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PEDIATRIC INFECTIOUS DISEASES (I BROOK, SECTION EDITOR)

Prevalence and Resistance Patterns of *Streptococcus pneumoniae* Recovered from Children in Western Asia

Yasser M. Matran[1,2] · Ahmed M. Al-Haddad[3] · Divakar Sharma[4] · Nitin Pal Kalia[5] · Sarika Sharma[6] · Manoj Kumar[7] · Sandeep Sharma[2]

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Abstract

Purpose of Review Despite the available pneumococcal conjugate vaccination (PCV), children in developing countries suffer significant morbidity and mortality from pneumococcal illness. This review outlines the pneumococcal carriage rate, common serotypes, antibiotic resistance, and PCV coverage among western Asian children.

Recent Findings The carriage rate and prevalence of PCV serotypes remain high among children in Western Asia. In recent times, the national immunization rates have increased, but there was a considerable rate of invasive pneumococcal diseases (IPD) strains and non-invasive pneumococcal diseases (NIPD) serotypes with high antimicrobial resistance rates and many communities in western Asian countries are experiencing the phenomenon of pneumococcal vaccine serotype replacement (PVSR).

Summary An accurate and updated disease surveillance in Western Asia is urgently needed to guide immunization efforts and protect children effectively. Increasing the PCV covering rate and antimicrobial stewardship is crucial for countries to implement strict systems and effectively minimize the high rate of resistance.

Keywords S. pneumoniae · Nasopharyngeal · Epidemiology · Western Asian Countries

✉ Divakar Sharma
divakarsharma88@gmail.com

✉ Sandeep Sharma
sandeep.23995@lpu.co.in

1 Department of Para-Clinic, Unit of Clinical Microbiology, Faculty of Medicine and Health Sciences, University of Aden, Aden, Yemen

2 Department of Medical Laboratory Science, Lovely Professional University, Phagwara, Punjab 144411, India

3 Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Hadhramout University, Al Mukalla, Yemen

4 Department of Microbiology, Lady Hardinge Medical College, New Delhi 110001, India

5 Department of Biological Sciences (Pharmacology & Toxicology), National Institute of Pharmaceutical Education and Research (NIPER), Balanagar, Hyderabad, Telangana 500037, India

6 Department of Sponsored Research, Lovely Professional University, Phagwara, Punjab 144411, India

7 Research Department, Maternal and Child Health Program, Sidra Medicine, Doha, Qatar

Introduction

Pneumococcal carriage is prevalent in low- and lower-middle-income countries, particularly among children, and encompasses a broad range of serotypes [1]. According to the World Health Organization (WHO), *Streptococcus pneumoniae* is responsible for the mortality of over 300,000 children under the age of 5 globally on an annual basis. The majority of fatalities take place in developing nations [2]. The carriage of *S. pneumoniae* in the nasopharynx, even in the absence of symptoms, is a crucial factor in the transmission of this pathogen. It typically occurs prior to the onset of invasive pneumococcal diseases [3]. The pneumococcal carriage, antimicrobial resistance, and pneumococcal conjugate vaccination (PCV) coverage vary across regions, influenced by various factors, such as the socioeconomic status of the population, vaccination rate, and antibiotic misuse [4•]. The year 1977 was an important historical event, with the licensing of the first pneumococcal vaccine in the USA which was composed of 14 pneumococcal serotypes, and in 1983 had licensed a 23-valent polysaccharide vaccine, but this vaccine was not effective in protecting children; the suffering continued until the year 2000, in which the first 7-valent pneumococcal conjugate vaccine was licensed in children followed by a 13-valent pneumococcal conjugate vaccine in 2010 that contains the PCV7 vaccine (4, 6B, 9 V, 14, 18C, 19F, 23 F), as well as serotypes 1, 3, 5, 6A, 7F, and 19A [5, 6]. The rise of pneumococcal strains resistant to penicillin and other antibiotics is a global challenge, although the PCV saved the life of many children and decreased the prevalence of antibiotic-resistant strains related to the included strains of vaccine; it associates with PVSR which is characterized by antibiotic resistance [7•, 8, 9].

Understanding and addressing *S. pneumoniae* involve considering crucial factors. The pneumococcal carriage rate helps assess the bacterium's burden, while identifying common serotypes informs vaccine and treatment strategies. Monitoring antibiotic resistance guides treatment decisions and stewardship efforts. Assessing PCV coverage evaluates protection and program impact. By considering these factors, comprehensive strategies can combat pneumococci in populations with high carriage, antimicrobial resistance, and low PCV coverage. In this paper, we review these factors, emphasizing continuous surveillance, increased PCV coverage, antimicrobial resistance, and antimicrobial stewardship.

Method

To conduct this review, we conducted a literature search on English publications related to the children of Western Asian countries during the last two decades. Using Google Scholar and PubMed, we combined the primary terms Pneumococci or *S. pneumoniae* with keywords like Prevalence, Incidence, Burden, Surveillances, Epidemiology, Colonization, Nasopharyngeal, Carriage, Serotype, Children, Infant, paediatric, Invasive, Non-invasive Pneumococcal diseases, MDR, Antibiotic Resistance, and antimicrobial susceptibility, or name of Western Asian countries. For this review, we focused on articles written in English and published between January 1, 2000, and April 30, 2023. We conducted a search and found 227 articles, but only 42 of them were relevant to the specific topic covered in this review. The present article is predicated upon extant research and does not encompass any novel investigations involving human or animal subjects that were conducted by the authors themselves.

Pneumococcal Carriage Rate

There has been a scarcity of information pertaining to the prevalence of pneumococcal carriage and disease in the countries of Western Asia over the past 20 years, although the prevalence of nasopharyngeal carriage of pneumococci among children under the age of 5 exhibits a considerable range, with rates varying from 42 to over 90% [10, 11]. The rate and serotype distribution among children in the community can provide insights into invasive illness, antibiotic resistance, and the potential impact of future deployment of national PCV [12, 13]. Between 2005 and 2019, six studies conducted in children under the age of 4 in Jordan reported the nasopharyngeal carriage rate of *S. pneumoniae* to vary between 19.5 and 56.2% cases per 3720 healthy children [4•, 7•, 14–16, 17•]. Among Western Asian children, Jordan had the highest rate of pneumococcal carriage through the studies included in the current review. Similarly, the prevalence was observed in children from the Occupied Palestinian Territory, where the rate of pneumococcal carriage ranged from 30 to 55.7% among 3531 individuals under 5 years of age for the period from 2009 to 2013 [18–20]. While the rate was similar between Cyprus, a developed country, and Egypt, classified as a developing country, it ranged from 25.3 to 35.3% in healthy Cypriot children under 5 years of age during the period from 2007 to 2014, with a total of 1507 participants [9, 21]. In Egypt, the rate ranged from 29.2 to 32.9% among 534 children under 5 years of age during the time from 2012 to 2017 [12, 22•]. On the other hand, in Iran, where the vaccine was only administered to the high-risk group, the carriage rate ranged from 2.2 to 44.1% among 2432 children aged from 6 months to 14 years [23, 24, 25•]. Additionally, the pneumococcal rate among Turkish children under 18 years of age ranged from 6.4 to 21.9% across 4346 healthy participants for the period from 2011 to 2020 [26–28, 29•]. In a cross-sectional report conducted in Iraq among 1092 healthy children aged 6 to 13 years, the rate was found to be 20.5% [13]. On the contrary, the carriage rate in Yemen was low, with only 5.6% among 602 healthy children during 2006 [30]. The pneumococcal carriage among the children of Western Asia was consistent with the rate which found in asymptomatic and symptomatic Ethiopian children aged 0–15 years old where it ranged from 25.3 to 43.8% in healthy children and 21.5% among the symptomatic cohort [31–33]. The pneumococcal carriage rate indeed differs between regions, depending on factors such as the socioeconomic status of the population, access to medical care, and the availability of the PCV, particularly in low- and middle-income countries. A study conducted in India prior to the introduction of PCV into the vaccination program discovered that the pneumococcal carriage rate was 74.7% among children with pneumonia and 54.5% among healthy children [8]. A similar study conducted in Pakistani urban and rural districts prior to the introduction of PCV10 found that the rate of pneumococcal carriage among healthy children was 73.6% and 79.5% [34]. The findings of the two previous studies were slightly similar to those found in some studies conducted in western Asian regions where the vaccine is not introduced [4•, 7•, 15, 16, 17•, 22•, 35]. Additionally, the rate of western Asian regions was near that found in Sri

Lanka 31.8% and 39.8% among asymptomatic and symptomatic children, respectively [36]. Furthermore, the rate was consistent with the rate that found in third-world countries as Bangladesh, Nepal, and Indonesia, where the prevalence rates among healthy children under 5 years ranged between 35 and 45% [37–39].

Unfortunately, during the journey of data searching for studies that were published in the last two decades, there has been a lack of updated data regarding the carriage rate in Arab Gulf states, including Lebanon. However, some data has been available focusing on the common serotypes in IPD, NIPD, and the antimicrobial resistant rate in those countries. In contrast to this, there is a lack of available data from Syria, and the data from Yemen is not up to date (Table 1).

In general, these findings indicate that the prevalence of pneumococcal carriage remains high among children in the Western Asian region. Despite the significant heterogeneity in the data presented in different studies, there is an urgent need for comprehensive surveillance to improve our understanding of the carriage rate, as well as IPD and NIPD in this region of the world. This surveillance can help in the development of effective vaccination strategies and reduce the burden of pneumococcal disease among children in Western Asia. Additionally, further research is required to identify risk factors associated with pneumococcal carriage and disease in this region.

The Burden of Pneumococcal Disease Among Western Asian Children

The serotypes of IPD and NIPD were the most identified in both invasive and non-invasive pneumococcal specimens collected from children in Western Asian countries over the past two decades (Table 1). In developing nations, the prevalence of IPD poses a significant challenge for individuals of all ages due to a lack of comprehensive surveillance investigations [49]. Despite the inclusion of PCV in most West Asian children's immunization program since a long time, the persistently high mortality rate linked to IPD remains concerning [51]. The yearly case fatality rate of pneumococcal infection in Egyptian children was 33.3%. This rate was higher in IPD cases (75%) compared to non-IPD cases (12.5%) [60], while the mortality rate in Lebanon significantly increased from 12.5% during the PCV7 era to 24.8% during the PCV13 era [50•]. In addition, the case fatality rate of IPD in Oman was higher in children under 5 years, at 14.2% [51]. In the case of Saudi Arabia (KSA), the case fatality rate due to meningitis and sepsis caused by *S. pneumoniae* was reported to be 12% in the period from 2001 to 2007 [61]. Moreover, another recent report from KSA found that *S. pneumoniae* was associated with 45.6% of sinusitis cases in the pediatric age group in KSA [62•]. Furthermore, the mortality rate for IPD among patients aged 14 years and older in Kuwait from 2010 to 2014 was 14.4% [63]. Also in Iran, the PCV13 serotypes were common prevalent in 130 cases of IPD and non-IPD during the period from 2017 to 2019, representing 83% and 84% of the isolated pneumococcal strains, respectively [42•]. It is worth noting that the PCV13 vaccine is not currently included in the Irani national vaccine program as a routine immunization. Consequently, pneumococcal meningitis is a significant public health issue in Iran, with a prevalence rate of 25% [64]. Unfortunately, in the absence of PCV, it is estimated that 18,713,211 children under 5 years of age contracted the pneumococcal disease in the last 10 years (2014–2023). This figure includes 519,412 cases of pneumonia, 18,148,116 cases of acute otitis media, 6,884 cases of meningitis, and 38,799 cases that are neither pneumonia nor meningitis [65]. Moreover, the bacterial meningitis can be caused by multiple serotypes of *S. pneumoniae*, which may not be detected if all serotypes are not thoroughly tested for in cerebrospinal fluid samples [66•]. Over and above, a recent survey from the USA indicated that, even in the era of vaccines, the highest disease incidence estimates were observed for pneumococcally related acute otitis media, with a rate of 2756 cases per 100,000 individuals [67•]. It is worth noting that the USA has a high vaccination rate compared to Western Asian countries. Likewise, there have been recent alarming reports from Lebanon regarding the emergence of serotype 24F in invasive infections. This serotype exhibits high virulence and antimicrobial resistance, which is a cause for concern. It is important to note that serotype 24F is not included in the current PCV [68•]. Because of the significant incidence of IPD among young children residing in developing nations, there has been a swift implementation of second-generation PCVs. These vaccines encompass a greater number of pneumococcal serotypes and are being incorporated into the Expanded Program on Immunization of low- and lower-middle-income countries [69]. Moreover, there are plans to launch the third generation of pneumococcal conjugate vaccines (PCV15 and PCV20) to overcome PVSR. This is intended to sustain the high vaccination coverage rate, following 13 years of using PCV13 in clinical settings to address the emergence of non-PCV13 serotypes [70•].

In addition, the ongoing political instability and civil war in some parts of Western Asia have exacerbated the situation. This is particularly evident in Yemen, where the negative impact on vaccination coverage has coincided with an increasing prevalence of acute bacterial meningitis in the country. Pneumococci has emerged as the dominant causative pathogen in these cases [71•].

Despite the diverse data from Western Asian countries that were reviewed in this study, the findings regarding serotypes underscore the importance of continuous surveillance.

Table 1 Prevalence of common circulating serotypes of *S. pneumoniae* among children of Western Asia

Countries	Study publication	Total study population	Carriage rate	Common serotypes	PCV covering rate	Ref.
Bahrain	2020	100 serotypes isolated from invasive and non-invasive samples collected from children and elderly people	Not available	19, 6, 23, 3, and 14	It was 66.7% in children < 2 years old	[40•]
Cyprus	2016–2017	1507 healthy children < 5 years old	25.3–35.3%	1, 6BC, 5AB, 19A, and 23AB	- PCV7 was 2.1–22.2% - PCV10 was 23.8% - PCV13 was 10.4–28.6%	[9, 21]
Egypt	2015–2020	1143 nasopharyngeal swabs from healthy children < 5 years old	56.5–65% (RT-PCR) 29.2–32.9% (culture)	1, 6ABC, 5, 18ABC, 19A, 19F, and	- PCV10 was 65.5% - PCV13 72.4–77.4%	[12, 22•,41]
Iran	2012–2022	- 2432 healthy children aged from 6 months to 14 years old in 4 studies - 130 infected cases age from 10 days to 92 years - 2049 clinical specimens from children younger than 18 years	2.2–44.1%	1, 3, 6, 9 V, 14, 17, 19, 20, 21, and 23	- PCV7 was 33.7–38.56% - PCV10 was 34.9 –65.1% - PCV13 was 66.2–83.5%,	[23, 24, 25•, 42•, 43, 44•, 45•, 46•]
Iraq	2019	- 1092 healthy children aged 6–13 years old	20.5%	Not available	Not available	[13]
Jordan	2014–2021	3720 healthy children under 1 month to 4 years old	19.5–56.2%	6A, 6B, 14, 9 V, 11A, 15A/B, 19F, 23A, 23F, and 35B	- PCV7 was 27.8–52.3% - PCV10 was 48.2–62.2% PCV13 was 49.4–73.2%	[4•, 7•, 14–16, 17•]
Kuwait	2008	397 isolates from different clinically infected patients, only 193 for children ≤ 15 years	Not available	23F, 19F, 6B, 14, and 9A	Covering rate of Pre-vaccination period: - PCV7 was 53.26% - PCV13 was 72.6% Covering rate of vaccination period: - PCV7 decreased to 32.7% and 6.6%	[47, 48]
Lebanon	2012–2022	850 pneumococci isolated from symptomatic children and adults	Not available	1, 3, 5, 6, 14, 19F,	- PCV7 was 50–51%, - PCV10 was 45.6–74%, - PCV13 was 63–80%,	[49, 50•]
Oman	2011–2019	252 strains isolated from symptomatic children and adults	Not available	3, 6B, 9A, 12, 14, 15, 19A, 19F, and 23F	- PCV7 was 46.1% then become 15.9% - PCV10 was 24.2% - PCV13 was 37.1%	[51, 52]
Occupied Palestine Territory	2012–2015	3531 healthy children ≤ 5 years	30–55.7%	6A/B, 14, 19F, and 23F	- PCV7 was 34.4% - PCV10 was 36.5% - PCV13 was 49.2%	[18–20]
Qatar	2007–2016	282 strains isolated from children and adult who have IPD and NIPD	Not available	1, 3, 6A, 6B, 9 V, 11 A, 14, 15B, 19A, 19F, and 23 F	- PCV7 was 43–52% - PCV10 was 52–679% PCV13 was 75–78.3%	[53, 54]

Table 1 (continued)

Countries	Study publication	Total study population	Carriage rate	Common serotypes	PCV covering rate	Ref.
Saudi Arabia	2005–2016	- 78 strains isolated from children and adult who have IPD and NIPD - 1051 children aged less than 15 years with IPD and NIPD	Not available	1, 5, 6 7, 14, 15, 19, 18, 22, and 23	- PCV7 was 30–77% - PCV10 was 81% PCV13 was 90%	[55–59]
Syria		Data not available				
Turkey	2014–2021	4346 healthy children < 18 years	6.4–21.9%	19F, 6A, 6B, 9 V, 11A, 12F, 15ABF, 19F, 22AF, 23A, and 23F	- PCV7 was 46.2% - PCV13 was 27.2–60%	[26–28, 29•]
United Arab Emirates	Data not available					
Yemen	2008	602 healthy children (nasopharyngeal swabs)	5.6%	1, 2, 4, 5, 15, 19, and 22	Data not available	[30]

Monitoring shifts in serotype distribution through surveillance is crucial for informing the development of vaccines.

Misuse of Antibiotics and Development of Resistance

Although many factors contribute to antimicrobial resistance (AMR), increased antibiotic use has been linked to an increase in the prevalence of pneumococcal resistance in the population [72]. Reduced antibiotic usage will continue to be the most important intervention in our efforts to reduce the emergence of antimicrobial resistance [73]. The public health sector continues to face a significant threat from the antimicrobial resistance exhibited by *S. pneumoniae*. According to the CDC, it is estimated that each year in the USA alone, antibiotic-resistant bacteria cause over 2 million illnesses and approximately 23,000 deaths [74]. In the isolates from children in Western Asian countries over the past two decades, the rate of antimicrobial resistance was found to be high (Table 2).

In certain Western Asian regions, the practice of obtaining antibiotics without a medical prescription is prevalent, with self-medication rates ranging from 19 to 82% [79]. In Yemen, a study conducted in 2015 observed that among 200 local pharmacies in Sana'a City, 73.3% of them provided antibiotics to customers without requiring a medical prescription. The prescribed antibiotics included penicillin (48.5%), sulfonamides (12.5%), macrolides (10.6%), fluoroquinolones (8.8%), metronidazole (7.8%), cephalosporins (6%), β-lactam, and β-lactamase (5.8%). Among the various simulated scenarios, the highest percentage of antibiotics dispensed was for the sore throat scenario (99.5%), followed by cough (92%), diarrhea (75.5%), and otitis media (52%). The lowest percentage of antibiotics dispensed was observed in the UTI scenario, with only 48% [80•]. Also according to the Centers for Disease Control and Prevention (CDC), it is estimated that 30% of antibiotics prescribed in outpatient clinics are deemed unnecessary [74]. Likewise, a recent survey demonstrated a high rate of antimicrobial resistance in Yemen, where it was reported that 74% of antimicrobial prescribers were under pressure to administer broad-spectrum antibiotics. In addition to that, it was established that 81% of prescribed cases did not perform an antimicrobial sensitivity test in order to advise antibiotic choice. Additionally, many pharmacies (67%) sold antibiotics without demanding a prescription. Amoxicillin, including amoxicillin-clavulanate, was the most frequently prescribed (63%) and dispensed (82%) antibiotic [81•]. The highest rate of penicillin resistance (80–95.8%) was observed in Jordan among 3720 healthy children during the period from 2005 to 2019 [4•, 7•, 14–16, 17•]. Similarly, in Yemen, the rate of penicillin resistance ranged from 85 to 93.3% among

Table 2 Antimicrobial resistance among children of Western Asian Countries

Antibiotics/countries	PNC	CTX	CRO	ERY	TET	TMX	References
Bahrain	32.7%	NA	NA	40.8%	34.6%	NA	[40•]
Cyprus	27.9–40.8%	0	5.8%	28.2–39.6%	12.9–31.9%	17.1–58.2%	[9, 21]
Egypt	15.8–55%	1–16%	0	20.1–50%	49–72.6%	55–96.7%	[22•, 41]
Iran	20.8–95.3%	2.9–69.8	4.5%	71.4–74.4%	41.9–69.9%	11.8–81.3%	[43, 44•, 75]
Iraq	53–57.6%	13–87%	45.1%	15.6–83%		89%	[13, 76]
Jordan	80–95.8%	3.6–29.2%	NA	46–78.2%	32.3–53.8%	61.4–86.6%	[4•, 7•, 14–16, 17•]
Kuwait	64%	NA	NA	NA	NA	NA	[48]
Lebanon	13.2–29.1%	12.8–18.3%		30.8–40.7%	NA	NA	[49]
Oman	40.9–44%	0.8%	0.8–1%	25.8%	NA	26.5%	[51, 52]
Occupied Palestine Territory	12.6–70.1%	0%	NA	30.3	NA	45.9%	[18–20]
Qatar	27% increased to 43.8%	2% shift to 16.6%	NA	22.8–30%	38.14%	56.78%	[53, 54]
Saudi Arabia	30–46%	6–10%	NA	26–77%	NA	43.5–100%	[55–59]
Syria	NA						
Turkey	62–73%	47.7%	13%	43%	NA		[26, 27]
United Arab Emirates	40.2–41.3%	NA	6.7–18.8%	52.6%	37%	45.5%	[77]
Yemen	85–93.3%	NA	NA	0	NA	20%	[30, 78]

PNC penicillin, *CTX* cefotaxime, *CRO* ceftriaxone, *ERY* erythromycin, *TET* tetracycline, *TMX* trimethoprim-sulfamethoxazole, *NA* not available

the studied population [30, 78]. In addition, in Iran, the rate of penicillin resistance ranged from 9.2 to 95.3% among 2165 children of the studied population during the period from 2008 to 2016 [23, 43, 75], while in Turkey, the rate of penicillin resistance ranged from 62 to 73% among 3266 children aged under 18 years old in the period from 2011 to 2013 [26, 27]. Also, the rate of penicillin resistance in the remaining countries was fairly closed (Table 2). Antibiotic resistance is a problem of the second millennium, especially in developing countries. According to the report published by the Asian Network at the beginning of the second millennium, the rate of pneumococcal penicillin resistance in Asia was 35.8%. Among the countries in Asia, Taiwan had the highest rate of resistance at 91.3% [82]. Another Asian investigation found that 52.4% of *S. pneumoniae* isolates tested from 14 centers in 11 Asian countries conducted between 2000 and 2001 were resistant to penicillin with Vietnam having the highest rate of resistance (92.1%) [83]. There has been a significant increase in the resistance of pneumococci to ceftriaxone and cefotaxime in Iraq, Iran, and Turkey. In Iraq, the resistance rate for ceftriaxone was 45.1%, and for cefotaxime, it ranged from 13 to 87% during the interval from 2014 to 2016 [13, 76]. In Iran, the rate was ranged between 2.9 and 69.8% for cefotaxime during the time from 2008 to 216, while in Turkey, the resistance rate for cefotaxime was 47.7% during the period from 2008 to 2011 [26, 27]. Significant resistance rates to erythromycin were observed in Iran, Iraq, Jordan, and Saudi Arabia, as indicated in Table 2. Additionally, there was a notable variation in the rates of resistance to tetracycline and trimethoprim-sulfamethoxazole across the different populations studied, as shown in Table 2. Besides, the prevalence of multi-drug-resistant (MDR) pneumococcal strains varied across different countries in the region. In Saudi Arabia, the prevalence ranged from 63 to 75% in three reviewed studies [55, 56, 61]. In Oman, it was 18.9%, while in Qatar, it was 32.46% [51, 53]. In Cyprus, the prevalence was 24.1%, and in Egypt, it was 41% [12, 21]. While in Iran, the prevalence ranged from 51 to 69.4% [44•]. Jordan reported a range of 14.6 to 56.9%, and in the Occupied Palestine Territory, the range was from 30 to 34.1% in pneumococcal isolates from children [14, 16, 18, 20, 84].

Even though antibiotic resistance rates vary considerably from one investigation to another, these variations are nevertheless causes for concern. They highlight the need for enhanced surveillance and access to new strategies to defend against the possible spread of drug-resistant bacteria, particularly in middle- and low-income countries like Western Asian areas. It is crucial to understand and consider the individual-, social-, and national-level factors that impact antimicrobial resistance when designing and implementing effective containment programs.

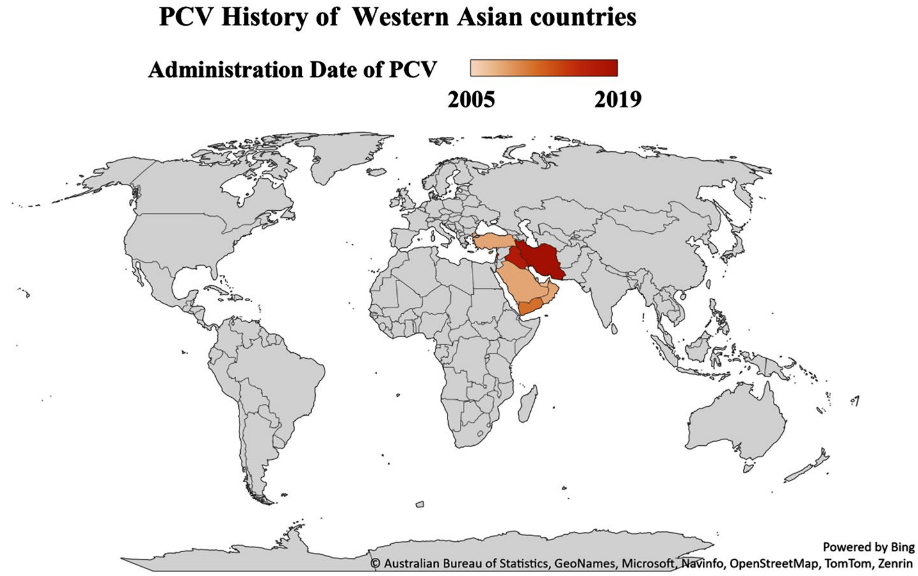

Fig. 1 The date of administration of PCV into the national immunization programs of Western Asian countries: Arab Gulf States, Cyprus, and Turkey introduced PCV7 between 2005 and 2008, which was later replaced by PCV10 or directly by PCV13. In Yemen, PCV13 was introduced under financial support from the WHO in 2011. Lebanon, Iraq, and Iran were introduced to PCV in 2005, 2017, and 2019, respectively. PCV has not been introduced to the national programs of Egypt and Jordan according to WHO. Moreover, there was no data from Syria and Occupied Palestine Territory according to the WHO website

Coverage of Pneumococcal Conjugate Vaccine

In numerous countries including Western Asian regions, the Global Alliance for Vaccines and Immunizations has played a crucial role in enhancing access to immunizations for life-threatening infectious diseases, including pneumococcal disease [85]. It was found that the introduction of PCV13 to certain regions of Western Asia has the potential to prevent numerous cases of pneumococcal disease and could contribute to a reduction of 38% in all pneumococcus-related deaths [65]. Furthermore, there was significant evidence indicating that PCV plays a critical role in reducing the isolation rate of penicillin-resistant pneumococci in clinical settings. However, the use of PCV has led to the emergence of many pneumococcal strains that are not covered by the vaccine composition [9]. The relationship between pneumococci and other bacteria that coexist can affect how well vaccines work. There is a natural balance between these microorganisms that influence vaccine efficacy [86]. In most Western Asian countries, the introduction of the pneumococcal conjugate vaccines occurred without prior knowledge of the prevalent serotypes [47]. Most countries of this region introduced the PCV shortly after the vaccine was licensed (Fig. 1). Although there is limited data regarding the distribution of pneumococcal serotypes in the post-vaccination era, it is possible that some countries, like Cyprus and Kuwait, may have experienced the phenomenon of PVSR [9, 21, 47]. To address the issue of serotype replacement and combat invasive infections among children, it is crucial to introduce the third generation of PCV once it becomes available [57]. Similarly, in countries where the PCV has not yet been introduced or has been recently introduced, serotypes included in PCV13 are likely to continue circulating in the population at a considerable rate. This is observed in countries such as Egypt, Jordan, Iran, and Iraq [87]. Unfortunately, there is no available data regarding the distribution of pneumococcal serotypes in Yemen after 12 years of the introduction of PCV into the national vaccination program. The extent of vaccine hesitancy regarding PCV coverage in the Western Asian regions remains to be examined, and this lack of data is putting many children's lives at risk.

Future Challenges

In Western Asian countries, there is a common occurrence of invasive pneumococcal strains and the emergence of multidrug-resistant serotypes [45•, 46•, 56, 88]. This issue is further exacerbated by the PVSR phenomenon and shows highly virulent and antimicrobial-resistant pneumococcal strains like 15A and 24F in this region [9, 53, 68•]. A study conducted in Cyprus on vaccinated children found that the number of vaccine serotypes had decreased significantly. Out of the total isolated pneumococcal strains, PCV10 and PCV13 serotypes accounted for 2.1% and 10.4%, respectively, while NVS represented 76.8% [9]. Furthermore, a Turkish case report emphasized that the potential outcome of PCV13 vaccine's inefficacy is the occurrence of a complex form of pneumonia accompanied by empyema [89]. Comparatively, a recent study in Japan including hospitalized children aged 5 years with community-acquired pneumonia found a rise in penicillin G resistance for NVS 15A and 35B in period between 2016 and 2018 [90•]. Moreover, the vaccination rate in most of Western Asian countries still below the desired level as shown among Yemeni children aged < 2 years was 71.4% according to a report published in 2020 [91•]. As of 2021, only 54% of individuals in Western Asian countries only have received the final dose of the PCV. While there has been progress, there is still a significant gap in achieving optimal vaccine coverage [87]. To deal with these future problems, governments, international organizations, healthcare professionals, and communities will need to work together to put an emphasis on preventing pneumococcal disease, improve healthcare infrastructure, increase vaccine coverage, encourage the right use of antibiotics, and strengthen health systems overall.

Conclusion

The Western Asian region exhibits a notably high rate of IPD serotypes and NIPD strains with a considerable fatality rate [17•, 22•, 46•]. There was a significant rate of pneumococcal resistance to penicillin, erythromycin, tetracycline, and trimethoprim-sulfamethoxazole. Therefore, it is not advisable to use these antibiotics for empiric treatment of suspected pneumococcal infections without antimicrobial susceptibly test (AST), and it is necessary to understand the links between different factors promoting self-medication practices [4•, 7•, 75, 79,]. Despite the significant progress made by many Western Asian countries in combating pneumococcal disease through the inclusion of PCV in their vaccination programs, the vaccination rate remains relatively low in this region [87]. Overcoming certain challenges is necessary to track the high rates of pneumococcal carriage and circulating IPD serotypes and spread of antibiotic-resistant strains. Initially, in this geographical area, sustained surveillance is crucial to monitoring the resistance patterns of *S. pneumoniae* and the distribution of serotypes [12, 13]. Besides, it is important for countries to implement strict systems for dispensing antimicrobial agents to minimize the high rate of resistance [79]. Eventually, changing trends need to be assessed to inform the development of educational interventions targeting both the public and healthcare professionals. Furthermore, the challenge of non-prescription antibiotic use can be addressed by enforcing regulations on the matter [80•, 81•].

If Western Asian countries do not intervene to minimize the factors that contribute to high carriage rates, the circulation of IPD serotypes, and resistant strains of pneumococci, it is anticipated that the observed increase in these rates, along with high fatality rates of IPD strains and significant pneumococcal resistance to antibiotics, will persist. Additionally, the relatively low vaccination rates in the region are also likely to continue. While the importance of antibiotic stewardship for antibacterial therapy is widely recognized in developed countries, there is a notable gap in the application of antibiotic stewardship in Western Asian countries, which raises considerable concern. To effectively address pneumococcal resistance, a comprehensive approach is necessary. This approach involves carefully assessing the use and selection of antibiotics by AST and promoting responsible antibiotic use by clinicians and public education awareness. These measures are vital for ensuring a low rate of IPD and reducing the high rate of antimicrobial resistance among children in this region.

Availability of Data and Materials The data used to support the findings of this study are included within the article.

Compliance with Ethical Standards

Conflict of Interest None to be declared.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Recently published papers that are of particular interest have been highlighted as:
• Of importance

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4.• Al-Lahham A, Khanfar N, Albataina N, et al. Urban and rural disparities in pneumococcal carriage and resistance in Jordanian children, 2015–2019. Vaccines. 2021;9(7):789. https://doi.org/10.3390/vaccines9070789. **This study investigates urban and rural disparities in pneumococcal carriage and resistance in Jordanian children from 2015 to 2019.**
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