensory disturbances, liver injury convulsions, shocks and renal failure. Long-term Cd exposure can cause certain fatal effects such as kidney, liver, bone and blood damages (Satarug et al. 2011; Sommar et al. 2013).

The Al levels were found to be higher in ground and lake water samples as compared to domestic treated water. Normally, the ingested Al is not frequently absorbed through gastrointestinal tract (transfer factor to blood is low); most of it is excreted unabsorbed in the feces. What little is absorbed is soon excreted in the urine, although some of it may be retained in the skeleton. However, the protective function of the intestinal barrier is less effective in end stage of renal disease patients than in healthy individuals (Neiva et al. 2002). In exposed areas where water treatment system is unavailable, the people mostly use alum for water purification, which enhances the level of the Al concentration in drinking water. The exposure of Al via drinking water by healthy referents with normal urological system may not be affected significantly, but for those with kidney disorders, the toxicity due to Al becomes severe. Al-induced damage to body organs has already been reported in several studies

and accumulation in the kidney has been related to worsening its function (Khan et al. 2011). Our results are also consistent with those of literature-reported study, which observed striking increases in serum Al in uremic patients in long-term hemodialysis (Sargazi et al. 2006).

The general population is exposed to Cd by consumption of contaminated water and the inhalation of tobacco smoke (Järup and Åkesson 2009). Tobacco is a major source of Cd uptake in smokers, as the tobacco plant usually accumulates a relatively high level of Cd in its leaves, which is the major route of exposure to smokers (Kazi et al. 2009b). Concentration of total Al was high in all cigarettes; one would imagine that smoking could be one of the sources of Al exposure (Kazi et al. 2009b). During smoking, the toxic metal content originally present in the filler tobacco of cigarettes, partitions among the mainstream smoke, side stream smoke, ash and cigarette or filter (Torrence et al. 2002). The filler tobacco of different branded and non-branded cigarette smoking by study population was analyzed for Al and Cd contents. It was reported in our previous work that the percentage of Cd in ash of different branded and non-branded cigarettes was observed in the ranges of 23.2–28.7 %, while in smoke 55.2–69.6 % of total contents of filler tobacco was observed (Kazi et al. 2009c). The percentage of Al in ash of different branded and non-branded cigarettes was observed in the ranges of 97.8–98.5 %, while in smoke only 0.0494–0.89 % of total contents of filler tobacco was observed. Cigarette ash contains major contents up to 99 % of Al, while 40–50 % of Cd plays an important role in terms of toxic metal distribution toward human health and environmental pollution. According to reported data, by smoking 10 cigarettes a day, approximately, 10 µg of Al while 18 µg of Cd/person/day is inhaled by the smoker or spreads into the environment (Ebisike et al. 2004).

The Cd accumulation in the kidney can induce impaired tubular function, salt retention and volume overload, which may lead to hypertension (Satarug et al. 2005). The Cd is efficiently retained in kidney and liver with a very long biological half-life, ranging from 10 to 30 years (Järup and Åkesson 2009; Andrée et al. 2010). Cd inhaled through cigarette smoke is more easily taken up by the body than through food or water. From 40 to 60 % of Cd inhaled in smoke is absorbed into the bloodstream, whereas only 5 to 10 %

absorbed through foods. Each cigarette contains roughly 3–4 µg of Cd, and smokers absorb an additional 1–3 µg of Cd into their systems daily for every pack they smoke. Some recent studies have raised the possibility that levels of Cd and other heavy metal intake via cigarette smoke may have toxic, genetic effects and peripheral arterial disease (Coen et al. 2001; Jin et al. 2003; Carpenter et al. 2002). Smoking and drinking contaminated water synergistically increases the carcinogenic effect of Cd (Flora et al. 2008).

The most prominent early pathological change associated with Al toxicity is the accumulation of neurofibrillary tangles in many regions of the brain (El-Rahman 2003) Furthermore Al also competes with and alters calcium metabolism in several organ systems including the brain (Klaassen 2001). Al has a fixed oxidation number and therefore cannot participate in redox reactions. However, as previously noted, Al can displace iron from binding sites and therefore result in an increase in catalytically active iron (Savory et al. 1996). Thus, Al in tobacco smoke may enhance iron-dependent free radical-induced tissue damage via an indirect mechanism (Johnston et al. 1993).

Finally, it is suggested that the proper awareness of the people in the study area regarding the toxic effect of tobacco smoking and drinking contaminated water, which create health risks, are carried out. The government should provide treated/clean water with supply line, far away from solid waste, sludge and sewage sites, while ban smoking in the public places should be implemented properly. The farmers should also be trained to avoid the over using of agrochemicals for their agricultural lands which are responsible for contamination of surface and ground water. The population of both exposed and non-exposed area should be educated properly with water knowledge through awareness and training programs needed for sustainable use and management of drinking water.

Conclusion

The present work indicated that the Cd and Al co-exposure to human from non-branded cigarettes smoking and drinking water (lake an underground) gives rise to more pronounced kidney disorders than those patients who were consume branded cigarette

and drinking water with low levels of these toxicants. The strong positive correlation was found between smoking and drinking water to kidney impaired function. Concentration of toxic metals in blood of kidney patients was significantly higher ($p < 0.001$) than in the referents'. The adverse impact of both toxic elements produces nephrotoxicity in humans, as indicated by increased NAG values and decreased clearance of urea creatinine in EP, which was higher than in NEP. Further studies are needed, possibly including additional new biomarkers and improved exposure assessment technology, to firmly establish this interaction.

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