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Pneumococcal Disease Burden and Pediatric Invasive Pneumococcal Serotype Shifts in Malaysia

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Research Article

Keywords:

Posted Date: August 14th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10379503/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

Streptococcus pneumoniae remains an important cause of invasive and non-invasive bacterial disease. However, nationwide data describing pneumococcal disease burden, antimicrobial susceptibility, and pediatric invasive pneumococcal disease (IPD) serotype shifts in Malaysia remain limited.

Methods

This retrospective study analyzed culture-confirmed pneumococcal infections reported to the National Surveillance for Antibiotic Resistance (NSAR) database submitted via WHONET from 2017 to 2023 to evaluate disease burden and antimicrobial susceptibility trends. A separate serotype analysis of invasive pneumococcal isolates from children aged $\leq$ 5 collected between 2018 to 2024 was conducted to describe pre- and post-vaccination serotype distribution and monitor the early impact of pneumococcal vaccines (PCVs) in Malaysia.

Results

A total of 10,237 culture-confirmed cases were identified, with an average incidence of 4.01 per 100,000 population. Incidence varied geographically, with higher rates in Peninsular Malaysia than in Sabah and Sarawak. Children aged ≤ 15 years represented the largest affected group, followed by adults aged $\geq$ 66 years, with a male predominance. Blood was the most common specimen source, indicating a substantial IPD contribution, although non-invasive specimens collectively accounted for a larger proportion of cases. Antimicrobial susceptibility was preserved for beta-lactams, levofloxacin, linezolid, and vancomycin, whereas resistance was highest to tetracycline, erythromycin, and co-trimoxazole. Among children aged $\leq$ 5 years with IPD, serotype distribution shifted after PCV10 introduction, with declining PCV10 serotype isolates and a proportional increase in serotypes 19A, 3, 19F, and non-vaccine serotypes (NVTs).

Conclusion

These findings provide baseline evidence to support integrated surveillance of pneumococcal disease burden, antimicrobial resistance, serotype replacement, and PCV impact in Malaysia.

Background

Streptococcus pneumoniae (pneumococcus) is a Gram-positive opportunistic bacterial pathogen responsible for a wide spectrum of infections, including otitis media, community-acquired pneumonia, bacteremia, sepsis, and meningitis [1]. The bacterium commonly colonizes the upper respiratory tract, particularly in children who serve as an important reservoir for transmission [1, 2]. Although carriage is often commensal, the bacterium can be disseminated locally, be aspirated into the lower respiratory tract, or invade normally sterile sites, including the bloodstream and central nervous system. These invasive processes result in clinical disease, with epidemiology influenced by geographical, demographic, and serotype-related factors [1, 2].

S. pneumoniae remains one of the leading bacterial pathogens responsible for community-acquired lower respiratory tract infections (LRTI) in both children and adults worldwide [3]. Although non-invasive pneumococcal disease (NIPD) is more frequently reported than invasive pneumococcal disease (IPD), IPD remains a key surveillance endpoint as it reflects severe disease and is typically confirmed through culture from normally sterile sites. This is particularly important for serotype surveillance, as invasive isolates provide valuable information for monitoring vaccine-type (VT) disease, serotype replacement, and the impact of pneumococcal conjugate vaccine (PCV) programs [4, 5]. In Malaysia, although previous studies have described pneumococcal disease, carriage, serotype distribution, and antimicrobial susceptibility in selected populations and regions, comprehensive national-level data remain limited [6–9].

Antimicrobial resistance (AMR) in *S. pneumoniae* remains a major global public health concern as it compromises the effectiveness of standard therapy, contributes to treatment failure, and increases both disease burden and healthcare costs [10, 11]. Beta-lactam antibiotics, including penicillin and third-generation cephalosporins, are standard treatment options for pneumococcal diseases. Although reduced penicillin susceptibility mediated by alterations in penicillin-binding proteins (pbp) has been documented worldwide, clinical resistance to beta-lactams remains low [11, 12]. In contrast, resistance to non-beta-lactam antibiotics, including macrolides, tetracyclines, and trimethoprim–sulfamethoxazole (co-trimoxazole), is more widespread, with recent Asian studies also reporting high resistance to these antibiotics despite sustained beta-lactam susceptibility [13–15]. A similar pattern has previously been observed in Malaysia, where non-susceptibility to the same antibiotic classes has been reported [6, 7, 16].

Capsular serotype distribution is a key determinant of pneumococcal epidemiology and vaccine-preventable disease burden, with over 100 serotypes described based on antigenic differences in the polysaccharide capsule and identified using type-specific antisera through the Quellung reaction [1, 17]. The capsule is the primary pneumococcal virulence factor and the main target of protective antibodies, forming the basis of PCVs, in which capsular polysaccharides are chemically conjugated to carrier proteins to induce T-cell dependent immunity and immunological memory [18]. The introduction of PCV7 in 2000 marked an important milestone in pneumococcal disease prevention, leading to substantial reductions in IPD among children and providing indirect protection through reduced nasopharyngeal carriage and transmission [19, 20].

However, the emergence of non-vaccine types (NVTs) has reduced the long-term impact of PCV7, prompting the sequential development of higher-valency vaccines, including PCV10, PCV13, PCV15, and PCV20 [18, 21]. Following World Health Organization recommendations to include PCVs in immunization

programme [22], PCV implementation has reduced childhood IPD [4, 23, 24], while higher-valency formulations provide broader serotype coverage to address evolving pneumococcal epidemiology [20, 25]. Most countries have since incorporated PCVs into routine infant immunization schedules, with PCV10 and PCV13 among the most widely used formulations [4, 23, 24, 26]. In Malaysia, PCV10 has been included in National Immunization Programme (NIP) for all newborns since late 2020 [7]. Despite global reductions in VT disease, residual IPD is increasingly influenced by persistent VTs such as 19A and 3, alongside the emergence of NVTs through serotype replacement [5, 21].

Pneumococcal transmission and disease burden are influenced by multiple factors, including age, circulating serotypes, antimicrobial resistance, regional epidemiology, and vaccine implementation. Therefore, defining the current epidemiology of *S. pneumoniae* in Malaysia is important to support evidence-based policy and strategies for immunization. Despite introduction of PCV10 into Malaysia's NIP, nationwide data remain limited for assessing disease burden, identifying affected population groups, and monitoring early post-vaccination changes. This study aimed to evaluate the disease burden, demographic distribution, clinical sources, and antimicrobial susceptibility patterns of culture-confirmed pneumococcal infections in Malaysia using NSAR data, and to describe pediatric IPD serotype distribution across the pre- and post-PCV periods.

Methodology

A retrospective cross-sectional study was conducted using the National Surveillance for Antibiotic Resistance (NSAR) database (https://imr.nih.gov.my/MyOHAR/index.php/site/archive_rpt). The database was screened for *S. pneumoniae* isolates obtained from Malaysian patients, which had been submitted to the WHONET system between January 2017 and December 2023. WHONET is a free Windows-based software application for the management and analysis of microbiology laboratory data, particularly on antimicrobial resistance surveillance [27]. The system is developed by the World Health Organization Collaborating Centre for Antimicrobial Resistance Surveillance and Research to support AMR surveillance initiatives (https://www.who.int/initiatives/glass/network) [28].

A culture-confirmed pneumococcal infection was defined as the isolation of *S. pneumoniae* from at least one clinical specimen. To avoid duplication, only one isolate per patient per year was included to represent a single episode of infection. Where multiple isolates were available for the same patient, the earliest isolate based on specimen collection date was selected. Data for each included isolate were reviewed for patient demographics (gender, age, geographical location, specimen source). Race, occupation, comorbidities, and clinical outcomes were excluded from analysis due to incomplete data within the NSAR network.

Annual and mean incidence rates of pneumococcal infection per 100,000 population were calculated at the state level, using the fourth quarter 2025 population estimates from the Department of Statistics Malaysia (DOSM) as a baseline reference denominator (https://www.dosm.gov.my/uploads/release-content/file_20260305153346.pdf). Mean annual incidence (2017–2023) was calculated at both national and state levels, then further stratified into Peninsular Malaysia and Malaysian Borneo (Sabah and Sarawak). For comparative analyses, the study timeline was stratified into pre-PCV (2017–2020) and post-PCV (2021–2023) periods, based on the introduction of PCV10 into Malaysia's NIP in late 2020. Age was analyzed using predefined age groups with additional sub-stratification among cases from pediatric cohort (aged $\leq$ 15) to characterize the burden of childhood IPD. Specimen types were classified as invasive (blood and cerebrospinal fluid) and non-invasive (sputum, tracheal aspirate, swabs including eye, ear, and vaginal, endotracheal tubing, nasopharyngeal aspirate, and pus). Antimicrobial susceptibility testing of pneumococcal isolates was performed by participating laboratories in accordance with the Clinical and Laboratory Standards Institute (CLSI) M100 guidelines (27th edition, 2017).

To address the limited availability of data on pneumococcal serotype distribution, a separate analysis was conducted using data from the National Surveillance of *Streptococcus pneumoniae* Serotypes in Malaysia, coordinated by the Bacteriology Unit, Institute for Medical Research (IMR), Ministry of Health Malaysia. The analysis included serotype data from invasive pneumococcal isolates collected from Malaysian children aged ≤ 5 years between 2018 and 2024. For this analysis, invasive isolates were defined as *S. pneumoniae* recovered from blood or cerebrospinal fluid (CSF) specimens. Pneumococcal serotyping was performed using the Neufeld Quellung reaction with type-specific antisera (Statens Serum Institut, Denmark), in accordance with the manufacturer's instructions.

Results

Burden, Incidence, and Demographic Characteristics of Pneumococcal Infection in Malaysia

A total of 10,237 culture-confirmed pneumococcal infections were reported through the WHONET-based NSAR network between 2017 and 2023. The mean national incidence was 4.01 cases per 100,000 population. The annual number of reported cases decreased markedly in 2020 (n = 368) compared with the pre-pandemic years, followed by a gradual increase from 2021 onwards. The geographical distribution of pneumococcal infection incidence across Malaysian states is shown in Fig. 1. Mean incidence was higher in Peninsular Malaysia than in Malaysian Borneo, at 4.33 and 2.10 cases per 100,000 population respectively. The state with highest incidence was in Terengganu (8.20 per 100,000 population), followed by Kelantan, Pahang, Melaka, and Negeri Sembilan (5.68–4.02 per 100,000 population). In contrast, lower incidence rates were reported in Johor and Sabah (2.43 and 1.11 per 100,000 population). These findings demonstrate notable geographical variation in reported pneumococcal infection incidence across Malaysia.

Demographic characteristics of the 10,237 culture-confirmed pneumococcal infections (Table 1) showed male predominance across all study years among the 8,843 cases with available gender data, with a male-to-female ratio ranging from 1.46:1 to 1.88:1. Among the 8,680 cases with confirmed age data, individuals aged ≤ 15 years accounted for the largest proportion of infections (n = 2,811, 32.4%), followed by adults aged $\geq$ 66 years (n = 1,570, 18.1%).

Within the pediatric cohort (≤ 15 years), children aged 1–5 years accounted for the highest proportion of infections (*n* = 1,649, 58.7%), followed by infants aged ＜1 year (*n*=752, 26.8%), while lower proportions were observed among those aged 6–10 years (*n*=245, 8.7%) and 11–15 years (*n*=164, 5.8%).

Table 1

Demographic and geographical characteristics of pneumococcal infections reported to the National Surveillance for Antibiotic Resistance (NSAR) database, Malaysia, 2017–2023.

Factors		**Year of isolation**						
		2017	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**
Number of isolates (*n* = 10237)		2248	2034	2119	368	718	1265	1485
Gender ratio (Male: Female) (*n* = 8843; 5416:3427)		1.58:1	1.69:1	1.46:1	1.68:1	1.88:1	1.57:1	1.52:1
Age group, n (%) (*n* = 8680)								
≤15 (*n* = 2811),		669 (35.5)	526 (33.0)	688 (36.7)	83 (24.9)	116 (17.8)	344 (30.2)	385 (32.0)
16–25 (*n* = 463)		108 (5.7)	96 (6.0)	110 (5.9)	24 (7.2)	50 (7.7)	37 (3.2)	38 (3.2)
26–35 (*n* = 845)		153 (8.1)	140 (8.8)	186 (9.9)	49 (14.7)	68 (10.4)	130 (11.4)	119 (9.9)
36–45 (*n* = 882)		166 (8.8)	152 (9.5)	169 (9.0)	39 (11.7)	80 (12.3)	119 (10.5)	157 (13.1)
46–55 (*n* = 873)		175 (9.3)	148 (9.3)	163 (8.7)	29 (8.7)	102 (15.6)	129 (11.3)	127 (10.6)
56–65 (*n* = 1236)		261 (13.8)	248 (15.6)	234 (13.5)	48 (14.4)	120 (18.4)	150 (13.2)	175 (14.6)
≥66 (*n* = 1570)		353 (18.8)	284 (17.8)	325 (17.3)	62 (18.6)	116 (17.8)	230 (20.2)	200 (16.7)
Age group distribution of patients aged ≤ 15 years, n (%)								
＜1 (*n* = 752)		181 (27.1)	113 (21.5)	136 (19.8)	18 (21.4)	30 (25.9)	139 (40.4)	135 (35.1)
1–5 (*n* = 1649)		425 (63.5)	351 (52.5)	442 (64.3)	48 (57.1)	60 (51.7)	151 (43.9)	172 (44.7)
6–10 (*n* = 245)		41 (6.1)	40 (7.6)	65 (9.5)	12 (14.3)	12 (10.3)	29 (8.4)	46 (11.9)
11–15 (*n* = 164)		22 (3.3)	22 (4.2)	44 (6.4)	6 (7.1)	14 (12.1)	25 (7.3)	32 (8.3)
Number of patients by location, n (%)								
Peninsular Malaysia (*n* = 7731)	Perlis	22 (1.2)	35 (2.1)	21 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Kedah	182 (9.6)	165 (9.8)	30 (1.8)	49 (15.3)	31 (4.9)	72 (6.7)	91 (7.4)
	Pulau Pinang	12 (0.6)	92 (5.4)	120 (7.0)	26 (8.1)	18 (2.9)	75 (7.0)	90 (7.3)
	Perak	190 (10.0)	150 (8.9)	144 (8.4)	0 (0.0)	44 (7.0)	84 (7.8)	97 (7.8)
	Selangor	601 (31.6)	295 (17.4)	362 (21.2)	38 (11.9)	177 (28.0)	224 (20.8)	242 (19.6)
	Wilayah Persekutuan	134 (7.0)	148 (8.8)	115 (6.7)	22 (6.9)	12 (1.9)	11 (1.0)	17 (1.4)
	Negeri Sembilan	102 (5.4)	53 (3.1)	86 (5.0)	17 (5.3)	28 (4.4)	32 (3.0)	32 (2.6)
	Melaka	70 (3.7)	52 (3.1)	33 (1.9)	0 (0.0)	32 (5.1)	57 (5.3)	62 (5.0)
	Johor	136 (7.1)	147 (8.7)	168 (9.8)	31 (9.7)	49 (7.8)	99 (9.2)	84 (6.8)
	Pahang	55 (2.9)	138 (8.2)	161 (9.4)	2 (0.6)	84 (13.3)	105 (9.8)	104 (8.4)
	Terengganu	133 (7.0)	142 (8.4)	173 (10.1)	9 (2.8)	43 (6.8)	95 (8.8)	121 (9.8)
	Kelantan	94 (4.9)	110 (6.5)	132 (7.7)	93 (29.1)	64 (10.1)	114 (10.6)	151 (12.2)
Borneo (*n* = 839)	Sabah	60 (3.2)	39 (2.3)	40 (2.3)	21 (6.6)	14 (2.2)	42 (3.9)	76 (6.1)
	Sarawak	114 (6.0)	125 (7.4)	123 (7.2)	12 (3.8)	36 (5.7)	66 (6.1)	71 (5.7)

[1]: Wilayah Persekutuan includes the Kuala Lumpur and Putrajaya region

The distribution of clinical specimen sources (Fig. 2) indicated that blood was the most common specimen yielding *S. pneumoniae* (37.7%), followed by sputum (19.8%), tracheal aspirate (14.5%), and swab specimens (13.5%). Less frequently reported sources included nasopharyngeal aspirate (5.5%), endotracheal tubing (4.8%), pus (3.3%), and cerebrospinal fluid (0.8%). Overall, invasive specimens (blood and cerebrospinal fluid) accounted for approximately 38.5% of isolates, with the remainder classified as non-invasive.

Antimicrobial Susceptibility and Resistance in Streptococcus pneumoniae

Antimicrobial susceptibility testing of *S. pneumoniae* isolates from 2017 to 2023 revealed variable resistance patterns across different antibiotic classes in Malaysia (Supplementary Table 1). Susceptibility to penicillin G, amoxicillin–clavulanate, cefotaxime, and ceftriaxone was determined using the Epsilometer test (E-test), while disk diffusion was applied for the remaining antimicrobials. High susceptibility was observed for beta-lactam antibiotics, including penicillin G (89.8%), amoxicillin–clavulanate (97.3%), cefotaxime (98.2%), and ceftriaxone (92.0%), as well as for levofloxacin (99.7%), linezolid (99.5%), and vancomycin (99.5%). In contrast, resistance was the most prominent for tetracycline (41.9%), erythromycin (32.8%), and co-trimoxazole (30.3%), with lower resistance observed for clindamycin (19.4%) and chloramphenicol (9.8%).

By clinical source, non-invasive isolates showed higher resistance than invasive isolates for several antibiotics (Supplementary Table 2). Penicillin G susceptibility was slightly higher in invasive isolates (91.3%) than non-invasive isolates (88.9%). Similar higher susceptibility was noted among invasive isolates than non-invasive isolates in amoxicillin-clavulanate (98.3% vs 96.8%) and ceftriaxone (92.5% vs 91.7%), whereas cefotaxime susceptibility was marginally higher among non-invasive strains (98.5% vs 97.9%). Higher resistance in non-invasive isolates was observed for tetracycline (46.1% vs 35.1%), erythromycin (35.5% vs 27.8%), and co-trimoxazole (34.0% vs 23.6%). Clindamycin resistance was also higher among non-invasive isolates (22.7%) than in invasive isolates (14.4%). Resistance to vancomycin, linezolid, and levofloxacin remained low ($<$1.0%) in both groups.

Comparison of AMR profiles between pre- and post-PCV periods (Supplementary Table 3) showed increased resistance to penicillin G (7.8% to 11.8%), cefotaxime (0.6% to 3.6%), ceftriaxone (7.0% to 8.1%), and chloramphenicol (8.7% to 12.5%). Conversely, resistance decreased for amoxicillin–clavulanate (1.8% to 0.6%), erythromycin (33.5% to 31.5%), tetracycline (43.6% to 37.2%), and co-trimoxazole (31.4% to 27.9%). The slight increase of resistance to levofloxacin, linezolid, and vancomycin was identified, but remained consistently low ($<$1.0%) across both periods.

Invasive Pneumococcal Disease and Serotype Distribution in Children Aged 5 Years

Invasive Pneumococcal Disease and Serotype Distribution in Children Aged $\leq$ 5 Years
A total of 305 invasive *S. pneumoniae* isolates from children aged ≤ 5 years were analyzed for their serotype distribution (Fig. 3) across the pre-PCV (2018–2020) and post-PCV periods (2021–2024), with their demographic information analyzed (Table 2). Overall, isolates were most frequently identified among children aged 1–2 years, followed by infants aged 4–12 months, children aged 3–5 years, and infants aged < 3 months. Age distribution differed between the vaccination periods (Supplementary Table 4). During the pre-PCV period, most IPD cases were among children aged 1–2 years (*n* = 93, 42.5%) and infants aged 4–12 months (*n* = 71, 32.4%). In contrast, cases were more evenly distributed between children aged 1–2 years and 3–5 years during the post-PCV period, each accounting for 33.7% (*n* = 29) of cases. The proportion of cases increased among children aged $<$3 months (5.9% to 12.8%), and children aged 3–5 years (19.2% to 33.7%), while it decreased among infants aged 4–12 months (32.4% to 19.8%).

Table 2

Demographic analysis of invasive pneumococcal isolates from Malaysian paediatric patients aged ≤5 by serot

Serotype	14	6B	19F	23F	18C	1	7F	4	5	9V	19A	6A	3	33F	2
Age Group, *n* (%)															
< 3 months (*n* = 25)	3 (4.5)	1 (2.2)	3 (13.0)	1 (6.7)	1 (12.5)	- (0.0)	1 (50.0)	1 (100.0)	- (0.0)	- (0.0)	4 (10.0)	1 (4.3)	7 (31.8)	- (0.0)	- (
4–12 months (*n* = 84)	15 (22.7)	18 (40.0)	3 (13.0)	5 (33.3)	2 (25.0)	1 (11.1)	1 (50.0)	- (0.0)	- (0.0)	- (0.0)	10 (25.0)	11 (47.8)	3 (13.6)	- (0.0)	- (
1–2 years (*n* = 124)	26 (39.4)	18 (40.0)	9 (39.1)	7 (46.7)	3 (37.5)	4 (44.4)	- (0.0)	- (0.0)	1 (100.0)	- (0.0)	15 (37.5)	10 (43.5)	10 (45.5)	- (0.0)	- (
3–5 years (*n* = 73)	22 (33.3)	8 (17.8)	8 (34.8)	2 (13.3)	2 (25.0)	2 (22.2)	- (0.0)	- (0.0)	- (0.0)	1 (100.0)	11 (27.5)	1 (4.3)	2 (9.1)	1 (100.0)	- (
Gender															
Male:Female Ratio	1.5:1	1.3:1	1.3:1	1:1	1:1.7	1.3:1	2:0	0:1	1:0	1:0	1.9:1	1.9:1	1:1.2	1:0	-
Race, n (%)															
Malay (*n* = 245)	62 (93.9)	29 (64.4)	19 (82.6)	13 (86.7)	4 (50.0)	6 (66.7)	2 (100.0)	1 (100.0)	1 (100.0)	- (0.0)	31 (77.5)	21 (91.3)	18 (81.8)	- (0.0)	- (
Chinese (*n* = 10)	- (0.0)	2 (4.4)	1 (4.3)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	3 (7.5)	- (0.0)	- (0.0)	- (0.0)	- (
Indian (*n* = 5)	1 (1.5)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	- (0.0)	2 (9.1)	- (0.0)	- (
Sabah & Sarawak Aboriginals (*n* = 45)	3 (4.5)	14 (31.1)	3 (13.0)	2 (13.3)	4 (50.0)	1 (11.1)	- (0.0)	- (0.0)	- (0.0)	1 (100.0)	5 (12.5)	2 (8.7)	2 (9.1)	1 (100.0)	- (
State, n (%)															
Perlis (*n* = 10)	2 (3.0)	- (0.0)	1 (4.3)	1 (6.7)	- (0.0)	1 (11.1)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	2 (5.0)	- (0.0)	2 (9.1)	- (0.0)	- (
Kedah (*n* = 16)	3 (4.5)	1 (2.2)	3 (13.0)	- (0.0)	1 (12.5)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	3 (13.0)	1 (4.5)	- (0.0)	- (
Pulau Pinang (*n* = 15)	1 (1.5)	1 (2.2)	1 (4.3)	1 (6.7)	2 (25.0)	1 (11.1)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	2 (5.0)	1 (4.3)	- (0.0)	- (0.0)	- (
Kelantan (*n* = 11)	5 (7.6)	1 (2.2)	- (0.0)	1 (6.7)	- (0.0)	- (0.0)	2 (100.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	- (0.0)	- (0.0)	- (0.0)	- (
Terengganu (*n* = 21)	6 (9.1)	3 (6.7)	1 (4.3)	1 (6.7)	1 (12.5)	- (0.0)	- (0.0)	- (0.0)	1 (100.0)	- (0.0)	2 (5.0)	1 (4.3)	2 (9.1)	- (0.0)	- (
Perak (*n* = 21)	3 (4.5)	3 (6.7)	2 (8.7)	3 (20.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	5 (12.5)	3 (13.0)	- (0.0)	- (0.0)	- (
Pahang (*n* = 15)	5 (7.6)	4 (8.9)	- (0.0)	- (0.0)	- (0.0)	2 (22.2)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	1 (4.3)	- (0.0)	- (0.0)	- (
Selangor (*n* = 67)	14 (21.2)	6 (13.3)	7 (30.4)	2 (13.3)	- (0.0)	- (0.0)	- (0.0)	1 (100.0)	- (0.0)	- (0.0)	9 (22.5)	4 (17.4)	11 (50.0)	- (0.0)	- (
Wilayah Persekutuan* (*n* = 29)	10 (15.2)	6 (13.3)	- (0.0)	3 (20.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	4 (10.0)	3 (13.0)	1 (4.5)	- (0.0)	- (

* Wilayah Persekutuan includes the Kuala Lumpur and Putrajaya regions

Serotype	14	6B	19F	23F	18C	1	7F	4	5	9V	19A	6A	3	33F	2
Age Group, *n* (%)															
Negeri Sembilan (*n* = 19)	9 (13.6)	3 (6.7)	- (0.0)	- (0.0)	1 (12.5)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	2 (5.0)	2 (8.7)	1 (4.5)	- (0.0)	- (
Melaka (*n* = 8)	2 (3.0)	3 (6.7)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	2 (8.7)	- (0.0)	- (0.0)	- (
Johor (*n* = 12)	2 (3.0)	2 (4.4)	- (0.0)	1 (6.7)	1 (12.5)	1 (11.1)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (2.5)	- (0.0)	1 (4.5)	- (0.0)	- (
Sarawak (*n* = 37)	1 (1.5)	8 (17.8)	6 (26.1)	1 (6.7)	2 (25.0)	2 (22.2)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	6 (15.0)	3 (13.0)	3 (13.6)	1 (100.0)	- (
Sabah (*n* = 24)	3 (4.5)	4 (8.9)	2 (8.7)	1 (6.7)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	- (0.0)	1 (100.0)	3 (7.5)	- (0.0)	- (0.0)	- (0.0)	- (
* Wilayah Persekutuan includes the Kuala Lumpur and Putrajaya regions															

By ethnicity, most isolates were reported among Malay children (*n* = 245, 80.3%), followed by Sabah and Sarawak Indigenous (*n* = 45, 14.8%), Chinese (*n* = 10, 3.3%), and Indian children (*n* = 5, 1.6%). Geographically, the highest number of isolates was reported from Selangor (*n* = 67, 22.0%), followed by Sarawak (*n* = 37, 12.1%), Wilayah Persekutuan (Kuala Lumpur and Putrajaya) (*n* = 29, 9.5%), Sabah (n = 24, 7.9%), Perak (*n* = 21, 6.9%) and Terengganu (*n* = 21, 6.9%). Regarding gender distribution, isolates were approximately twice as frequent in males as in females for serotypes 19A and 6A (male-to-female ratios of 1.9:1 for both). Male predominance was also observed for serotypes 14 (1.5:1), 6B (1.3:1), and 19F (1.3:1). In comparison, serotype 3 had a slight female predominance (1:1.2) compared to the prevalent serotypes in this study.

Figure 3 shows the serotype distribution of isolates among the pediatric cohort. Overall, the most common pediatric IPD serotypes were 14 (*n* = 66, 21.6%), 6B (*n* = 45, 14.8%), 19A (*n* = 40, 13.1%), 19F and 6A (*n* = 23 each, 7.5%), 3 (*n* = 22, 7.2%), and 23F (*n* = 15, 4.9%). Serotype 14 predominated before PCV implementation (*n* = 56, 25.6%), followed by 6B (*n* = 39, 17.8%), 19A (*n* = 25, 11.4%), 6A (*n* = 19, 8.7%), 19F (*n* = 15, 6.8%), and 23F (*n* = 12, 5.5%). In the post-PCV period, serotype 19A was the predominant serotype (*n* = 15, 17.4%), followed by 3 (*n* = 13, 15.1%), 14 (*n* = 10, 11.6%), 19F (*n* = 8, 9.3%), 6B (*n* = 6, 7.0%), 6A (*n* = 4, 4.7%), and 23F (*n* = 3, 3.5%).

Following PCV introduction, isolates of serotypes 14, 6B, 6A, and 23F declined, offset by increases in serotypes 19A, 3, and 19F. The proportion of post-PCV NVTs increased from 11.4% (*n* = 25) to 23.3% (*n* = 20). This shift was driven by changes in dominant NVTs, from serotypes 23A (*n* = 5), 6D (*n* = 4), 23B (*n* = 3), and 15A (*n* = 3) pre-PCV to serotypes 15C and 23A (*n* = 5 each), alongside 19B and 19C (*n* = 2 each) post-PCV. The proportion of PCV10 serotype isolates decreased from 63.0% pre-PCV to 36.0% post-PCV. PCV13 serotype isolates decreased from 87.2% to 73.3% but they remained the predominant cause of pediatric IPD post-PCV.

Discussion

S. pneumoniae remains an important public health concern in Malaysia, particularly among young children and older adults. This study provides a nationwide overview of culture-confirmed pneumococcal infections reported through NSAR, alongside a separate national pediatric IPD serotype surveillance analysis. The mean incidence rate of 4.01 per 100,000 population was higher than earlier Malaysian estimates based mainly on IPD, which reported an incidence below 1.00 per 100,000 population [9]. This difference is attributable to the inclusion of both invasive and non-invasive infections in the NSAR dataset. Regional variation in pneumococcal disease burden from Southeast Asia is also evident, with Singapore reporting IPD incidences of 3.9 per 100,000 children and up to 11.1 per 100,000 older adults, while Thailand has reported IPD and NIPD incidences of 4.05 and 10.92 per 100,000 population respectively [23, 29, 30]. The reduction in reported cases during 2020–2021, followed by the subsequent resurgence aligns with global observations of reduced respiratory infections during the COVID-19 pandemic and subsequent rebound following relaxation of public health measures [31, 32].

Geographical variation was observed across Malaysian states, with the highest incidence reported in Terengganu, followed by Kelantan, Pahang, Melaka, and Negeri Sembilan. These differences may reflect variation in healthcare access, diagnostic practices, reporting completeness, population density, and local transmission dynamics. Household crowding may also contribute to pneumococcal transmission, as a Klang Valley childcare study reported that household size greater than five was significantly associated with pneumococcal carriage among healthy children [33]. Similarly, higher carriage rates in the East Coast compared to Klang Valley may reflect differences in household size and crowding levels [34]. Collectively, these findings highlight the importance of local surveillance data for understanding regional pneumococcal epidemiology and guiding targeted public health interventions.

The demographic profile across study period showed male predominance similar to previous Malaysian pneumococcal studies reporting higher male carriage and infection rates [6, 7, 33, 35]. This pattern may be influenced by differences in exposure, comorbidities, or healthcare-seeking behavior, as population-based studies have shown a higher prevalence of risk factors such as smoking, alcohol use, and immunocompromising conditions among men [36]. Children aged ≤ 15 years accounted for the highest infection incidence, particularly those aged 1–5 years, while older adults aged $\geq$ 66 years formed a secondary peak. This age distribution mirrors the global surveillance that identifies young children and older adults as main risk groups for pneumococcal disease [37]. This is relevant in the context of PCV implementation, as young children serve as major reservoirs for pneumococcal carriage and transmission,

while reductions in VT carriage in this group may confer indirect protection to older adults through herd immunity [19]. However, this study could not directly assess herd immunity because vaccination status, carriage data, and adult serotype information were not available.

Blood was the most common single specimen source, indicating a substantial contribution of IPD among reported cases. Nevertheless, non-invasive specimens collectively represented a larger proportion of isolates, in line with previous reports showing that pneumococcal disease burden extends beyond IPD alone [7, 38]. This underscores the importance of maintaining surveillance for both invasive and non-invasive pneumococcal infections, as reliance on IPD data alone may underestimate the overall clinical burden of *S. pneumoniae*.

Pneumococcal isolates in this study showed persistently high resistance to tetracycline, erythromycin, and co-trimoxazole, while susceptibility to beta-lactam antibiotics, levofloxacin, linezolid, and vancomycin remained. These resistance profiles align closely with previous local and regional pneumococcal studies [6, 7, 13, 15]. Macrolide and tetracycline resistance remains common among pneumococci in Asia, which has been associated with antimicrobial exposure and selective pressure [39, 40]. The generally high susceptibility to beta-lactams, particularly amoxicillin–clavulanate, cefotaxime, and ceftriaxone underscore their continued clinical relevance in treating pneumococcal infections in Malaysia, although reduced susceptibility to penicillin G was observed. The robust efficacy of third-generation cephalosporins mirrors regional reports on low cefotaxime and ceftriaxone resistance among pneumococcal isolates across Asia [13–15].

Non-invasive pneumococcal isolates demonstrated higher resistance rates to tetracycline, erythromycin, co-trimoxazole, and clindamycin compared to invasive isolates. This trend corroborates previous studies, particularly among respiratory isolates, which consistently exhibit elevated resistance profiles [41–43]. This divergence may reflect the greater antimicrobial exposure in the respiratory tract, where commensal and pathogenic bacteria facilitate the circulation and horizontal transfer of AMR determinants to colonizing pneumococcal strains [44, 45].

The pediatric serotype surveillance analysis showed changes in the age distribution of IPD among children aged $\leq$ 5 years between the pre-PCV and post-PCV periods. Lower proportions of cases were observed among infants aged 1–3 months and 4–12 months, while a higher proportion occurred among children aged 3–5 years in the post-PCV period. This may reflect early shifts in the age profile of pediatric IPD observed after PCV introduction, consistent with age-related changes reported in other settings after PCV implementation [46]. In line with the broader NSAR dataset, male predominance was observed among pediatric IPD cases across most serotypes. However, the female predominance in serotype 3 contrasts with findings from the Netherlands where serotype 3 IPD incidence was significantly higher among males [47, 48].

Malaysia introduced PCV10 into the NIP in late 2020 as part of the routine vaccination for infants [8]. Following implementation, PCV10 serotype isolates declined from 63.0% in the pre-PCV period to 36.0% in the post-PCV period, supporting early evidence of vaccine impact in Malaysia. Similar results have been reported from other countries showing reductions in VT pediatric IPD post-PCV [13, 23]. In this study, serotype 14 was predominant in the pre-PCV period, followed by 6B, 19A, 6A, 19F, and 23F, indicating that VT serotypes were major contributors to pediatric IPD prior to PCV immunization. The present findings also align with previous pre-PCV study in Malaysia reporting serotype 14 as a predominant strain [6].

Following PCV introduction, the lower proportions of serotypes 14, 6B, 6A, and 23F contrasted with the rising prevalence of 19A, 3, and 19F, are important in the context of PCV10 implementation. Serotypes 19A and 3 which are not included in PCV10 formulation, have been reported to persist or increase in several PCV10 settings, including Sweden, Nepal, Lithuania, and Colombia [26, 49–51]. Although PCV10 serotype isolates declined, PCV13 serotype isolates remained predominant in the post-PCV period, despite decreasing from 87.2% to 73.3%. This reflects the continued contribution of serotypes covered by PCV13 but not in PCV10, particularly 19A, 3, and 6A. Although PCV15 and PCV20 provide broader potential serotype coverage, this pediatric IPD dataset did not show a marked additional contribution serotypes specific to these higher-valency PCVs beyond those already covered by PCV13. These findings suggest that PCV13 serotypes represent the main residual VT disease burden and provide baseline evidence for monitoring future serotype changes following the introduction of broader-valency PCV formulations in Malaysia.

The shifting pneumococcal serotype landscape was further characterized by the increase in NVTs, which nearly doubled from 11.4% pre-PCV to 23.3% post-PCV. The emergence of serotypes 15C and 23A reflects global patterns of vaccine-driven serotype replacement, when reductions in VTs are accompanied by expansion of NVTs [13, 21, 23]. A pre-PCV nasopharyngeal carriage study among children attending childcare centers in Klang Valley found NVTs accounted for 43.6% of pneumococcal carriage isolates, suggesting that these serotypes were well-established in the pediatric carriage reservoir and may contribute to future shifts in IPD serotype distribution [33].

This study has several limitations. Although the NSAR dataset provided nationwide coverage across all age groups, the laboratory-based data includes only culture-confirmed *S. pneumoniae* cases. This may underestimate the true burden of clinically diagnosed pneumococcal infections, particularly NIPD. Serotype analysis was restricted to invasive isolates from children aged $\leq$ 5 years, which precludes the interpretation of serotype distribution, vaccine impact, herd immunity, and serotype replacement among adolescents and adults. Furthermore, the absence of data regarding individual vaccination status, pneumococcal carriage, clinical severity, comorbidities, and patient outcomes further limited assessment of vaccine effectiveness and disease burden. Despite these constraints, the findings provide important baseline evidence for monitoring pneumococcal epidemiology, antimicrobial resistance, serotype replacement, and the early impacts of PCV implementation in Malaysia. Strengthening the integration of laboratory, clinical, vaccination, and serotype data within national surveillance systems would support more comprehensive evaluation of pneumococcal disease and inform future vaccine policy, including broader-valency PCV strategies.

Conclusion

This study provides a nationwide assessment of the burden, demographics, antimicrobial susceptibility, and serotype distribution of *S. pneumoniae* infections in Malaysia across the pre- and post-PCV periods. Pneumococcal disease remains an important public health concern, particularly as pediatric IPD continues

to evolve during the early post-PCV period. The persistence of PCV13 serotypes and increasing contribution of NVTs highlights the dynamic nature of pneumococcal epidemiology following vaccine introduction. These findings provide important baseline evidence for the future evaluation of Malaysia's PCV programme and strategic planning of broader valency vaccines to improve serotype coverage and reduce residual pediatric IPD burden. Continued integrated surveillance combining epidemiological data, serotype distribution, antimicrobial resistance profiling, and genomic characterization will be essential to monitor serotype replacement, detect emerging resistant clones, and guide future pneumococcal disease prevention strategies in Malaysia.

Abbreviations

AMR
Antimicrobial Resistance
CLSI
Clinical and Laboratory Standards Institute
CSF
Cerebrospinal Fluid
DOSM
Department of Statistics Malaysia
E-test
Epsilometer test
GLASS
Global Antimicrobial Resistance Surveillance System
IMR
Institute for Medical Research
IPD
Invasive Pneumococcal Disease
LRTI
Lower Respiratory Tract Infections
NIP
National Immunization Programme
NIPD
Non-Invasive Pneumococcal Disease
NMRR
National Medical Research Register
NSAR
National Surveillance for Antibiotic Resistance
NVT
Non-Vaccine Type
pbp
Penicillin-Binding Protein
PCV
Pneumococcal Conjugate Vaccine
VT
Vaccine-Type
WHO
World Health Organization
WHONET
World Health Organization Network

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia (Protocol ID: NMRR ID-24-01370-HHE). The requirement for informed patient consent was waived by the committee due to the retrospective nature of the data analysis and complete anonymization of patient records. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki.

Informed consent

Informed consent to participate was not applicable as this was secondary data.

Consent for publication

Not applicable.

Competing interests

Thea authors declare that they have no competing interests.

Funding

This study was funded by Ministry of Health, Malaysia (NMRR 24-01370-HHE).

Author Contribution

R.A.: Conceptualization, Visualization, Methodology, Formal analysis, Writing-Original Draft, Writing-review & editing. C.-N.T.: Investigation, Formal analysis, Writing-original draft. M.R.M.A: NSAR Project administration. N.A.N.A: NSAR Project administration. N.S.: Investigation, Resources, Validation R.H.: NSAR Project administration, Supervision., Resources.

Acknowledgements

We would like to thank the Director General of Health Malaysia for allowing us to publish our findings. We would also like to acknowledge all participating microbiology laboratories for contributing antimicrobial susceptibility data to the National Surveillance for Antibiotic Resistance (NSAR) programme in Malaysia.

Data Availability

All datasets used and analyzed in this study are available within the article and its supplementary materials.

References

1. Narciso AR, Dookie R, Nannapaneni P, Normark S, Henriques-Normark B. *Streptococcus pneumoniae* epidemiology, pathogenesis and control. Nat Rev Microbiol. 2025;23:256–71. https://doi.org/10.1038/s41579-024-01116-z.
2. Weiser JN, Ferreira DM, Paton JC. *Streptococcus pneumoniae*: transmission, colonization and invasion. Nat Rev Microbiol. 2018;16:355–67. https://doi.org/10.1038/s41579-018-0001-8.
3. Sirota SB, Bender RG, Dominguez R-MV, Movo A, Swetschinski LR, Araki DT, et al. Global burden of lower respiratory infections and aetiologies, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023. Lancet Infect Dis. 2026;26:343–61. https://doi.org/10.1016/S1473-3099(25)00689-9.
4. Bennett JC, Deloria Knoll M, Kagucia EW, Garcia Quesada M, Zeger SL, Hetrich MK, et al. Global impact of ten-valent and 13-valent pneumococcal conjugate vaccines on invasive pneumococcal disease in all ages (the PSERENADE project): a global surveillance analysis. Lancet Infect Dis. 2025;25:457–70. https://doi.org/10.1016/S1473-3099(24)00665-0.
5. Garcia Quesada M, Peterson ME, Bennett JC, Hayford K, Zeger SL, Yang Y, et al. Serotype distribution of remaining invasive pneumococcal disease after extensive use of ten-valent and 13-valent pneumococcal conjugate vaccines (the PSERENADE project): a global surveillance analysis. Lancet Infect Dis. 2025;25:445–56. https://doi.org/10.1016/S1473-3099(24)00588-7.
6. Arushothy R, Ahmad N, Amran F, Hashim R, Samsudin N, Azih CRC. Pneumococcal serotype distribution and antibiotic susceptibility in Malaysia: A four-year study (2014–2017) on invasive paediatric isolates. Int J Infect Dis. 2019;80:129–33. https://doi.org/10.1016/j.ijid.2018.12.009.
7. Dzaraly ND, Mohd Desa MN, Muthanna A, Masri SN, Taib NM, Suhaili Z, et al. Antimicrobial susceptibility, serotype distribution, virulence profile and molecular typing of piliated clinical isolates of pneumococci from east coast, Peninsular Malaysia. Sci Rep. 2021;11:8220. https://doi.org/10.1038/s41598-021-87428-z.
8. Lister AJJ, Le CF, Cheah ESG, Desa MNM, Cleary DW, Clarke SC. Serotype distribution of invasive, non-invasive and carried *Streptococcus pneumoniae* in Malaysia: a meta-analysis. Pneumonia. 2021;13:9. https://doi.org/10.1186/s41479-021-00086-7.
9. Sundaramurthy SSR, Allen KE, Fletcher MA, Liew KF, Borhanuddin B, Ali M, et al. Retrospective database analysis for clinical diagnoses commonly associated with pneumococcal diseases in the Malaysian healthcare system over a 3-year period (2013–2015). BMC Infect Dis. 2024;24:79. https://doi.org/10.1186/s12879-023-08611-3.
10. Naghavi M, Vollset SE, Ikuta KS, Swetschinski LR, Gray AP, Wool EE, et al. Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Lancet. 2024;404:1199–226. https://doi.org/10.1016/S0140-6736(24)01867-1.
11. World Health Organization. Global antibiotic resistance surveillance report 2025. 2025. https://iris.who.int/server/api/core/bitstreams/139d068a-1086-43f7-a47d-575d0118d034/content. Accessed 9 Jun 2026.
12. Wang J-L, Lai C-C, Ko W-C, Hsueh P-R. Global trends in non-susceptibility rates of *Streptococcus pneumoniae* isolates to ceftriaxone: Data from the antimicrobial testing leadership and surveillance (ATLAS) programme, 2016–21. Int J Antimicrob Agents. 2024;63:107072.

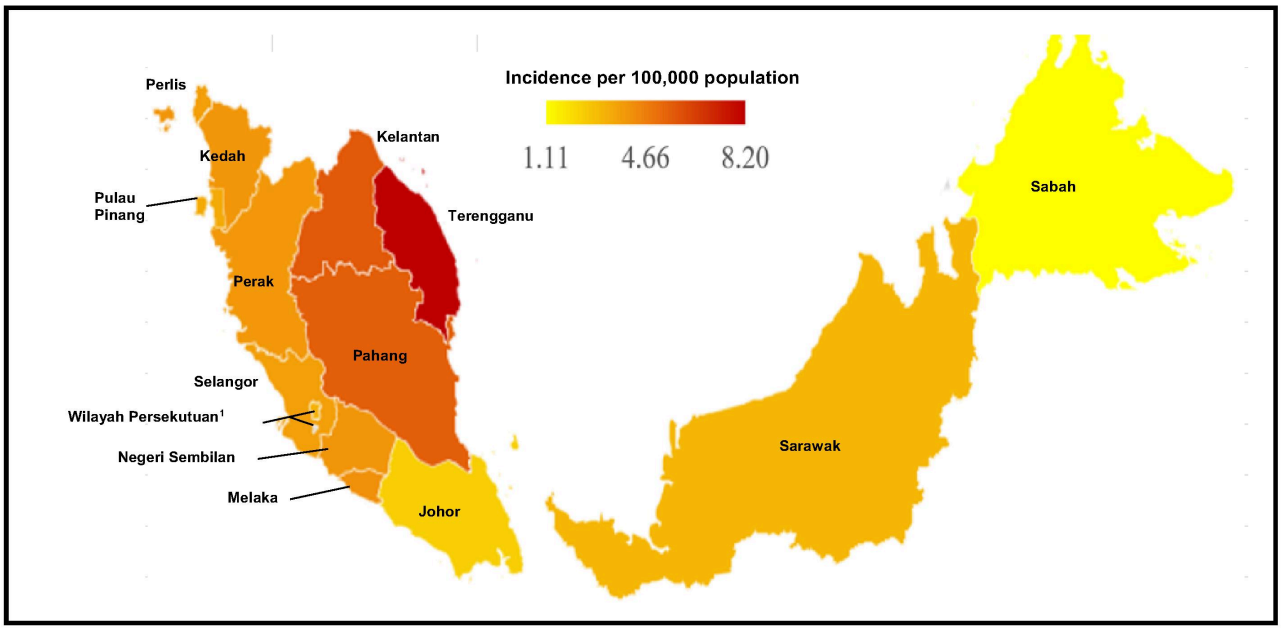
https://doi.org/10.1016/j.ijantimicag.2023.107072.

13. Cheng H-CR, Kuo S-C, Lai J-F, Wu H-C, Chen F-J, Sytwu H-K, et al. Genomic analysis of the *Streptococcus pneumoniae* in Taiwan: a nationwide study from 2006 to 2022. Microb Genom. 2025;11. https://doi.org/10.1099/mgen.0.001498.
14. Kawaguchiya M, Aung MS, Urushibara N, Ohashi N, Kobayashi N, Kudo K, et al. Molecular characterization and antimicrobial resistance of *Streptococcus pneumoniae* isolated from adult patients with invasive pneumococcal disease in northern Japan, 2017–2023. IJID Reg. 2025;16:100693. https://doi.org/10.1016/j.ijregi.2025.100693.
15. Shin J-I, Cho S-Y, Chu J, Park C, Lee M, Song JY, et al. Genomic analysis and pneumococcal population dynamics across PCV implementation in South Korea, 1997–2023. Microb Genom. 2025;11. https://doi.org/10.1099/mgen.0.001433.
16. Wan Mahmud WN, Hassan SA, Abd Rahman Z, Wan Abdul Wahab WNA, Ismail N. Detection of macrolide-resistant *Streptococcus pneumoniae* genes and its clinical outcomes in a tertiary teaching hospital in Malaysia. Malaysian J Med Sci. 2024;31:188–98. https://doi.org/10.21315/mjms2024.31.2.17.
17. Berical AC, Harris D, Dela Cruz CS, Possick JD. Pneumococcal vaccination strategies. An update and perspective. Ann Am Thorac Soc. 2016;13:933–44. https://doi.org/10.1513/AnnalsATS.201511-778FR.
18. Musher DM, Anderson R, Feldman C. The remarkable history of pneumococcal vaccination: an ongoing challenge. Pneumonia. 2022;14:5. https://doi.org/10.1186/s41479-022-00097-y.
19. Davis SM, Deloria-Knoll M, Kassa HT, O'Brien KL. Impact of pneumococcal conjugate vaccines on nasopharyngeal carriage and invasive disease among unvaccinated people: Review of evidence on indirect effects. Vaccine. 2013;32:133–45. https://doi.org/10.1016/j.vaccine.2013.05.005.
20. Sgrulletti M, Mastrototaro MF, Beni A, Mantuano G, Costagliola G, Santilli V, et al. Toward universal protection: A comprehensive review of pneumococcal disease, emerging vaccination challenges and future perspectives. Vaccines (Basel). 2025;13:1237. https://doi.org/10.3390/vaccines13121237.
21. Sunmonu GT, Lo SW, Sheppard AE, Ogunniyi AD. Serotype replacement and mobile genetic elements in *Streptococcus pneumoniae*: a systematic review. Microb Genom. 2025;11. https://doi.org/10.1099/mgen.0.001497.
22. World Health Organization. WHO position paper: Pneumococcal conjugate vaccines in infants and children under 5 years of age. 2019. https://iris.who.int/server/api/core/bitstreams/dc6b2135-4a01-4783-a16c-6fc50a060aa0/content. Accessed 8 Jun 2026.
23. Li J, Yung CF, Kam K-Q, Nadua K, Tan NWH, Thoon KC, et al. Invasive pneumococcal disease and impact of 7- and 13-valent pneumococcal conjugate vaccines in Singapore children over 24 years. Open Forum Infect Dis. 2025;12. https://doi.org/10.1093/ofid/ofaf093.
24. Izurieta P, AbdelGhany M, Borys D. Serotype distribution of invasive and non-invasive pneumococcal disease in children ≤ 5 years of age following the introduction of 10- and 13-valent pneumococcal conjugate vaccines in infant national immunization programs: a systematic literature review. Front Public Health. 2025;13. https://doi.org/10.3389/fpubh.2025.1544359.
25. Principi N, Argentiero A, Campana B, Esposito S. PCV20 in pediatric pneumococcal prevention: expanded coverage, remaining challenges. Front Immunol. 2026;16. https://doi.org/10.3389/fimmu.2025.1707345.
26. Yamba Yamba L, Uddén F, Dalence S, de Bruijn A, Köster W, Ahl J, et al. Pneumococcal serotype epidemiology and resistance after PCV13 replacement with PCV10, Sweden. J Infect. 2026;92:106723. https://doi.org/10.1016/j.jinf.2026.106723.
27. Stelling JM, O'Brien TF. Surveillance of antimicrobial resistance: the WHONET program. Clinical Infectious Diseases. 1997;24 Supplement_1:S157–68. https://doi.org/10.1093/clinids/24.Supplement_1.S157
28. Wahl B, O'Brien KL, Greenbaum A, Majumder A, Liu L, Chu Y, et al. Burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000–15. Lancet Glob Health. 2018;6:e744–57. https://doi.org/10.1016/S2214-109X(18)30247-X.
29. Leong HN, Leong CK, Kurup A. The status of pneumococcal diseases and pneumococcal vaccination in Singaporean adults. Singap Med J. 2024. https://doi.org/10.4103/singaporemedj.SMJ-2023-113.
30. Ngamprasertchai T, Kerdsin A, Ruenroengbun N, Srisompong J, Dhitinanmuang W, Kajeekul R, et al. Interrupted time-series analysis of nationwide surveillance in Thai adult pneumococcal diseases over 14 years: evidence to inform policy in resource-limited countries. Expert Rev Vaccines. 2026;25. https://doi.org/10.1080/14760584.2026.2645382.
31. Camilli R, Giancristofaro S, Boros S, Bellini B, D'Ambrosio F, Urciuoli R, et al. Invasive pneumococcal diseases before and after the COVID-19 pandemic in Italy (2018–2023). Microorganisms. 2025;13:2734. https://doi.org/10.3390/microorganisms13122734.
32. Rybak A, Assad Z, Levy C, Bonarcorsi S, Béchet S, Werner A, et al. Age-specific resurgence in invasive pneumococcal disease incidence in the COVID-19 pandemic era and its association with respiratory virus and pneumococcal carriage dynamics: A time-series analysis. Clin Infect Dis. 2024;78:855–9. https://doi.org/10.1093/cid/ciad746.
33. Arushothy R, Tan CN, Nor Amdan NA, Mohd Ali MR, Mohd Tap R, Paliappan PA, et al. Serotype diversity and risk factors for pneumococcal carriage among healthy children in Klang Valley, Malaysia: A pre-vaccination cross-sectional study. IJID Reg. 2026;18:100814. https://doi.org/10.1016/j.ijregi.2025.100814.
34. Gunasegaran H, Ramzi NH, Hoong Tan AC, Johari NA, Nathan AM, Sulaiman NA, et al. Prevalence of pneumococcal carriage and risk factors for pneumonia and carriage among under-5 children in Malaysia: findings from the MY-Pneumo study. Pneumonia. 2025;17:24. https://doi.org/10.1186/s41479-025-00177-9.
35. Abdullah AFA, Kee SY, Razali K, Mohamed TJ, Abdul Wahab Z, Othman N. Invasive pneumococcal disease in a tertiary paediatric hospital in Malaysia. Malaysian J Paediatrics Child Health. 2017;23:74–82.
36. Forcadell-Peris MJ, Vila-Córcoles Á, de Diego-Cabanes C, Torras Vives V, Ochoa-Gondar O, Satué-Gracia EM. Evaluating sex differences in pneumococcal disease burden and vaccination effectiveness in adults: A population-based study. J Infect Dis. 2025;231:1455–64.

https://doi.org/10.1093/infdis/jiae624.

37. Anglemyer A, Ren X, Gilkison C, Kumbaroff Z, Morgan J, DuBray K, et al. The impact of pneumococcal serotype replacement on the effectiveness of a national immunization program: a population-based active surveillance cohort study in New Zealand. Lancet Reg Health West Pac. 2024;46:101082. https://doi.org/10.1016/j.lanwpc.2024.101082.
38. Le C-F, Palanisamy NK, Mohd Yusof MY, Sekaran SD. Capsular serotype and antibiotic resistance of *Streptococcus pneumoniae* isolates in Malaysia. PLoS ONE. 2011;6:e19547. https://doi.org/10.1371/journal.pone.0019547.
39. Skalet AH, Cevallos V, Ayele B, Gebre T, Zhou Z, Jorgensen JH, et al. Antibiotic selection pressure and macrolide resistance in nasopharyngeal *Streptococcus pneumoniae*: A cluster-randomized clinical trial. PLoS Med. 2010;7:e1000377. https://doi.org/10.1371/journal.pmed.1000377.
40. Albrich WC, Monnet DL, Harbarth S. Antibiotic selection pressure and resistance in *Streptococcus pneumoniae* and *Streptococcus pyogenes*. Emerg Infect Dis. 2004;10:514–7. https://doi.org/10.3201/eid1003.030252.
41. Higgs C, Kumar LS, Stevens K, Strachan J, Sherry NL, Horan K, et al. Population structure, serotype distribution and antibiotic resistance of *Streptococcus pneumoniae* causing invasive disease in Victoria, Australia. Microb Genom. 2023;9. https://doi.org/10.1099/mgen.0.001070.
42. Lau JC, Cheung KW, Yu Q, Wu P, Wong S, Cheng VC, et al. Disease pattern and risk factors of antimicrobial resistance in patients with pneumococcal infection in the Hong Kong population. Int J Infect Dis. 2025;161:108174. https://doi.org/10.1016/j.ijid.2025.108174.
43. Gupta V, Yu KC, Schranz J, Gelone SP. A multicenter evaluation of the US prevalence and regional variation in macrolide-resistant *S. pneumoniae* in ambulatory and hospitalized adult patients in the United States. Open Forum Infect Dis. 2021;8. https://doi.org/10.1093/ofid/ofab063.
44. Lattar SM, Wu X, Brophy J, Sakai F, Klugman KP, Vidal JE. A mechanism of unidirectional transformation, leading to antibiotic resistance, occurs within nasopharyngeal pneumococcal biofilm consortia. mBio. 2018;9. https://doi.org/10.1128/mBio.00561-18.
45. Nishimoto AT, Dao TH, Jia Q, Ortiz-Marquez JC, Echlin H, Vogel P, et al. Interspecies recombination, not *de novo* mutation, maintains virulence after β-lactam resistance acquisition in *Streptococcus pneumoniae*. Cell Rep. 2022;41:111835. https://doi.org/10.1016/j.celrep.2022.111835.
46. Jovicevic M, Kabic J, Kekic D, Kovacevic-Jovanovic V, Vasiljevic Z, Hadzi-Simovic O, et al. Impact of sequential pediatric pneumococcal conjugate vaccination (PCV10/PCV13/PCV10) on serotype distribution and antimicrobial resistance in invasive and non-invasive *Streptococcus pneumoniae* isolates in Serbian children. Front Microbiol. 2026;17. https://doi.org/10.3389/fmicb.2026.1801133.
47. Lodi L, Catamerò F, Sarli WM, Moriondo M, Nieddu F, Ferraro E, et al. Serotype 3 invasive pneumococcal disease in Tuscany across the eras of conjugate vaccines (2005–2024) and anthropic-driven respiratory virus fluctuations. Hum Vaccin Immunother. 2025;21. https://doi.org/10.1080/21645515.2025.2510005.
48. Wagenvoort GHJ, Sanders EAM, Vlaminckx BJ, de Melker HE, van der Ende A, Knol MJ. Sex differences in invasive pneumococcal disease and the impact of pneumococcal conjugate vaccination in the Netherlands, 2004 to 2015. Eurosurveillance. 2017;22. https://doi.org/10.2807/1560-7917.ES.2017.22.10.30481
49. Gutiérrez-Tobar IF, Londoño-Ruiz JP, Mariño-Drews C, Beltrán-Higuera S, Camacho-Moreno G, Leal-Castro AL, et al. Epidemiological characteristics and serotype distribution of culture-confirmed pediatric pneumococcal pneumonia before and after PCV 10 introduction, a multicenter study in Bogota, Colombia, 2008–2019. Vaccine. 2022;40:2875–83. https://doi.org/10.1016/j.vaccine.2022.03.022.
50. Shrestha S, Gurung M, Amatya P, Bijukchhe S, Bose AS, Carter MJ, et al. Effect of the of 10-valent pneumococcal conjugate vaccine in Nepal 4 years after introduction: an observational cohort study. Lancet Glob Health. 2022;10:e1494–504. https://doi.org/10.1016/S2214-109X(22)00281-9.
51. Petrutienė A, Sinotova J, Pupienienė N, Marcinonytė R, Padvilikytė I, Razmuk J, et al. A decade of 10-valent pneumococcal conjugate vaccine use in Lithuania: trends in invasive pneumococcal serotype dynamics. Front Public Health. 2025;13. https://doi.org/10.3389/fpubh.2025.1633396.

Figures

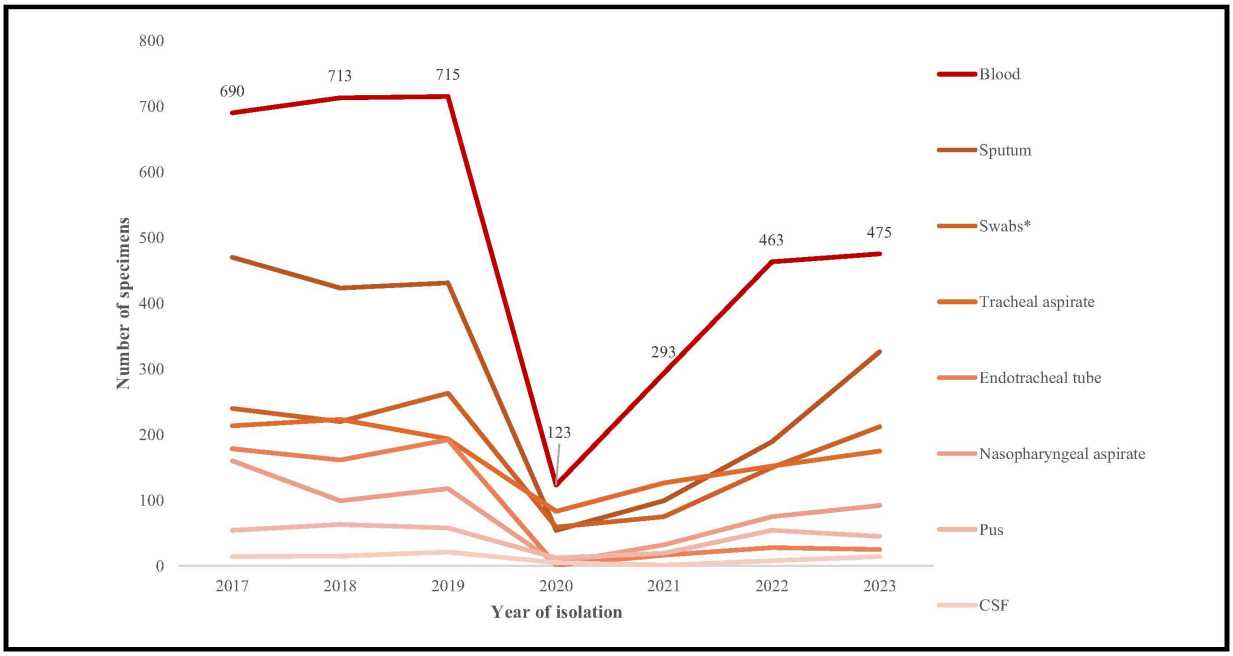


[1]Wilayah Persekutuan includes the Kuala Lumpur and Putrajaya region

Figure 1. Geographical distribution of mean annual reported incidence of pneumococcal infections per 100,000 population by states from 2017-2023. The color gradient indicates incidence rates ranging from 1.11 (light yellow) to 8.20 (dark red).

Figure 1

See image above for figure legend.



*Swabs include eye, ear, and vaginal swabs

Figure 2. Distribution of clinical specimen sources for pneumococcal infection cases. Line graphs represent the number of different clinical specimens collected each year. The red line with bold data labels represents the count of blood samples.

Figure 2

See image above for figure legend.

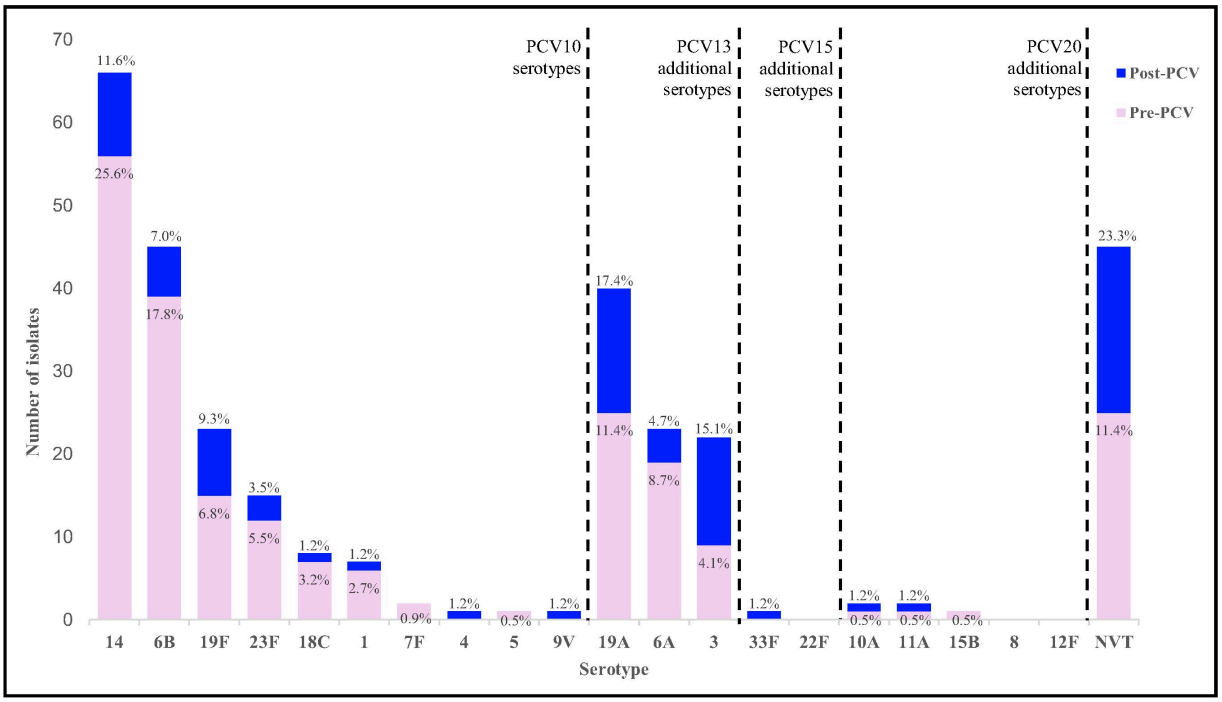


Figure 3. Serotype distribution of pneumococcal isolates from Malaysian paediatric patients aged ≤5. Light pink bars represent the pre-PCV10 period (2018-2020), while blue bars represent the post-PCV10 period (2021-2024). Vertical dashed lines categorize the serotypes based on their inclusion in successive pneumococcal conjugate vaccine formulations: PCV10, PCV13 additional serotypes, PCV15 additional serotypes, and PCV20 additional serotypes. Percentages within and above the segments indicate the proportion of total isolates contributed by respective serotype in pre-PCV and post-PCV period.

Figure 3

See image above for figure legend.

Supplementary Files

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- SupplementaryTables.docx