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MAJOR ARTICLE

Childhood Bacterial Meningitis Surveillance in Southern Vietnam: Trends and Vaccination Implications From 2012 to 2021

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Background. This retrospective hospital-based surveillance aimed to assess the epidemiology, causative pathogens trend, and serotypes distribution of pneumococcal meningitis among children aged under 5 years with bacterial meningitis in Southern Vietnam after the introduction of pentavalent vaccine in the Expanded Program on Immunization (EPI).

Methods. From 2012 to 2021, cerebrospinal fluid samples were collected from children aged under 5 years with suspected bacterial meningitis at Children's Hospitals 1 and 2 in Ho Chi Minh City. Probable bacterial meningitis (PBM) cases were identified using biochemistry and cytology. Real-time polymerase chain reaction was used to confirm cases of confirmed bacterial meningitis (CBM) caused by *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Neisseria meningitidis*. *Streptococcus pneumoniae* serotyping was performed.

Results. Of the 2560 PBM cases, 158 (6.2%) were laboratory-confirmed. The CBM proportion decreased during the 10-year study and was associated with age, seasonality, and permanent residence. *Streptococcus pneumoniae* was the most common pathogen causing bacterial meningitis (86.1%), followed by *H influenzae* (7.6%) and *N meningitidis* (6.3%). The case-fatality rate was 8.2% (95% confidence interval, 4.2%–12.2%). Pneumococcal serotypes 6A/B, 19F, 14, and 23F were the most prevalent, and the proportion of pneumococcal meningitis cases caused by the 10-valent pneumococcal conjugate vaccine (PCV) serotypes decreased from 96.2% to 57.1% during the PCV eras.

Conclusions. *Streptococcus pneumoniae* is the most frequent causative agent of bacterial meningitis in children aged under 5 years in Southern Vietnam over the last decade. Policymakers may need to consider introducing PCVs into the EPI to effectively prevent and control bacterial meningitis.

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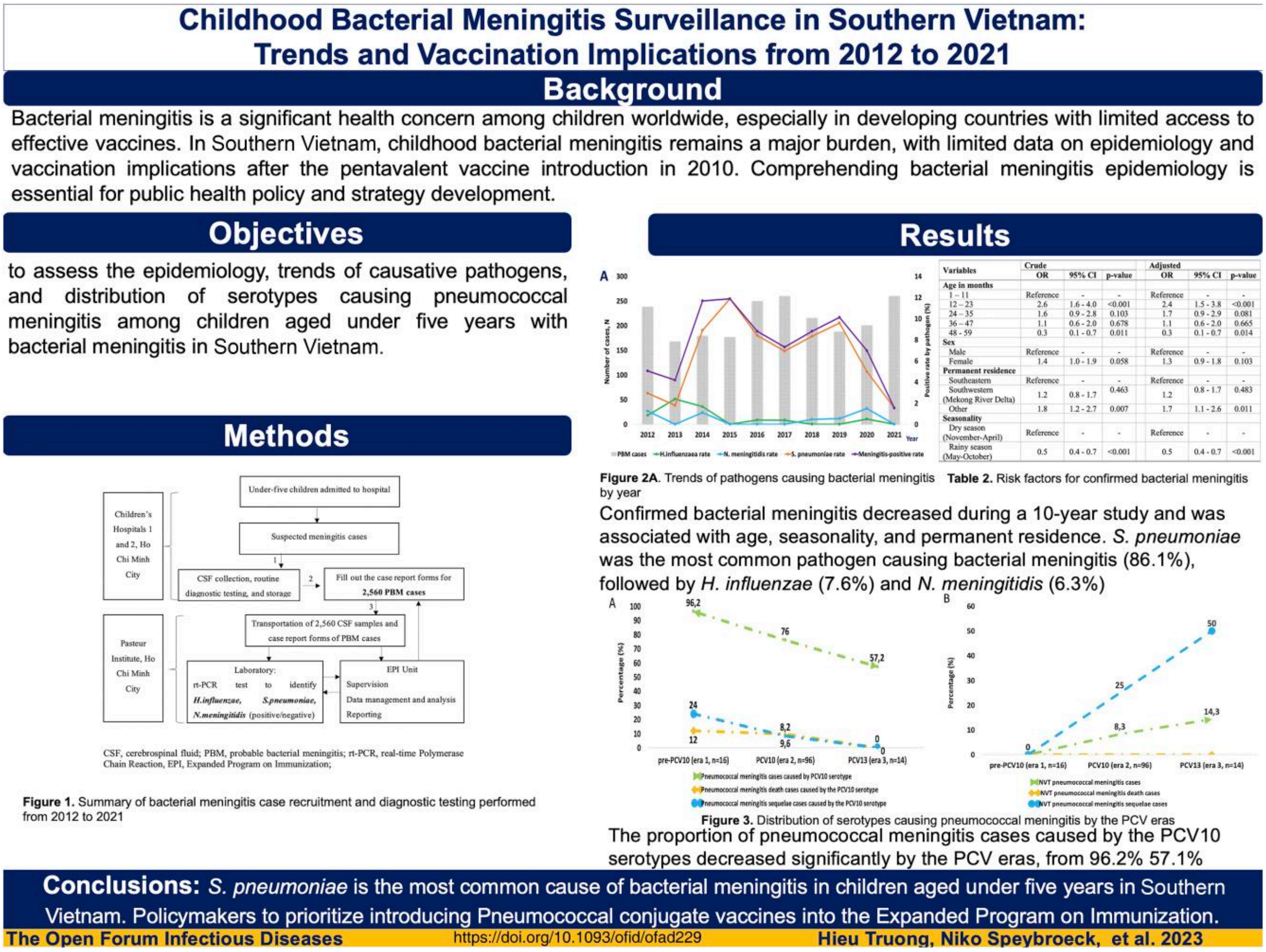
Graphical Abstract



Keywords. childhood bacterial meningitis; epidemiology; surveillance; vaccination implications; Vietnam.

Acute bacterial meningitis is a life-threatening disease that causes central nervous system damage and can lead to high rates of morbidity and mortality, particularly in developing countries [1–3]. Children under 5 years of age are the most vulnerable group, accounting for half of all cases and deaths. The most common bacterial pathogens causing meningitis are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*, which can be prevented and reduced by vaccination [4]. It is notable that 8% to 15% of affected children died within 1–2 days of the onset of symptoms, and approximately 13% of survivors experienced severe sequelae, including brain damage, hearing loss, and learning disabilities [4, 5].

According to the Global Burden of Disease Study in 2019, the number of meningitis cases increased from 2.50 million in 1990 to 2.82 million in 2016 worldwide [6]. Meningitis was ranked sixth among the leading causes of health burden in children [7]. However, the burden of *H influenzae* and pneumococcal meningitis in high-income countries has significantly decreased after the *H influenzae type* b (Hib) and pneumococcal conjugate vaccines (PCVs) were introduced into the Expanded Programs on Immunization (EPI). Conversely, bacterial meningitis is still a significant public health concern in low- and middle-income countries due to low PCVs coverage or the unavailability of these vaccines in their EPI [5, 8, 9].

In 2002, a population-based study was conducted in Hanoi, Vietnam, estimating the incidence rate of *H influenzae* meningitis to be approximately 12 per 100 000 among children under 5 years of age [10]. More recent research from 2007 to 2010 in Vietnam revealed that *H influenzae* remained the predominant pathogen in children [11]. In June 2010, Vietnam introduced a pentavalent vaccine against diphtheria, pertussis (whooping cough), tetanus, hepatitis B, and Hib into the EPI, which is administered in 3 doses to infants under 1 year of age [12]. To date, there has only been 1 study on meningitis in Vietnam based on a small sample (33 children), which primarily described clinical and laboratory characteristics in children under 15 years of age with meningitis between 2019 and 2021 [13]. To the best of our knowledge, limited research has been conducted on bacterial meningitis among children aged under 5 years after the introduction of the pentavalent vaccine in 2010. Therefore, this study aims to assess the epidemiological characteristics, trends of causative pathogens, and distribution of serotypes causing pneumococcal meningitis among children aged under 5 years with bacterial meningitis in Southern Vietnam from 2012 to 2021.

METHODS

Surveillance Program and Design

This retrospective, hospital-based sentinel, surveillance study was conducted at Children's Hospitals 1 and 2 in Ho Chi Minh City (HCMC) among children under 5 years of age with suspected bacterial meningitis from 2012 to 2021. This surveillance was part of the Invasive Bacterial Vaccine-Preventable Diseases network, which was established by the Western Pacific Regional Office of the World Health Organization (WHO) and technically supported by the US Centers for Disease Control and Prevention (CDC). These 2 hospitals were selected as sentinel sites for Vietnam's Meningitis Encephalitis Surveillance Network, which was established in 1998 [14].

Case Enrollment

Surveillance guidelines for vaccine-preventable diseases from WHO were used to define cases of bacterial meningitis in this study [15].

Suspected Meningitis Cases

Suspected meningitis cases were any children presenting with the acute onset of fever (>38.5°C rectal or 38°C axillary) and 1 of the following signs/symptoms: headache, convulsion, altered consciousness, neck stiffness, behavioral change, vomiting, and bulging fontanel. Cases also included any children aged under 5 years hospitalized with a clinical diagnosis of meningitis.

Probable Bacterial Meningitis Cases

Probable bacterial meningitis (PBM) cases were any suspected meningitis cases with at least 1 of the following findings (on cerebrospinal fluid [CSF] examination): the turbid appearance, or leukocytosis (>100 cells/mm^3), or protein (>1 g/L), or leukocytosis (10–100 cells/mm^3) and protein (>0.45 g/L), or leukocytosis (10–100 cells/mm^3) and glucose (<2.2 mmol/L).

Confirmed Bacterial Meningitis Cases

Confirmed bacterial meningitis (CBM) cases were any cases that tested positive for 1 of the 3 causative pathogens (*H influenzae*, *S pneumoniae*, or *N meningitidis*) by real-time polymerase chain reaction (rt-PCR) testing. It is important to mention that bacterial culture from CSF samples for patient treatment has isolated other pathogens besides *H influenzae*, *S pneumoniae*, and *N meningitidis*. However, the surveillance system in this study specifically focuses on these 3 pathogens.

A schematic overview of the case recruitment is described in Figure 1. As part of standard clinical procedures in the selected hospitals, CSF samples were collected from all children aged under 5 years admitted with suspected bacterial meningitis. The CSF samples were analyzed by performing biochemistry, cytology, and bacterial culture following routine hospital procedures. Based on the findings of the biochemistry and cytology analysis, only those who met the standard PBM definition were included in the study. Due to the limited resources, only a subset of all standard PBM cases was selected for data collection and analysis in this study. Subsequently, the CSF samples from these PBM cases were sent to the Pasteur Institute in HCMC (PIHCMC) for confirmation by rt-PCR, regardless of the bacterial culture results obtained in the hospital.

Data Collection and Management

The sentinel hospitals used a standardized case report form (CRF), as outlined in Supplementary Methods 1, to gather data, which included demographic characteristics, vaccination records, date of admission, date of onset, clinical symptoms, outcomes, date of death (if applicable), discharge sequelae (seizures, hearing loss, limb weakness, ventriculitis, hydrocephalus, brain abscess, and learning disabilities), and laboratory findings such as CSF specimen collection and test results [15]. The completed CRFs were then forwarded monthly to PIHCMC. Subsequently, the PIHCMC surveillance team conducted data cleaning and entry into Microsoft Access 2010.

Seasonal, Permanent Residence, and Pneumococcal Conjugate Vaccine Era

The children's permanent residence was determined using information from their household books, as described in Supplementary Methods 2. Seasonality was classified as the dry season (November–April) and the rainy season (May–October) to highlight any seasonal trends. The pneumococcal conjugate vaccine (PCV) eras were defined based on the availability of the 10-valent PCV (PCV10) and the 13-valent PCV (PCV13) at private healthcare services in Vietnam: pre-PCV10 (era 1, January 2012–July 2014), PCV10 (era 2, August 2014–October 2019), and PCV13 (era 3, November 2020–December 2021, including PCV10).

Laboratory Procedures

Collecting Clinical Specimens

A CSF specimen was collected from a suspected meningitis case and divided into 3 tubes. Two tubes were used for routine diagnostics based on biochemistry, cytological analysis, and bacteriological culture at the hospital. The third tube was stored at

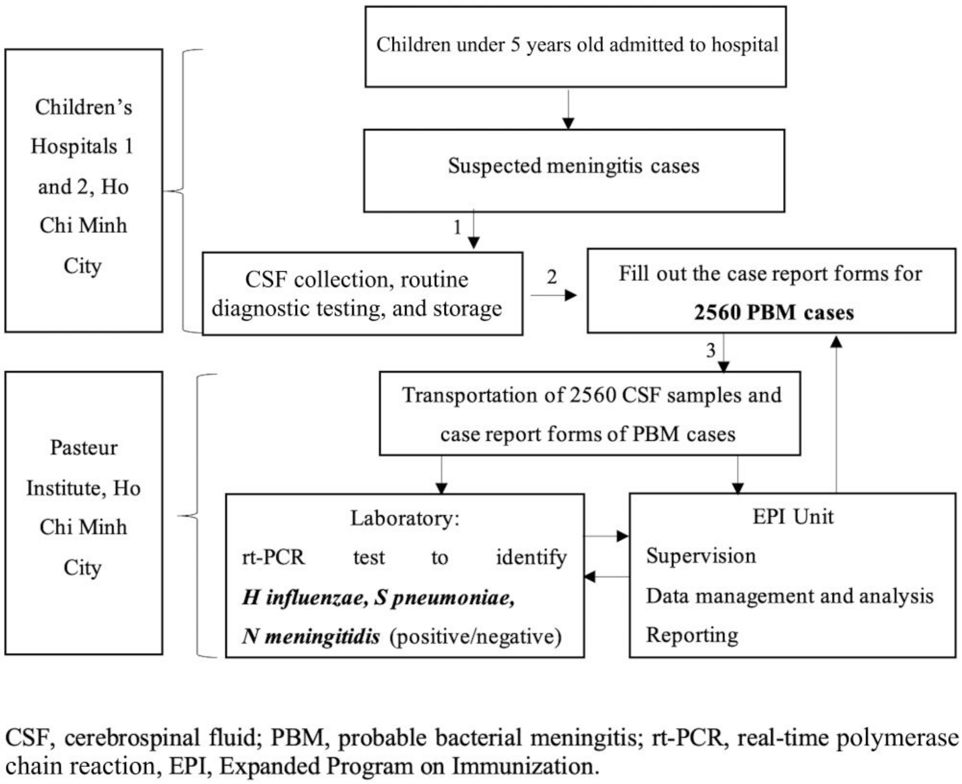


Figure 1. Summary of bacterial meningitis case recruitment and diagnostic testing performed over 10 years, from 2012 to 2021.

−80°C. This tube was then transported to the national reference laboratory at PIHCMC for confirmation of the pathogens by rt-PCR and serotyping or serogrouping when the case met the PBM criteria.

DNA Extraction and Real-Time Polymerase Chain Reaction Testing

Three main agents of bacterial meningitis, including *S pneumoniae*, *H influenzae*, and *N meningitidis*, were identified with monoplex rt-PCR targeting *lytA*, *hpd*, and *sodC* genes, respectively (for the CSF samples collected from 2012 to 2017) [16]. For those samples collected between 2018 and 2021, we applied a novel rt-PCR technique that relies on a Taq polymerase in PerfeCTa qPCR ToughMix Low Rox master mix (Quanta), allowing amplification of CSF directly without extracting DNA. This direct triplex rt-PCR approach detected the 3 pathogens simultaneously using the identical primer or probe sequences as the above-mentioned method, apart from *H influenzae* of which *hpd3* was additionally used for detection [17].

Serotyping and Serogrouping

From 2012 to 2017, a multiplex conventional PCR scheme was used to type 40 serotypes for positive samples of *S pneumoniae* [18]. Subsequently, between 2018 and 2021, a sequential direct triplex rt-PCR technique mentioned above was used to identify 21 serotypes of pneumococci [16]. These include 13 serotypes within 13-valent PCV and 8 important serotypes or serogroups [18, 19].

Statistical Analysis

Descriptive data analysis was performed to determine the proportion of PBM and confirmed bacterial meningitis, stratified by age group, sex, permanent residence, seasonality, vaccination history (including Hib, PCV, and meningococcal vaccines), outcomes, sequelae at discharge, and pathogens. The case-fatality rate (CFR) was calculated with a 95% confidence interval (CI). Logistic regression models were used to identify the risk factors (sex, age group, seasonality, and permanent residence) that differentiate confirmed bacterial meningitis from nonbacterial meningitis. The trend of serotypes causing pneumococcal meningitis and PCV eras was assessed using the linear-by-linear association test. Percentages, proportions, median, and interquartile range (IQR) were calculated and presented in tables, figures, and text. All statistical analyses were performed using Stata version 17.0 (released in April 2021) and R version 4.2.2.

Patient Consent Statement

The study has been reviewed and approved by the Institutional Review Boards of the Pasteur Institute in Ho Chi Minh City (approval reference: 27/GCN-PAS).

RESULTS

Demographic Characteristics

Through a hospital-based sentinel surveillance system for bacterial meningitis in Southern Vietnam from 2012 to 2021, a total of 2560 children aged under 5 years with PBM cases were enrolled and processed to detect bacterial pathogens by rt-PCR technique (Figure 1). Among these cases, 1623 (63.4%) were male, and 1706 (66.6%) were children under 1 year. The overall CFR for PBM cases was 1.2% (30 of 2560; 95% CI, .8%–1.6%). Overall, 158 CBM cases (6.2%) were detected by using the rt-PCR approach. Of these, 89 patients (56.3%) were male, and their median age was 8 months (IQR, 5–21 months). The highest percentage of CBM was observed in patients aged 1 to 11 months (97 cases, 61.4%), whereas the lowest (3.2%) was seen in the age group of 48–59 months. Further details on the demographic characteristics of bacterial meningitis cases are summarized in Table 1.

Epidemiologic Characteristics and Risk Factors of Confirmed Bacterial Meningitis Cases

Figure 2 presents the proportion of CBM among PBM cases and pathogens distribution by month and year. The CBM proportion decreased during the 10-year study, from 8.2% in 2015 to 2.5% in 2021 (Figure 2A), and was more prevalent during the dry season than the rainy season (60.8% vs 39.2%) (Table 1 and Figure 2B). More than half of CBM (52.5%) cases were found in the southeastern region. Most of the CBM cases were unvaccinated or had an unknown vaccination history for Hib, PCV, and meningococcal vaccines, with 84.8%, 98.1%, and 100%, respectively. The highest number of CBM cases were detected as *S pneumoniae* (86.1%, 136 of 158), followed by *H influenzae* (7.6%, 12 of 158) and *N meningitidis* (6.3%, 10 of 158). The CFR of CBM varied by the causative pathogens. For instance, *S pneumoniae* was responsible for the most deaths (92.3% of 13 deaths), with a mortality rate of 8.8% (12 of 136; 95% CI, 4.0%–13.6%). However, *N meningitidis* caused 1 death out of 13, but its mortality rate was 10% (1 of 10; 95% CI, 8.6%–28.6%). The overall CFR for CBM was 8.2% (13 of 158; 95% CI, 4.2%–12.2%). At discharge, 11.4% of CBM cases had sequelae.

The multivariate logistic model is presented in Table 2. As a result, children aged between 12 to 23 months, those living permanently outside the Southern region, and those infected during the dry season had a higher risk for bacterial meningitis caused by the 3 most common bacterial pathogens.

Trends of Bacterial Pathogens

Over the course of a decade, the annual prevalence of CBM among children aged under 5 years admitted to the 2 pediatric hospitals varied from 4.5 per 100 000 in 2013 to 13 per 100 000 in 2020 (Supplementary Table 1). The proportion of PBM cases that tested positive for at least 1 of the 3 common pathogens was 6.2% (158 of 2560 cases), and it showed monthly and yearly fluctuations. The CBM cases caused by *S pneumoniae* were evenly distributed throughout the year. On the other hand, CBM cases caused by *H influenzae* were mostly observed from August to February of the following year, whereas the CBM cases caused by *N meningitidis* were scattered in March, April, May, August, October, and December of the year (Figure 2B).

Based on Figure 2C, *S pneumoniae* was identified as the primary causative pathogen of CBM cases over the 10-year study period. All 3 bacterial pathogens were detected in 2012, 2014, and 2020, of which *S pneumoniae* was the most prevalent (58.3%, 76.2%, and 71.4%, respectively). In 2013, *H influenzae* was responsible for the majority (57%) of bacterial meningitis cases, but *S pneumoniae* became the predominant pathogen, causing more than 95% of cases in the 5 consecutive years from 2015 to 2019 and in 2021.

Distribution of Serotypes Causing Pneumococcal Meningitis

A total of 136 pneumococcal meningitis cases were isolated to identify the circulating serotypes. The analysis determined 12 different serotypes, among which serotypes 6A/B were found to be the most predominant, accounting for 36.0% of pneumococcal meningitis cases, followed by serotypes 19F (20.6%), 14 (11.0%), 23F (9.6%), and 19A (4.4%). Moreover, 7.4% of the cases were classified as non-vaccine serotypes (NVT), and 8.8% were non-typeable due to low DNA concentration in the specimens. PCV10 and PCV13 provided coverage against 77.9% and 83.8% of pneumococcal meningitis serotypes, respectively (Supplementary Table 2).

The distribution of pneumococcal meningitis serotypes during the PCV eras is illustrated in Figure 3. The proportion of pneumococcal meningitis cases caused by the PCV10 serotypes decreased significantly during the PCV eras, from 96.2% in the pre-PCV10 era to 76.0% in the PCV10 era and further down to 57.1% in the PCV13 era ($P_{\text{trend}} = .0032$) (Figure 3A). By contrast, the proportion of NVT pneumococcal meningitis increased from 0% to 8.3%, reaching up to 14.3% by the 3 PCV eras as described above ($P_{\text{trend}} = .0779$) (Figure 3B). Among death-related pneumococcal meningitis cases, serotypes 6A/B, 14, 19F, and 19A were the most common, all of which are covered by PCV10 (83.3%) and PCV13 (100%). There was a linear association between the proportion of sequelae in pneumococcal meningitis cases caused by the PCV10 serotypes and the different PCV eras ($P_{\text{trend}} = .02$) (Figure 3A). The sequelae proportion decreased from 100% in the pre-PCV10 era to 66.7% in the PCV10 era and declined to 0% in the PCV13 era.

DISCUSSION

To the best of our knowledge, this study represents one of the initial attempts to assess bacterial meningitis in children aged

Table 1. **Demographic and Epidemiologic Characteristics of Bacterial Meningitis Cases**

Variables	PBM Cases (N = 2560) n (%)	CBM Cases (N = 158) n (%)	No. CBM Case by Pathogen		
			Haemophilus influenzae (N = 12) n (%)	*Streptococcus pneumoniae* (N = 136) n (%)	*Neisseria meningitidis* (N = 10) n (%)
Age in months, median (IQR)	4 (1–24)	8 (5–21)	6.5 (4.5–47)	8 (5–20)	(5 (3–30)
1–11	1706 (66.6)	97 (61.4)	7 (58.3)	84 (61.8)	6 (60.0)
12–23	208 (8.1)	28 (17.7)	0	28 (20.6)	0
24–35	170 (6.6)	15 (9.5)	0	13 (9.6)	2 (20.0)
36–47	203 (7.9)	13 (8.2)	3 (25.0)	8 (5.9)	2 (20.0)
48–59	273 (10.7)	5 (3.2)	2 (16.7)	3 (2.2)	0
Sex					
Female	937 (36.6)	69 (43.7)	8 (66.7)	75 (55.2)	6 (60.0)
Male	1623 (63.4)	89 (56.3)	4 (33.3)	61 (44.8)	4 (40.0)
Permanent Residence					
Southeastern	1531 (59.8)	83 (52.5)	6 (50.0)	72 (52.9)	5 (50.0)
Southwestern (Mekong River Delta)	660 (25.8)	41 (26.0)	5 (41.7)	32 (23.5)	4 (40.0)
Other	369 (14.4)	34 (21.5)	1 (8.3)	32 (23.5)	1 (10.0)
Seasonality					
Dry season (November–April)	1185 (46.3)	96 (60.8)	9 (75.0)	81 (59.6)	6 (60.0)
Rainy season (May–October)	1375 (53.7)	62 (39.2)	3 (25.0)	55 (40.4)	4 (40.0)
Hib Vaccination History					
Yes	251 (9.8)	24 (15.2)	1 (8.3)	22 (16.2)	1 (10.0)
No or Unknown	2039 (90.2)	134 (84.8)	11 (91.7)	114 (83.8)	9 (90.0)
PCV Vaccination History					
Yes	18 (0.7)	3 (1.9)	0	3 (2.2)	0
No or Unknown	2542 (99.3)	155 (98.1)	12 (100)	133 (97.8)	10 (100)
Meningococcal Vaccination History					
Yes	7 (0.3)	0	0	0	0
No or unknown	2553 (99.7)	158 (100)	12 (100)	136 (100)	10 (100)
Outcome at Discharge					
Recovery or improved	2037 (79.6)	121 (76.6)	9 (75.0)	105 (77.2)	7 (70.0)
Referred to other hospital	23 (0.9)	2 (1.3)	0	2 (1.5)	0
Death	30 (1.2)	13 (8.2)	0	12 (8.8)	1 (10.0)
Unknown	470 (18.3)	22 (13.9)	3 (25.0)	17 (12.5)	2 (20.0)
Case-fatality rate, % (95% CI)	1.2 (0.8–1.6)	8.2 (4.2–12.2)	0	8.8 (4.0–13.6)	10.0 (8.6–28.6)
Sequelae at discharge	74 (2.9)	18 (11.4)	1 (8.3)	16 (11.8)	1 (10.0)

Abbreviation: CBM, confirmed bacterial meningitis; CI, confidence interval; IQR, interquartile range; Hib, *Hemophilus influenzae* type b; Nm, meningococcus vaccine; PBM, probable bacterial meningitis; PCV, pneumococcal vaccine.

under 5 years in Vietnam over the last decade. Utilizing hospital-based surveillance data from 2012 to 2021, our research provides evidence of shifts in bacterial meningitis patterns after the introduction of the Hib vaccine in the Vietnam EPI in June 2010. Although *H influenzae* was the primary causative pathogen of bacterial meningitis between 2007 and 2010, our study shows that *S pneumoniae* has become the predominant cause of bacterial meningitis among Vietnamese children aged under 5 years from 2012 to 2021.

Despite the availability of a "6-in-1" vaccine (diphtheria, whooping cough, tetanus, hepatitis B, Hib, and poliomyelitis) at private healthcare facilities in Vietnam in 2006, *H influenzae* remained the most prevalent pathogen among children between 2007 and 2010 [11]. However, our findings demonstrated that the prevalence of *H influenzae* meningitis decreased sharply after the Hib vaccine was introduced into the EPI in Vietnam. Specifically, the Hib vaccine coverage was consistently over 85% from 2012 to 2021 (except for 2013 and 2021, when vaccination was temporarily suspended due to adverse effects after immunization linked to a pentavalent vaccine and the coronavirus disease 2019 pandemic, respectively) (Figure 2C), resulting in a rapid decrease in *H influenzae* meningitis cases from 57% (2013) to 5% (2017) and no cases reported in 2018, 2019, and 2021.

In contrast, the proportion of pneumococcal meningitis cases increased from 43% in 2013 to over 94% for 5 consecutive years from 2015 to 2019, and in 2021, *S pneumoniae* became the most prevalent cause of bacterial meningitis from 2012 to 2021, despite the availability of PCV10 and PCV13 at private healthcare services in Vietnam. This result is similar to findings from studies conducted in India and Brazil, where *S pneumoniae* became the leading cause of bacterial meningitis after the Hib vaccine was introduced into their EPI [20, 21]. Our

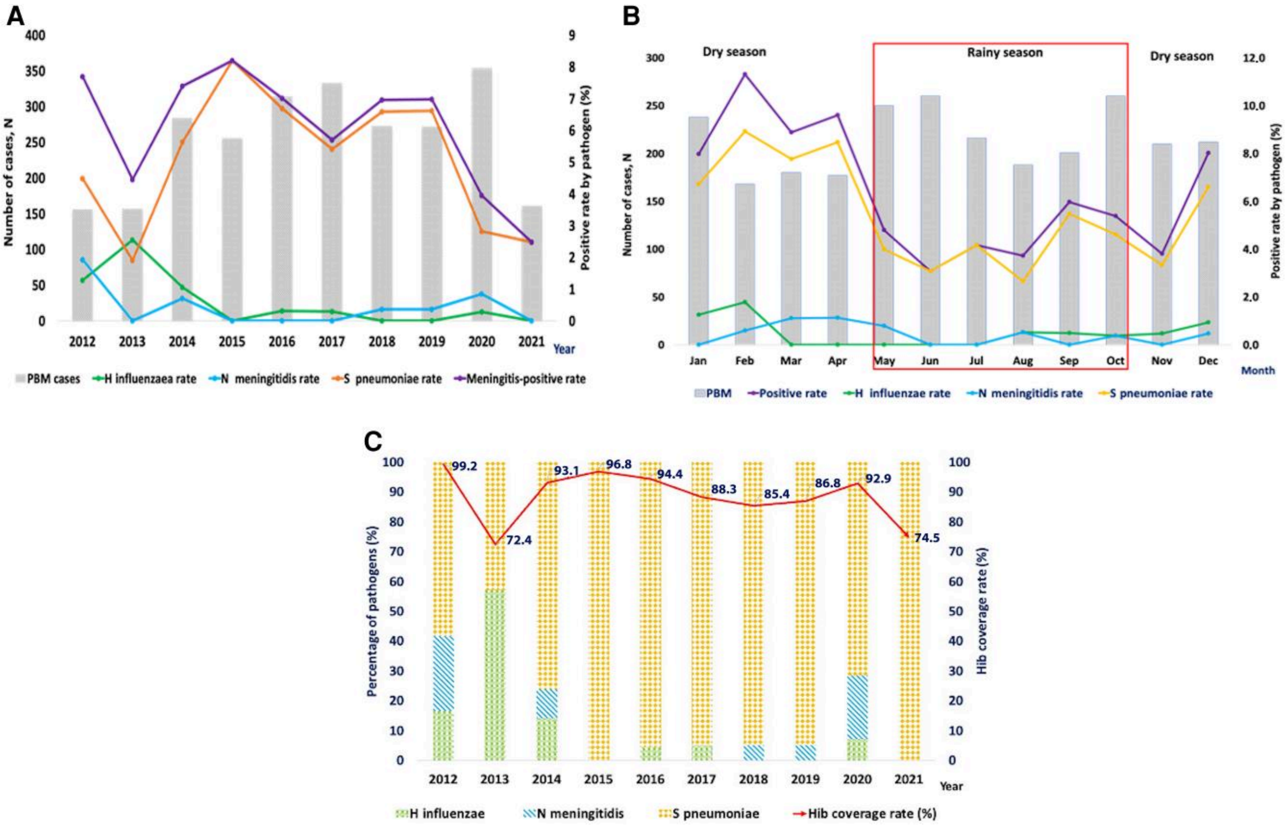


Figure 2. The bacterial meningitis positivity rate and pathogens distribution by month and year. (A) The yearly trend of pathogens causing bacterial meningitis. (B) Distribution of bacterial meningitis positivity by seasonality: meningitis cases were more prevalent during the dry season (from November to April) compared to the rainy season (May to October) (positivity 60.8% vs 39.2%; $P < .001$). (C) Distribution of pathogens causing bacterial meningitis and the *Hemophilus influenzae* type b (Hib) coverage rate by year. The Hib coverage rate data were obtained from the Expanded Program on Immunization unit in Southern Vietnam. *Streptococcus pneumoniae* was the primary causative pathogen of bacterial meningitis cases over the last 10 decades in Southern Vietnam.

Table 2. Risk Factors for Confirmed Bacterial Meningitis Cases

	Crude			Adjusted		
Variables	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Age in Months						
1–11	Reference	…	-	Reference	…	-
12–23	2.6	1.6–4.0	<.001	2.4	1.5–3.8	<.001
24–35	1.6	.9–2.8	.103	1.7	.9–2.9	.081
36–47	1.1	.6–2.0	.678	1.1	.6–2.0	.665
48–59	0.3	.1–.7	.011	.3	.1–.7	.014
Sex						
Male	Reference	…	-	Reference	…	-
Female	1.4	1.0–1.9	.058	1.3	.9–1.8	.103
Permanent Residence						
Southeastern	Reference	…	-	Reference	…	-
Southwestern (Mekong River Delta)	1.2	.8–1.7	.463	1.2	.8–1.7	.483
Other	1.8	1.2–2.7	.007	1.7	1.1–2.6	.011
Seasonality						
Dry season (November–April)	Reference	…	-	Reference	…	-
Rainy season (May–October)	0.5	.4–.7	<.001	0.5	.4–.7	<.001

Abbreviation: CI, confidence interval; OR, odds ratio.

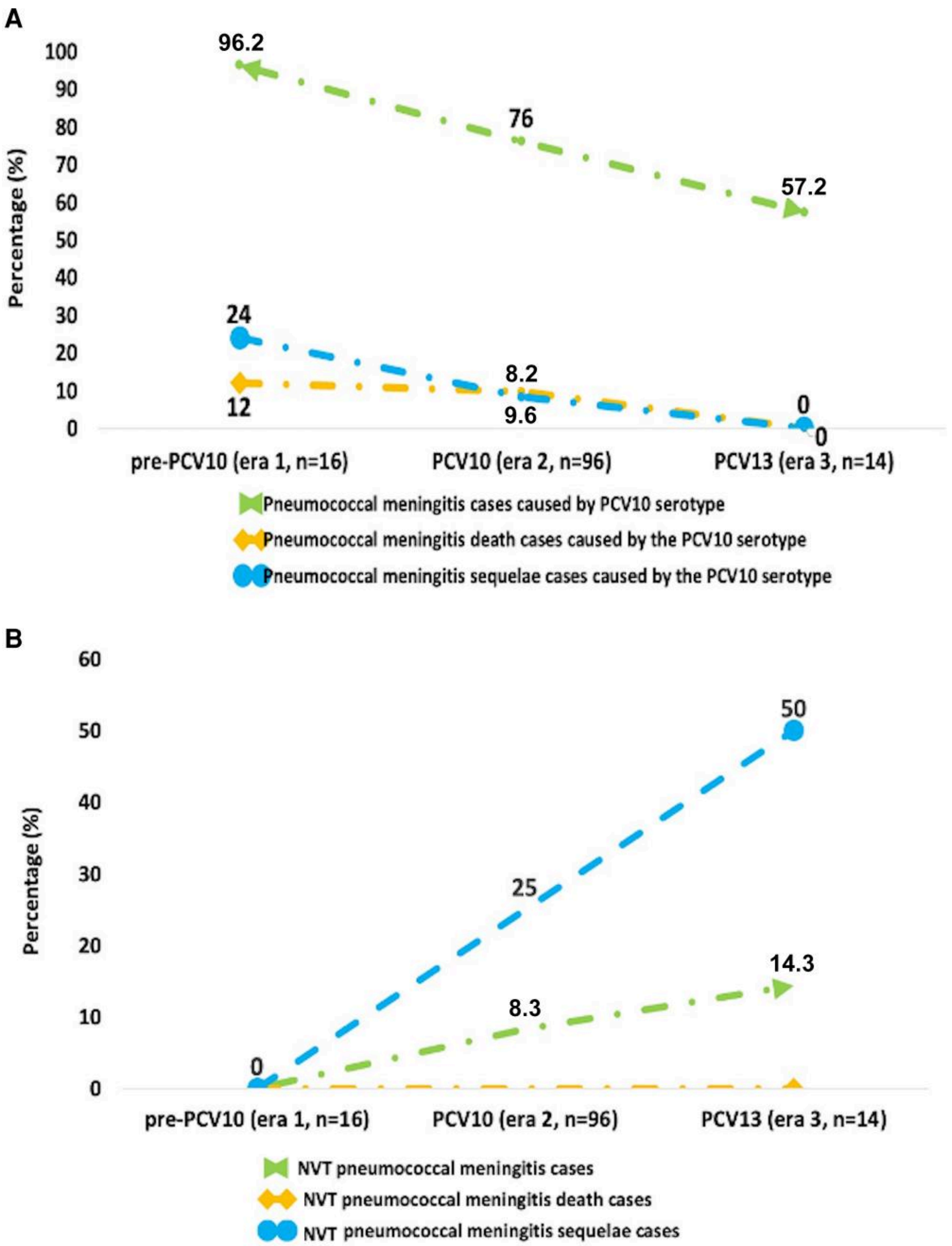


Figure 3. Distribution of serotypes causing pneumococcal meningitis during the pneumococcal conjugate vaccine (PCV) eras. (A) The cases, death cases, and sequelae cases of pneumococcal meningitis caused by the PCV10 serotypes by the PCV eras. Two linear-by-linear associations were observed between the pneumococcal meningitis cases caused by the PCV10 serotypes and the PCV eras ($P = .032$) as well as the pneumococcal meningitis sequelae cases caused by the PCV10 serotypes and the PCV eras ($P = .02$). (B) The nonvaccine serotypes (NVT) pneumococcal meningitis cases, death cases, and sequelae cases by the PCV eras. The proportion of NVT pneumococcal meningitis cases and sequelae cases increased from 0% in the pre-PCV era to 14.3% in the PCV10 era and 50% in the PCV13 era. There were nonlinear-by-linear association tests ($P = .0779$ and $P = .512$).

results underscore the impact of the Hib vaccine on bacterial meningitis, because it not only provided direct protection against *H influenzae* meningitis among vaccinated children but also conferred indirect protection for unvaccinated children by interrupting bacterial spread in communities through herd immunity [22]. Furthermore, our results also indicate that although PCV10 and PCV13 are available at private healthcare facilities in Vietnam, their impact on reducing overall morbidity has yet to be seen, because *S pneumoniae* remains the primary causative pathogen of bacterial meningitis. These findings emphasize the need to introduce PCV into the EPI to reduce the burden of pneumococcal meningitis in children aged under 5 years in Vietnam, similar to the effectiveness of the *H influenzae*-containing vaccines in the EPI.

Our study has demonstrated that 8.2% (13 of 158 cases) of CBM cases resulted in death, 92.3% (12 of 13 cases) of which were attributed to *S pneumoniae*. Among these, the most common serotype was 6A/B, followed by serotypes 14, 19F, and 19A, all of which are covered in PCV10 (83.3%) and PCV13 (100%). These findings are consistent with those found in a previous study in India, where serotypes 6A, 6B, 14, and 19F were identified as the primary serotypes of pneumococcal meningitis [23, 24]. Moreover, the introduction of PCV into EPI in several countries has resulted in a reduction in morbidity and mortality [25]. Therefore, based on our results, it is suggested that PCV be introduced into the EPI in Vietnam to reduce the incidence and mortality of pneumococcal meningitis.

Our research also found that the implementation of PCV10 in private healthcare services in Vietnam since July 2014 has resulted in an increase in NVT pneumococcal meningitis cases in children aged under 5 years, with 15A/F being the most common serotype. This phenomenon is consistent with similar observations reported in other countries [26]. However, a study conducted in Fiji did not detect any evidence of change in the incidence of invasive pneumoniae diseases, meningitis, or sepsis caused by non-PCV10 serotypes after the introduction of PCV10 to their immunization program [27]. Further studies are necessary to elucidate whether the use of PCV10 increases the risk of pneumococcal meningitis caused by non-PCV10 serotypes in children under 5 years of age in Vietnam. Continuous monitoring of the epidemiological characteristics of *S pneumoniae* is essential for more effective intervention in bacterial meningitis in children.

The proportion of PBM cases that tested positive for at least 1 of the 3 causative pathogens of *H influenzae*, *S pneumoniae*, or *N meningitidis* in Vietnam has decreased from 11.9% in 2015 to 7.0% in 2020 and 1.5% in 2021, which can be attributed to the Hib vaccine's impact in preventing bacterial meningitis. However, vaccine coverage has not yet reached the required rate. In our study, we found that the majority of CBM cases occurred in children with unvaccinated or unknown vaccination status, which suggests the accumulation of at-risk children and the development of an immunity gap among children under 5 years of age in the community. This could lead to the ongoing occurrence of bacterial meningitis. Our findings support the continued widespread vaccination of Vietnamese children under 5 years of age against bacterial meningitis and ongoing surveillance that monitors the burden of vaccine-preventable bacterial meningitis and any potential changes in serotypes distribution over time.

This study has several limitations that need to be acknowledged. First, the surveillance was conducted only in 2 pediatric hospitals in Ho Chi Minh City, which might have missed some local cases. However, because these pediatric hospitals are the main ones in Southern Vietnam, the majority of bacterial meningitis cases that occurred in the southeastern region would visit these 2 hospitals. The limited funding resulted in the inability to test all collected CSF samples, making it difficult for clinicians to decide which samples to choose for testing. In addition, samples for rt-PCR were delivered to the reference laboratory after a considerable time in hospital storage, which may have affected the quality of rt-PCR results. Finally, vaccination status information was primarily collected from parents' memories, which may not be entirely accurate because no vaccination records were available.

Despite these limitations, this study provides valuable insights into the proportion of the 3 causative pathogens of bacterial meningitis in children aged under 5 years in Vietnam. The study also demonstrates the positive impact of the Hib vaccine on preventing bacterial meningitis in children aged under 5 years in Vietnam since its introduction into the EPI. The findings suggest that similar changes in the burden of pneumococcal meningitis are likely to occur if PCV is brought into the national EPI. Our results can be used to inform immunization program managers and policymakers to prioritize the introduction of PCV into the EPI to further prevent bacterial meningitis, especially in children aged under 5 years.

CONCLUSIONS

Our surveillance highlighted that *S pneumoniae* is the most common causative pathogen of bacterial meningitis in children aged under 5 years in Southern Vietnam, after the introduction of the Hib vaccine in the EPI. These findings emphasize the essential need for policymakers to prioritize introducing PCV into the national EPI to effectively prevent and control bacterial meningitis. Furthermore, it is necessary to continue surveillance of bacterial meningitis to monitor changes in the distribution of causative pathogens, and emerging antibiotic resistance, and to identify the diversity of serotypes causing pneumococcal meningitis in Vietnam. This information is particularly important in low- and middle-income countries with limited resources for managing vaccine-preventable bacterial infectious diseases.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Author contributions. HCT was responsible for data acquisition, analysis, interpretation, writing the original draft, and preparing the manuscript. TTQP, TAH, TVH, QDP, and QCL contributed to data collection and data management at the Pasteur Institute. HTN, KHT, VCD, and NNMP contributed to data collection and data management at Children Hospital 1 and Children Hospital 2. TVP, TNLH, and DTTV performed laboratory tests. AS contributed to data analysis and reviewed the original draft. NS and TVN contributed to the study interpretation and critically revised the manuscript. All authors read and approved the final manuscript.

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Potential conflicts of interest. All authors: No reported conflicts of interest.

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