

HAEMOPHILUS INFLUENZAE TYPE B MENINGITIS AMONG CHILDREN IN HANOI, VIETNAM: EPIDEMIOLOGIC PATTERNS AND ESTIMATES OF *H. INFLUENZAE* TYPE B DISEASE BURDEN

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Abstract. From March 2000 to February 2002, a population-based study of *Haemophilus influenzae* type b (Hib) meningitis was conducted among children less than five years of age in Hanoi, Vietnam. Children with suspected bacterial meningitis were referred to hospitals and each patient underwent standardized clinical examination and microbiologic testing. In Hanoi, 580 children were evaluated for bacterial meningitis and 23 (4%) had confirmed or probable Hib meningitis. The incidence of all Hib meningitis was 12/100,000 child-years less than five years of age and 26/100,000 child-years less than two years of age. Nationally, an estimated 1,005 children less than five years of age are hospitalized for Hib meningitis and 5,107 are hospitalized for Hib pneumonia. Among children with Hib meningitis, at least 100 will develop severe neurologic sequelae and 40 will die. These data suggest there is a substantial burden of Hib disease in Vietnam. National leaders will be provided with these data to facilitate development of national vaccination policies for children in Vietnam.

INTRODUCTION

Globally, prior to introduction of conjugate vaccines directed against *Haemophilus influenzae* type b (Hib), there were an estimated 300,000–400,000 deaths and 2.2 million cases in children each year due to Hib disease.^{1,2} After the introduction of conjugate Hib vaccines into national childhood immunization programs, the decrease in incidence of

Hib disease in children in several countries has been well-documented.^{3–7} In 1999, the Global Alliance for Vaccines and Immunizations (GAVI) was launched to support improvement of immunization programs in developing countries. GAVI has also recognized that a major barrier to the rational introduction of Hib vaccine has been the limited availability of credible disease burden data among children.

In Vietnam, Tran and others in Ho Chi Minh City showed that Hib caused 53% of culture-proven bacterial meningitis in hospitalized children.⁸ In the northern region of Vietnam, a community-based survey showed that Hib was carried by 39% of the children and that 68% of the Hib isolates were resistant to at least one antibiotic.⁹ These data have suggested that the burden of disease was substantial, but few data are available to understand the incidence of Hib meningitis and the consequent neurologic sequelae. Despite these data, however, no population-based incidence rates of Hib meningitis have been available in Vietnam. To address the need for this information, we conducted a population-based study of bacterial meningitis in Hanoi, Vietnam.

METHODS

Study population. The study population consisted of 94,529 children \leq 59 months of age residing in the seven urban district of Hanoi, Vietnam.¹⁰ In this population, children with suspected meningitis were referred to one of three central hospitals in Hanoi: 1) National Pediatric Hospital, 2) St. Paul Hospital, and 3) Bach Mai Hospital. Because these hospitals are major tertiary care centers for children in the northern region of Vietnam, they also serve residents in the five outlying districts of Hanoi province (population = 1.2 million people). The study was reviewed and approved by the Institutional Review Board of the Research and Educational Institute at Harbor-UCLA Medical Center and by the Ethical Research Committee of the National Institute of Hygiene and Epidemiology (NIHE), (Hanoi, Vietnam). Informed consent for each subjects' participation was verbally obtained from each parent. Training workshops were conducted to provide

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standardized procedures for the referral of children with signs and symptoms of meningitis as well as the clinical and laboratory evaluations.

Clinical evaluation of patients. From March 4, 2000 through March 3, 2002, active surveillance for meningitis in children ≤ 59 months of age was established in Hanoi. Children residing outside the city in suburban areas of Hanoi and rural northern provinces were detected by passive surveillance. These children were evaluated for meningitis if they met the same referral and age criteria used for children in Hanoi. Children ≤ 59 months of age were referred for evaluation if they had a body temperature $> 37.5^{\circ}\text{C}$ (axillary) or $> 38.0^{\circ}\text{C}$ (orally) and had at least one of the following signs/symptoms: headache, bulging (tense) fontanelle, nuchal rigidity, forceful vomiting, or mental status changes including irritability, confusion, lethargy, or coma. Children were admitted to inpatient pediatric wards after the collection of blood and cerebrospinal fluid (CSF) to measure indices of inflammation (e.g., CSF glucose level) and perform bacterial culture testing. Medical histories and demographic data were obtained in interviews with parents or guardians, and laboratory data were collected using standardized case report forms and laboratory procedures. Neurologic sequelae were assessed clinically at the time of hospital discharge and were defined as any cranial nerve (e.g., hearing loss), motor (e.g., paralysis), or cognitive (e.g., vegetative state) deficit at the time of hospital discharge.

Case definitions. Abnormal CSF was defined by the presence of one or more of the following: 1) visibly turbid CSF, 2) CSF white blood cell count (WBC) > 30 cells/mm³ for neonates ≤ 1 month of age and > 10 cells/mm³ for older infants and children), 3) CSF neutrophils $> 70\%$ of total CSF WBCs, 4) CSF protein concentration > 170 mg/dL for neonates ≤ 1 month of age or > 75 mg/dL for older infants and children, or 5) CSF glucose concentration < 40 mg/dL.^{11,12} The following case definitions were used: 1) confirmed Hib meningitis: growth of Hib in CSF culture or abnormal CSF and growth of Hib in a blood culture; 2) confirmed bacterial meningitis: growth of a bacterial pathogen in CSF or abnormal CSF and growth of a bacterial pathogen in a blood culture; 3) probable Hib meningitis: presence of abnormal CSF findings and identification of Hib in CSF by Gram stain or detection by latex agglutination antigen (LA) or DNA polymerase chain reaction (PCR) tests; 4) suspected bacterial meningitis: presence of abnormal CSF with no identifiable bacterial pathogen by culture or other testing; 5) probable bacterial meningitis: according to the World Health Organization (WHO) a probable bacterial meningitis case requires a child to have one or more signs or symptoms of meningitis and either a CSF with turbid appearance or CSF protein > 100 mg/dL or glucose < 40 mg/dL or WBCs > 100 cells/mm³ with $> 80\%$ neutrophils and no identifiable bacterial pathogen.¹³

Laboratory evaluations. The CSF was sent to the laboratory within one hour of collection and a Gram stain was performed on uncentrifuged CSF. Two drops each of CSF were streaked onto commercially prepared blood and chocolate agar media (BBL®; Becton Dickinson, Franklin Lakes, NJ). Residual CSF was inoculated into 5% Fildes broth.¹⁴⁻¹⁶ The CSF broth was routinely sub-cultured after 24 hours, 72 hours, and 7 days of incubation. Blood was inoculated into BACTEC® Peds Plus®/F bottles (Becton Dickinson) with growth detected using either an automated blood

culture system or after routine subculture at one, three, and seven days of incubation. Bacterial identification was performed using standard microbiologic criteria.¹⁵ External proficiency testing was performed periodically throughout the study to ensure accuracy in bacterial growth on study media and identification.¹⁷ Abnormal CSF was tested for the presence of Hib, *S. pneumoniae*, and *Neisseria meningitidis* capsular polysaccharides by latex agglutination (Slidex Meningite®; BioMerieux; Marcy l'Etoile, France). The PCR was performed using a PCR enzyme-linked immunosorbent assay method to detect *H. influenzae* *bexA* gene and *S. pneumoniae* *ply* gene DNA using previously published methods.^{16,18}

Data management and statistical analysis. Case report forms were transmitted to the study data management center and entered into a computerized database at the NIHE in Hanoi. Study case report forms were compared with available data in hospital medical charts, and study databases were regularly inspected for accuracy of recorded data. Study investigators conducted microbiology laboratory record audits by comparing logbook (blood and CSF specimen records, bacterial culture records) information with study laboratory reports to identify missed meningitis cases.

Categoric comparisons were performed with the chi-square test. The Fisher exact test was used in analysis with expected cell sizes less than five (SAS® statistical software version 8.1; SAS, Inc., Cary, NC). Comparison of dimensional variables was performed with Student's *t*-test or the Mann-Whitney *U* test when data were not normally distributed. Test statistics were evaluated with a significance level of $P < 0.05$. Incidence rates were calculated using person-time denominators that incorporated the two-year period of prospective surveillance and 1999 census data for children ≤ 59 months of age in Hanoi.¹⁰ Ninety-five percent confidence intervals (CIs) for incidence rates were calculated by the Wilson score method.¹⁹ The estimated national burden of Hib meningitis (hospitalizations and deaths) was calculated directly from the Hib meningitis incidence and case-fatality rate (CFR) determined in this study. To estimate the incidence of Hib pneumonia, we assumed that the frequency of Hib pneumonia hospitalizations was five times the number of Hib meningitis hospitalizations.²⁰ This assumption, which was used in the WHO Rapid Assessment Tool for Hib disease, is based on the ratio of Hib pneumonia to Hib meningitis cases observed in two studies that described the burden of Hib pneumonia and Hib meningitis.^{21,22}

RESULTS

Characteristics of children with meningitis. Between March 4, 2000 and March 3, 2002, a total of 3,407 children from Hanoi, suburban Hanoi, and other northern provinces were prospectively evaluated for bacterial meningitis. Of these children, 580 lived in the Hanoi active surveillance study population (Table 1). In Hanoi, 47% of the children evaluated were ≤ 11 months of age, 24% were neonates (< 1 month of age), and 15% were 1-6 months of age. From parent-reported data, only 3 (0.5%) of the 580 children evaluated for bacterial meningitis in this study had received conjugate Hib vaccine (0 of the 3 had confirmed Hib meningitis or probable Hib meningitis) and 102 (18%) used antibiotics prior to hospitalization.

TABLE 1

Demographic characteristics and incidence of bacterial meningitis (suspected and probable) and meningitis due to *Haemophilus influenzae* type b (Hib) (confirmed and probable) in children \leq 59 months of age, Hanoi, Vietnam, March 4, 2000–March 3, 2002*

Characteristic Age (months)	Patients enrolled No. (%)	Meningitis case category					
		Suspected bacterial meningitis		Probable bacterial meningitis		Confirmed Hib meningitis and probable Hib meningitis	
		No.	Incidence (CI)	No.	Incidence (CI)	No.	Incidence (CI)
< 1	139 (24)	49	1,773 (1,199–2,615)	54	1,954 (1,346–2,829)	0	–
1–11	133 (23)	45	148 (98–224)	34	112 (70–179)	11	36 (16–82)
12–23	76 (13)	26	89 (52–153)	19	65 (35–122)	5	17 (5–55)
24–35	67 (12)	31	98 (60–161)	12	38 (17–83)	2	6 (1–36)
36–47	80 (14)	45	133 (88–200)	23	68 (38–120)	3	9 (2–38)
48–59	85 (15)	55	89 (62–130)	24	39 (22–68)	2	3 (1–18)
Sex							
Male	357 (62)	152	155 (124–195)	106	108 (83–142)	12	12 (6–27)
Female	223 (38)	99	108 (82–143)	60	66 (46–94)	11	12 (5–27)
All	580 (100)	251	133 (111–158)	166	88 (71–109)	23	12 (7–22)

* Rates are expressed as children per 100,000 child-years per year with 95% confidence interval (CI) in parentheses.

Suspected and probable bacterial meningitis. In the Hanoi active surveillance population (Table 1) among children \leq 59 months of age, suspected bacterial meningitis was found in 251 (43%) of the 580 children evaluated. The annual incidence of suspected bacterial meningitis was 133/100,000 (95% CI = 111–156). The highest age-specific incidence rates for suspected bacterial meningitis were 1,773/100,000 (95% CI = 1,199–2,615) among neonates and 199/100,000 (95% CI = 123–321) among infants 1–6 months of age. Probable bacterial meningitis was found in 166 (29%) of 580 children evaluated and the annual incidence of probable bacterial meningitis was 88/100,000 children \leq 59 months of age (95% CI = 71–109). Age-specific incidence rates for probable bacterial meningitis were slightly lower than the corresponding age-specific incidence rates of suspected bacterial meningitis with the exception of neonates in whom the incidence was 1,954/100,000 (95% CI = 1,346–2,829) (Table 1). Among children living in either suburban Hanoi or rural provinces outside the Hanoi active surveillance area, 1,019 cases of probable bacterial meningitis and 1,265 cases of suspected bacterial meningitis were identified (Table 2).

Confirmed Hib and probable Hib meningitis. In the Hanoi active surveillance population, 13 children had confirmed Hib meningitis and 10 children had probable Hib meningitis (Table 1). All 10 children with probable Hib meningitis had CSF positive by the *H. influenzae* PCR, but none were positive by either CSF LA or Gram stain. For children \leq 59 months of age, the annual total incidence of confirmed Hib meningitis plus probable Hib meningitis was 12/100,000 (95% CI = 7–22) and the incidence for confirmed Hib meningitis alone was 7/100,000 (95% CI = 3–15). For children \leq 23 months of age, the annual total incidence rate of confirmed Hib meningitis plus probable Hib meningitis was 26/100,000 (95% CI = 13–51) including the 13 children with confirmed Hib meningitis (Figure 1). The highest age-specific rates of confirmed Hib meningitis plus probable Hib meningitis, 30/100,000 and 44/100,000, were found among infants 1–6 and 7–11 months of age, respectively. In children 24–60 months of age, no cases of confirmed Hib meningitis were identified, but 7 of the 10 children with probable Hib meningitis (CSF culture negative, *H. influenzae* PCR positive) were identified in this older age group.

TABLE 2

Clinical and cerebrospinal fluid (CSF) characteristics in children \leq 59 months of age with meningitis in Hanoi city (active surveillance area), suburban Hanoi, and other northern provinces (passive surveillance area), Vietnam, March 4, 2000–March 3, 2002*

Characteristic of meningitis	Confirmed Hib meningitis and probable Hib meningitis			Probable bacterial meningitis		
	Hanoi city (n = 23)	Suburban Hanoi and other provinces (n = 93)	Total (n = 116)	Hanoi city (n = 166)	Suburban Hanoi and other provinces (n = 1,019)	Total (n = 1,185)
Clinical characteristic						
Altered mental status	16 (70)	76 (82)	92 (79)	88 (53)†	771 (76)	859 (73)
Nuchal rigidity	16 (70)	68 (73)	84 (72)	55 (33)‡	248 (24)	303 (26)§
Seizure	8 (35)‡	61 (66)	69 (60)	49 (30)†	479 (47)	528 (45)§
Antibiotic pretreatment	5 (22)	34 (37)	39 (34)	23 (14)‡	244 (24)	267 (23)§
Length of hospitalization, mean (days)	11.5	17.7	16.5	6.5	11.6	10.9
CSF characteristic						
Total WBC count, cells/mm ³	10,845	16,149	15,079	1,364	805	884
Segmented neutrophils, %	80	76	77	52	47	48
Protein, mg/dL	104.2	161.0	149.6	63.1	108.6	102.2
Glucose, mg/dL	28.7	25.1	25.9	38.0	38.0	43.6

* Data are numbers with percent in parentheses. WBC = white blood cell.

† Two-sided $P < 0.01$ for comparison of Hanoi city vs. suburban Hanoi and northern provinces.

‡ Two-sided $P < 0.05$ for comparison of Hanoi city vs. suburban Hanoi and northern provinces.

§ Two-sided $P < 0.01$ for comparison of confirmed Hib meningitis and probable Hib meningitis vs. probable bacterial meningitis.

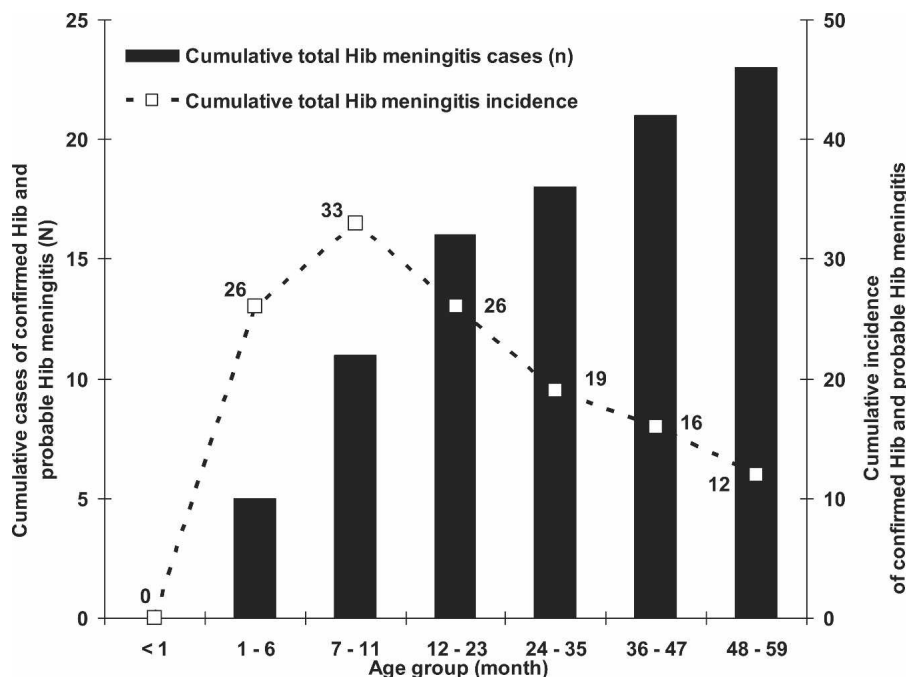


FIGURE 1. Cumulative incidence of *Haemophilus influenzae* type B (Hib) meningitis by age group among children ≤ 59 months of age in an active surveillance area of Hanoi, Vietnam, March 4, 2000 through March 3, 2002.

Among the presenting signs and symptoms of meningitis, altered mental status, nuchal rigidity, and seizure were more commonly observed among children with confirmed Hib meningitis and probable Hib meningitis compared with those having suspected bacterial meningitis (Table 2). Among cases determined to be confirmed Hib meningitis, probable Hib meningitis, probable bacterial meningitis, and suspected bacterial meningitis, those from suburban Hanoi or rural provinces presented with more severe disease compared with children from Hanoi. For each meningitis case category, children living in suburban Hanoi or rural provinces were also more likely to have received prior antibiotic treatment.

Other bacterial meningitis. In all surveillance areas (active and passive surveillance areas), there were 211 children ≤ 59 months of age identified with bacterial meningitis during the 24-month surveillance period. Of the 116 children with Hib meningitis, 51 had Hib isolated in both CSF and blood, 48 had Hib isolated in only CSF, and 17 children were categorized as probable Hib meningitis. Eighty percent (n = 93) of the confirmed Hib meningitis and probable Hib meningitis cases were identified from suburban Hanoi and other northern provinces.

Case-fatality and neurologic sequelae. In all areas of surveillance, the overall CFR in children with confirmed Hib and probable Hib meningitis was 4% (n = 5) (Table 3). All Hib

TABLE 3

Neurologic sequelae and deaths among children ≤ 59 months of age with meningitis in Hanoi, suburban Hanoi, and rural northern provinces, Vietnam, March 4, 2000–March 3, 2002*

Outcomes at hospital discharge	Confirmed Hib meningitis and probable Hib meningitis			Probable bacterial meningitis		
	Hanoi city (n = 23)	Suburban Hanoi and northern provinces (n = 93)	Total (n = 116)	Hanoi city (n = 166)	Suburban Hanoi and northern provinces (n = 1,019)	Total (n = 1,185)
Developmental delay	1 (4)	1 (1)	2 (2)	0 (0)	4 (0.4)	4 (0.3)
Hearing/vision loss	0 (0)	0 (0)	0 (0)	0 (0)	4 (0)	4 (0.3)†
Hydrocephalus	1 (4)	3 (3)	4 (4)	1 (1)	27 (3)	28 (2)
Paralysis	0 (0)	2 (2)	2 (2)	0 (0)	25 (2)	25 (2)
Seizure disorder	1 (4)	3 (3)	4 (4)	1 (1)	12 (1)	13 (1)
Vegetative state	0 (0)	1 (1)	1 (1)	0 (0)	21 (2)	21 (2)
No. of children with any neurologic sequelae‡	3 (13)	9 (10)	12 (10)	4 (2)	92 (9)	96 (8)
No. of deaths	0 (0)	5 (5)	5 (4)§	14 (8)	201 (20)	215 (18)

* Data are numbers with percent in parentheses.
 † Includes three patients with hearing loss and one patient with vision loss.
 ‡ Total number of children with at least one neurologic sequelae of all subjects. Includes neurologic sequelae prior to death.
 § Two-sided *P* < 0.01; total confirmed Hib meningitis and probable Hib meningitis vs. probable bacterial meningitis.

meningitis-associated deaths occurred in children from suburban Hanoi and rural provinces; no children died of Hib meningitis in Hanoi. Among children from Hanoi, suburban Hanoi, and rural provinces, neurologic sequelae were observed in 12 (10%) of 116 children with either confirmed Hib meningitis or probable Hib meningitis. Among these 12 children with Hib-associated sequelae, hydrocephalus ($n = 4$), developmental delay ($n = 2$), limb paralysis ($n = 2$), seizure disorder ($n = 4$), and vegetative state ($n = 1$) were identified.

Other invasive disease. *Streptococcus pneumoniae* was found among 11% ($n = 28$) and *N. meningitidis* was found in 4% ($n = 10$) of children with non-Hib invasive disease (bacterial isolates from normally sterile sites). In the Hanoi active surveillance population, there were three children with pneumococcal meningitis and one with pneumococcal bacteremia, giving an annual incidence rate for pneumococcal meningitis of 1.6/100,000 (95% CI = 0.4–6.9) in children ≤ 59 months of age. Using meningococcal cases ($n = 5$) identified in the active surveillance area of Hanoi, we found that the annual incidence rate of meningococcal meningitis was 2.6/100,000 in children ≤ 59 months of age (95% CI = 0.8–8.5), with the highest rate found in infants 7–11 months of age (21.8/100,000; 95% CI = 5.0–94.4).

Burden of Hib disease. Recent population census data show that Vietnam has 8,371,377 children ≤ 59 months of age. In addition, recent Vietnam population data report that there were 1,674,275 newborn babies in 2004. Based on the national population and Hib meningitis incidence from Hanoi, there are an estimated 1,005 hospitalizations each year for Hib meningitis with at least 40 deaths associated with Hib meningitis. Of the 1,005 children hospitalized for Hib meningitis, it is estimated that at least 100 children have severe neurologic sequelae as a result of Hib meningitis. Based on the population distribution of children ≤ 59 months of age, more than half (~553) of severe Hib meningitis cases that lead to hospitalization occur among infants. Based on expected ratio of Hib pneumonia to Hib meningitis cases, we would expect 115 cases of Hib pneumonia each year in Hanoi. Thus, the estimated incidence of Hib pneumonia among children ≤ 59 months of age was 61/100,000 (95% CI = 47–79) during the study period. Nationally, we estimate that there are at least 5,107 hospitalizations for Hib pneumonia each year among children ≤ 59 months of age.

DISCUSSION

In this prospective, population-based study of acute bacterial meningitis, Hib was the most common bacterial etiology among children in Hanoi, suburban districts of Hanoi, and other northern provinces of Vietnam. *Haemophilus influenzae* type B was responsible for 56% and 49% of culture- or PCR-positive bacterial meningitis cases in Hanoi, suburban Hanoi, and rural provinces, respectively. In Hanoi, the total Hib meningitis incidence (confirmed Hib meningitis and probable Hib meningitis) was 12/100,000 in children ≤ 59 months of age. In children ≤ 59 months of age, probable bacterial meningitis produced a sizable disease burden with an annual incidence rate of 88/100,000 children. All Hib meningitis-associated deaths were among children living outside Hanoi in either suburban Hanoi districts or rural provinces (CFR = 5% among 93 children with confirmed or probable Hib meningitis).

Our study has some limitations. First, we limited standard clinical evaluations and obtained cultures from children with meningitis or sepsis and we did not systematically evaluate and enroll children with cellulitis, pneumonia, epiglottitis, septic arthritis, or osteomyelitis. Second, the approach for estimating the incidence of Hib pneumonia is based on assumptions described in the Hib Rapid Disease Burden Assessment tool developed by a WHO expert panel. In this algorithm, it is assumed that five cases of serious Hib pneumonia occur for every one case of Hib meningitis, but we recognize that there may be some variations in this ratio by country or region. Third, although considerable efforts were made to use surveillance and laboratory methods that would enhance detection of meningitis, 34% of the children in Hanoi as well as suburban and rural Hanoi who were diagnosed with confirmed Hib meningitis and probable Hib meningitis had received antibiotics prior to hospital evaluation. In a survey from a community near Hanoi, Vietnam, Larsson and others noted that 91% of children with acute respiratory infection received treatment with antibiotics.⁹ Thus, in our study, the antibiotic usage information from parents/guardians who sought care likely underestimates the actual number of children pretreated with antibiotics because parents were instructed to report treatment as unknown if they could not precisely recall the use of an antibiotic. Also, in our study, a high proportion of children with abnormal CSF consistent with suspected or probable bacterial meningitis also had negative CSF Hib cultures and PCR test results. These results are consistent with previous studies showing that CSF in patients with antibiotic treatment may show abnormal test results even after cultures and/or antigen test results have become negative.^{23,24} Finally, our study detected patients who were sick enough for referral to hospitals. Patients (including those with fever as their only symptom) having less severe disease would have been more likely to receive immediate antimicrobial therapy at commune health centers or private clinics under national guidelines based on the Integrated Management of Childhood Illness protocols for Vietnam.²⁵ This may have prevented invasive Hib disease from being detected during surveillance.

The incidence rates of Hib meningitis observed in this study were in the lower range of incidence rates for Hib meningitis found globally. This range of Hib incidence includes some of the highest observed rates from indigenous populations in the United States (409/100,000 children < 5 years of age)²⁶ and Australia (150/100,000 children < 5 years of age)²⁷ to the lowest rates observed in several Asian countries including Thailand (4/100,000 children < 5 years of age), the Republic of Korea (6/100,000), and China (Hefei, 10/100,000).^{16,28,29} The total confirmed Hib meningitis and probable Hib meningitis incidence rates found in Hanoi are similar to those found in European countries such as Austria (9/100,000 children < 5 years of age), Spain (6/100,000), and Greece (8/100,000).^{30–32}

The higher incidence rate for Hib meningitis that we observed in Hanoi compared with data from other population-based studies in Asia may be due to at least two key features of our study design.³³ First, study investigators provided laboratory training, supervision, and enhanced microbiologic diagnostic capacity in each study hospital. This strengthened capacity was demonstrated in data from the National Pediatric Hospital where confirmed Hib meningitis was

detected nine times more often during the study period compared with the two-year period prior to our surveillance study (90 cases versus 10 cases). Our study also provided standardized microbiology methods as well as commercially prepared bacterial culture media containing IsoVitaleX® (BBL Microbiology Systems, Cockeysville, MD) for *Haemophilus influenzae* growth enhancement and reagents for bacterial identification.

A second feature of our study design was the inclusion of CSF testing by PCR that increased our detection of Hib meningitis by 77% compared with the use of bacterial culture alone. The added value of PCR was underscored by the results from older children 24–59 months of age in whom 7 of the 10 total probable Hib meningitis cases who were detected by CSF *H. influenzae* PCR testing. Although PCR detected several additional cases of Hib meningitis, no additional gains in Hib meningitis case detection occurred using latex agglutination Hib antigen detection. This finding may be due to a number of factors, including the reported lower sensitivity (86%) of latex agglutination antigen detection relative to bacterial culture.^{34,35} One study suggested that Hib latex agglutination may require $\geq 1,000$ bacteria/mL of CSF to yield a positive test result.³⁶

The present study provides evidence from population-based surveillance that Hib is the most common cause of bacterial meningitis among Vietnamese children living in urban and rural settings with high incidence rates observed in children < 24 months of age. Furthermore, there are an estimated 6,111 cases of severe Hib disease among Vietnamese children every year including 1,005 cases of Hib meningitis and 5,107 due to Hib pneumonia. These data will be provided to national decision-makers to help inform decisions regarding the introduction of conjugate Hib vaccine into the routine national childhood immunization schedule. Future Hib-related activities in Vietnam will focus on the development of a national Hib reference laboratory capacity and a reporting system for identifying persons with culture-confirmed invasive Hib disease.

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