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Epidemiology and outcomes of bacterial meningitis in Mexican children: 10-year experience (1993—2003)

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Summary
Background: Acute bacterial meningitis remains an important cause of morbidity, neurologic sequelae, and mortality in children in Latin America.
Methods: We retrospectively reviewed the hospital-based medical records of children diagnosed with acute bacterial meningitis, aged 1 month to 18 years, at a large inner city referral Hospital in Mexico City, for a 10-year period (1993—2003). To characterize the epidemiology, clinical features, and outcomes of acute bacterial meningitis, we subdivided our study into two time periods: the period prior to the routine use of *Haemophilus influenzae* type b (Hib) vaccine (1993—1998) and the period after the vaccine became available (1999—2003).
Results: A total of 218 cases of acute bacterial meningitis were identified during the study period. The most frequently affected age group was that of children aged between 1 and 6 months. Hib was the most commonly isolated pathogen, found in 50% of cases. However, its incidence declined significantly after the introduction of the combined diphtheria, tetanus, pertussis, hepatitis B, and conjugated Hib (DTP—HB/Hib) pentavalent vaccine into the universal vaccination schedule for children in 1998. *Streptococcus pneumoniae* followed as the second most commonly isolated bacterial pathogen. *Neisseria meningitidis* was isolated in only a few cases, confirming the historically low incidence of this pathogen in Mexico. Identified risk factors for death were found to include the presence of septic shock and intracranial hypertension, but were not attributable to any particular bacterial pathogen.
Conclusions: In our hospital, acute bacterial meningitis remains a severe disease with important sequelae and mortality. The incidence of Hib meningitis cases has declined since the introduction of the Hib vaccine. However, *S. pneumoniae* persists as an important cause of bacterial meningitis, highlighting the need for the implementation of vaccination policies against this pathogen.

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Introduction

Acute bacterial meningitis (BM) constitutes a significant global public health problem. Worldwide, it has been estimated that 1–2 million cases of BM occur annually.[1–4] The problem is more significant in resource-poor countries including those in some regions of Sub-Saharan Africa, Southeast Asia, and Latin America.[5,6]

The initial treatment approach to a child with suspected BM depends on early recognition of the meningitis syndrome, rapid diagnostic evaluation, and early antimicrobial and adjunctive therapy.[7–9] Once suspected, blood cultures, cranial computed tomography (CT scan) when indicated, and lumbar puncture to obtain cerebrospinal fluid (CSF) for examination is considered the standard of care. Management algorithms for BM in children include the initiation of dexamethasone plus empirical antimicrobial therapy.[10–12] However, BM remains a neurological and infectious disease emergency with a high mortality rate, despite advances in diagnostic techniques, antimicrobial chemotherapy, and adjuvant use of anti-inflammatory agents.[10] Sequelae, such as hearing loss, blindness, seizure disorders, hydrocephalus, developmental delay, and motor deficit occur even with the rapid institution of adequate therapy.[11,12] Indeed, BM can often be rapidly progressive, resulting in permanent sequelae in a relatively short period of time.[11] This is the reason why vaccination strategies to prevent the invasive bacterial disease of organisms capable of causing meningitis, such as *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*, are considered public health priorities.[13–19]While there are six serotypes of *Haemophilus influenzae* known to cause disease, type b is responsible for over 90% of BM in children.[5,16,18] Indeed, prior to the widespread use of conjugate vaccines against Hib, this organism was the most common cause of severe invasive infections in children, resulting in approximately 300 000 to 500 000 deaths annually worldwide. In the USA, with the advent of the Hib conjugate vaccine, Hib cases in children under 5 years of age declined by 99% from 1986 to 1995; this decline has also occurred in other resource-rich countries. This beneficial shift in the epidemiology of BM prompted the World Health Organization (WHO) to recommend that the Hib vaccine should be included in routine infant immunization programs for all children, as appropriate to national capacities and priorities.[5,15]With these dynamic changes in the epidemiology of BM in many areas of the world resulting in decreasing numbers of cases due to Hib, *S. pneumoniae* and *Neisseria meningitidis* have become the predominant causes of meningitis in children aged 1 month and older.[13] In fact, recent WHO estimates have suggested that approximately 1.6 million people die of pneumococcal disease every year, including 0.7–1 million children under 5 years of age, most of whom are from resource-poor countries.[11,13] This is the rationale behind the WHO and other leading public health agencies promoting the introduction of a conjugate pneumococcal vaccine into routine childhood immunization programs. In addition, countries are encouraged to conduct appropriate surveillance for pneumococcal disease to establish the baseline and monitor the impact of vaccination.[13]

In Mexico, BM remains an important cause of morbidity, neurologic sequelae, and mortality. However, there are limited epidemiologic and microbiologic data on this disease in children and adults.[7] In particular, there are limited data evaluating the impact of routine childhood vaccination against Hib, which was initiated in 1998. Therefore, we conducted this comprehensive, hospital-based retrospective study to describe the epidemiology, clinical features, and outcomes for Mexican children with BM aged 1 month and older, seen at the Hospital Infantil de México Federico Gómez, a major national pediatric referral center.

Methods

We retrospectively reviewed the hospital-based medical records of children diagnosed with acute BM, aged 1 month to 18 years (beyond the neonatal period), evaluated at the Hospital Infantil de México Federico Gómez (HIMFG), for a 10-year period (1993–2003). Founded in 1943, HIMFG is the oldest of Mexico's 12 National Institutes of Health, and is the leading national referral pediatric institution. The study period was subdivided into the period prior to the introduction of the conjugate Hib vaccine (1993–1998) and the period after its introduction (1999–2003).

We included 218 cases of BM based on the presence of clinical symptoms consistent with a meningitis syndrome and the following ancillary laboratory criteria: (1) positive bacterial culture in CSF; (2) CSF pleocytosis $\geq 5 \times 10^6$/l with a negative CSF culture plus one of the following: positive blood culture, positive CSF antigen test, positive Gram stain of the CSF, or a positive throat culture for *N. meningitidis* in patients with a purpuric rash; (3) CSF pleocytosis $\geq 5 \times 10^6$/l with a negative CSF culture, negative blood or throat culture, or negative co-agglutination test. We excluded patients with tuberculous meningitis, immunocompromised patients, and cases of nosocomial meningitis. Demographic data (including age and gender) and data on symptoms at presentation, physical examination on admission, previous vaccination schedule, laboratory results, CSF examination, CT scan results, and treatment and outcomes were collected using a standarized data collection form. Death due to BM was classified as meningitis-related if death was secondary to meningitis or any of its complications as recorded by the medical record and/or autopsy data.

Statistical analysis was carried out by proportion comparisons using the Mantel–Haenszel Chi-square test or Fisher's exact test as appropriate. The Wilcoxon rank sum test was used to compare medians of continuous variables when the two-sample *t*-test was not appropriate. All tests were two-sided and a *p*-value of ≤ 0.05 was considered significant. To determine the association between potential risk factors and death due to BM, logistic regression was used to estimate odds ratios (OR) and their 95% confidence intervals (CI). Those variables that in bivariate analysis would have achieved a significance level of 0.05 were included in the model as main effects, along with effect modifiers and confounders of the association between death and shock (our main outcome of interest). A hierarchical backwards elimination strategy was performed, with proper evaluation of interaction and confounding. The goodness of fit of the model was assessed using the Hosmer and Lemeshow Chi-square test. Assessment of collinearity was done by analyzing the condition indices and the respective variance decomposition proportions (VDPs). All statistical analyses were performed using SAS software (version 8.2, SAS Institute, Cary,

NC, USA). The study was approved by the research committee of the Hospital Infantil de México Federico Gómez.

Results

A total of 218 cases met the inclusion criteria for our study. Of these, 131 were male and 87 were female. When we divided the number of cases by age group, we identified 85 cases in infants between 1 and 6 months of age, 56 cases in those between 6 months and 12 months of age, 61 cases in children aged between 1 and 5 years, and 16 cases in children older than 5 years.

During the initial study period (1993–1998), there were 159 (73%) children with BM, while there were 59 (27%) cases during the second period (1999–2003) (Table 1). Overall, Hib was the most common pathogen (by CSF culture and/or co-agglutination testing in CSF), causing 50% (109/218) of the cases; *S. pneumoniae* was isolated in 31% (67/218) of cases and *N. meningitidis* in only 2% (4/218) during the two study periods. Other pathogens, particularly Gram-negative bacteria, were found in 6% (14/218) of cases. In 11% (24/218) of cases, no pathogen was identified but the patient met the clinical criteria for BM according to our study inclusion criteria.

With regards to the etiological cause of BM according to age group, we found that pneumococcal disease occurred in all age groups, but was more frequent in children $\geq$1 year of age. Cases of BM due to Hib occurred equally in all age groups; however we noted a trend for it to occur more frequently in children aged between 6 months and 3 years in the pre-vaccination period. In the period following the availability of the Hib vaccine, we noted that 6/8 (75%) Hib cases arose in children aged 4 years and over who had not previously been vaccinated. However, 2/8 (25%) cases occurred in children who had received at least two doses of Hib vaccine at the time BM was diagnosed (in the group of children aged between 6 and 12 months).

When we analyzed microbiological causes by study period (1993–1998 vs. 1999–2003), we identified that prior to the introduction of the Hib vaccine (1993–1998 period) the most frequent pathogen was Hib in 64% of cases; *S. pneumoniae* occurred in 22%, and *N. meningitidis* in 0.5% of cases. Other pathogens were found in 5.5% of cases and no bacterial pathogen was found in 8%.

The number of Hib meningitis cases during the 1999–2003 study period was eight (14%); *S. pneumoniae* was found in 54%, *N. meningitidis* in 5%, other pathogens in 8%, and no pathogen in 19% of cases (Table 1). Therefore, the incidence of Hib decreased from 64% to 14% ($p < 0.001$) following the introduction of the Hib vaccine, in absolute numbers and also by rates when adjusted to the number of admissions per year (data not shown). Cases of *S. pneumoniae* were not significantly different between the two periods.

With regards to the clinical manifestations of BM, 45 of the 218 (21%) patients presented at admission with the classic clinical triad of fever, altered mental status, and nuchal rigidity. The most common clinical features were fever in 92%, vomiting in 55%, irritability in 54%, and focal neurologic findings in 36% of patients. Fever was highly prevalent in all age groups. Focal neurologic findings were more commonly seen in children over 5 years of age ($p = 0.0006$). A history of seizure disorder occurring during hospitalization was present in 54% of our patients, and it was most commonly seen in children aged 6 to 12 months ($p = 0.0169$). In addition, the findings of neck stiffness and meningismus increased with increasing age, and these two signs were more frequent in children older than 5 years of age ($p = 0.0002$ and $p < 0.0001$, respectively). A bulging fontanelle was identified in 27% of children aged less than 6 months ($p < 0.0001$) (Table 2).

With respect to laboratory values, almost two thirds of patients with BM developed anemia during the course of their hospitalization. In addition, leukocytosis was present in 70% of patients. However, only 9% developed thrombocytopenia and most of these cases occurred during the course of septic shock episodes. Hyponatremia was found in 13% of patients during the course of their hospitalization. Blood cultures were positive in 6% of a total of 203 patients from whom blood cultures were obtained. Interestingly, of the 106 cases of Hib-related meningitis, 83% had anemia compared to only between 11% and 20% for other bacterial pathogens ($p = 0.003$).

Lumbar puncture was performed in 201 of the 218 BM cases; this procedure was contraindicated in the remaining cases due to a high risk of brain herniation. Cerebrospinal fluid pleocytosis was a common finding, identified in 96% of our patients. The CSF protein level was elevated in 95% of cases, and the glucose level was considered low in 78% of

Table 1 Number of cases of acute bacterial meningitis according to study period (1993–1998 and 1999–2003) and bacterial pathogen, among 218 pediatric patients with acute bacterial meningitis (Hospital Infantil de México Federico Gómez, 1993–2003)

Bacterial pathogen	Total No. cases (%)[a]	Period before the introduction of Hib vaccine, 1993–1998 No. cases (%)	Period after the introduction of Hib vaccine, 1999–2003 No. cases (%)
All pathogens	218 (100%)	159 (100%)	59 (100%)
Haemophilus influenzae type b	109 (50%)	101 (64%)	8 (14%)[b]
Streptococcus pneumoniae	67 (31%)	35 (22%)	32 (54%)
Neisseria meningitidis	4 (2%)	1 (0.5%)	3 (5%)
Other pathogen	14 (6%)	9 (5.5%)	5 (8%)
No pathogen[c]	24 (11%)	13 (8%)	11 (19%)

[a] Absolute numbers are shown in this table. Rates not shown.
[b] Six out of eight (75%) of the cases were in children aged 4 years and over who had not received previous Hib vaccination.
[c] Clinical cases of acute bacterial meningitis (by signs, symptoms, and CSF pleocytosis, but negative co-agglutination, CSF cultures, or blood cultures).

Table 2 Prevalence of clinical manifestations by age group among 218 pediatric patients with acute bacterial meningitis (Hospital Infantil de México Federico Gómez, 1993—2003)

Clinical manifestations ($N = 218$)	1—6 months	6—12 months	1—5 years	>5 years	Chi-square	*p*-Value	Fisher's exact test
Fever	89.4	92.8	98.3	81.25	NA		0.0498
Seizure disorder	54.1	75.4	40.9	25	5.7	0.0169	
Irritability	64.71	46.4	55.7	18.7	7.14	0.0075	
Altered mentation	23.5	35.7	49.1	56.2	12.94	0.0003	
Focal neurologic signs (sensory or motor deficits)	28.2	30.3	40.9	81.2	11.93	0.0006	
Vomiting	44.7	58.9	65.5	62.5	5.926	0.0149	
Meningeal signs	27.0	41.0	50.8	75.0	16.22	<0.0001	
Neck stiffness	48.2	51.7	68.8	93.75	13.54	0.0002	
Feeding avoidance	43.5	46.4	50.8	31.2	0.0026	0.9595	
Prostration	12.9	8.93	32.7	31.2	9.51	0.0020	
Headache	2.35	8.93	24.5	75.0	46.09	<0.0001	
Bulging fontanelle	27.06	17.8	4.9	0.00	15.65	<0.0001	

cases. The classic triad of CSF pleocytosis, increased total protein, and a low glucose level was present in 78% of cases. Only in 50% of patients was the Gram stain positive. Co-agglutination was clinically useful in confirming a diagnosis in 56% of cases when CSF culture was reported as negative.

Most patients in our series, 156 of the 218 (71%), underwent CT cranial imaging at some point during their hospital stay. Of these, 29% had findings that were consistent with cerebral edema, 43% manifested subdural effusion, 11% had a brain abscess, 14% had a cerebral infarct, 11% had hydrocephalus, and 13% had findings consistent with brain atrophy. The presence of headache ($p = 0.0278$), seizure disorder ($p = 0.0001$), and fever ($p = 0.021$) were independent risk factors for developing a hygroma in cranial CT imaging, while having a bulging fontanelle was a risk factor for cerebral edema ($p = 0.0031$) (Table 3).

A total of 36 (16%) patients died as a result of BM and its complications. In a multivariable logistic regression analysis, septic shock and intracranial hypertension were identified as independent risk factors for death. However, we did not find any statistically significant difference between bacterial pathogens for the risk of death (Table 4). The most common complication identified in our series was seizure disorder in 37% of patients, followed by subdural empyema in 26%, and shock in 24% of cases. A full recovery occurred in 82 (38%) patients. Of the remaining 100 (46%) patients who survived, the most common neurologic sequelae were persistent seizure disorder, occurring in 37%, followed by hearing loss (32%).

Discussion

Acute BM is a significant cause of morbidity and mortality in children in Latin America across all age groups. However, neurologic sequelae and mortality seem particularly high in the pediatric population.[18—21] The results of this study confirm that the clinical features and outcomes in children with BM are similar to those reported in previous studies from Latin America and other countries.[22,23] In addition, we found that anemia was most frequently associated with Hib meningitis, as has been reported in other series.[5,8,18] Regarding clinical outcomes, we identified that septic shock and intracranial hypertension were independent risk factors for death, but were unable to identify an increased risk attributable to any particular bacterial pathogen. Furthermore, we identified that among survivors there was a high rate of permanent neurologic sequelae including seizure disorder and/or hearing loss, confirming that these complications continue to occur despite the institution of adequate therapy in children.[5,6,11] In fact, the results of our study confirm that BM continues to be a medical, neurological, and sometimes neurosurgical emergency that requires a multidisciplinary approach.[10]

With regards to the specific complications that could be attributed to specific bacterial pathogens, it has been estimated that most of the mortality due to Hib in Latin America, and worldwide, occurs in children aged <5 years.[5,8,12,14,16—18] The long-term complications of Hib-associated BM, such as hearing loss, have been used as standard indicators for comparing Hib disease burden between and within countries.[5,16]

Many factors can affect the quality of population-based studies of Hib meningitis, including patient access to and utilization of medical services, pre-treatment of patients with antibiotics, and quality of laboratory diagnostic methods. We found that at our institution, the occurrence of Hib meningitis has decreased over time, while that of *S. pneumoniae* has remained constant.[16] The importance of preventive strategies such as the use of Hib and pneumococcal conjugate vaccination is highlighted by the fact that despite the effectiveness of current antibiotic regimens in clearing bacteria from the CSF, BM continues to cause substantial morbidity and mortality worldwide.[5,16] This may be due to the underlying pathogenesis of the disease, given the fact that much of the damage from this infection is believed to result from cytokines and the ensuing inflammatory infiltration within the CSF.[6,23,24]In Latin America, in 1994, Uruguay became the first country to include the Hib vaccine in their routine immunization program. Following the lead of Uruguay, Chile also introduced Hib vaccination, since many clinical trials to evaluate the safety, immunogenicity, and efficacy of the Hib vaccine were conducted in this country.[5] It

Table 3 Prevalence of cranial CT findings in association with clinical manifestations among 218 pediatric patients with acute bacterial meningitis (Hospital Infantil de México Federico Gómez, 1993–2003)

		Cerebral edema				Hygroma		
Clinical manifestations	No.	Prevalence (%)	Chi-square	*p*-Value	Fisher's	Prevalence (%)	Chi-square	*p*-Value
Fever								
Yes	201	19.40	NA		0.1269	32.84	5.32	0.021
No	17	32.29				5.88		
Seizures								
Yes	117	24.79	2.635	0.1045		41.88	14.67	0.0001
No	101	15.84				17.82		
Irritability								
Yes	118	22.88	0.784	0.376		34.75	1.93	0.1641
No	100	18.0				26.00		
Altered mentation								
Yes	79	25.32	1.645	0.1996		26.58	0.999	0.3177
No	139	17.99				33.09		
Focal neurologic signs								
Yes	79	22.78	0.346	0.5566		29.11	0.152	0.6966
No	139	19.42				31.65		
Vomiting								
Yes	121	23.97	1.827	0.1765		31.40	0.057	0.8109
No	97	16.49				29.90		
Meningeal signs								
Yes	82	22.47	0.306	0.5802		25.84	1.683	0.1946
No	129	19.38				34.11		
Neck stiffness								
Yes	127	21.26	0.071	0.7906		28.35	0.811	0.3679
No	91	19.78				34.07		
Feeding avoidance								
Yes	99	23.23	0.739	0.3899		32.32	0.214	0.6435
No	119	18.49				29.41		
Prostration								
Yes	41	21.95	0.053	0.8186		24.39	0.950	0.3297
No	117	20.34				32.20		
Headache								
Yes	34	17.65	0.220	0.6394		14.71	4.839	0.0278
No	184	21.20				33.70		
Bulging fontanelle								
Yes	36	38.89	8.724	0.0031		33.33	0.136	0.712
No	182	1703				30.22		

soon became clear that BM due to Hib had declined significantly in these two countries following the introduction of the Hib vaccine. By 1998, with the support of the Pan-American Health Organization (PAHO) revolving fund for joint purchases of vaccine, more than 15 other countries in Latin America and the Caribbean integrated the Hib vaccine into their routine immunization programs.[5,15,22]

Subsequent studies from Chile and Uruguay have demonstrated the importance of evaluating the epidemiology and burden of disease associated with BM in the region after the introduction of Hib vaccination.[5,16] In 1999, Mexico was the first country to introduce Hib vaccination using the pentavalent combination vaccine in a three-dose schedule without a booster.[25,26] The decision to use this combination vaccine was reached after documenting that high anti-PRP antibody concentrations were reached 1 month after vaccination, with 100% of seroprotected subjects in the combined vaccination group (antibody concentrations $\geq$0.15 μg/ml) against 99.4% in the separate injection vaccination group.[27] By the end of that year the DTP–HB/Hib vaccine had been distributed to 87% of Mexican children under 1 year of age.[25,26] By the end of 1999, more than 800 000 doses of pentavalent vaccine had been administered in Mexico.[26] It is noteworthy that in the study period following the introduction of the Hib combination vaccine, 6/8 (75%) of BM cases were in children who had not received previous Hib vaccination because they were

Table 4 Adjusted odds ratios for death among 218 pediatric patients with acute bacterial meningitis (Hospital Infantil de México Federico Gómez, 1993–2003)

Risk factors for death	OR	95% CI	*p*-Value
Shock			
Yes	25.56	9.19–71.10	<0.001
No	1.00		
Intracranial hypertension			
Yes	6.63	2.25–19.55	0.001
No	1.00		
Bacterial pathogen			
Haemophilus influenzae type b	0.35	0.11–1.08	0.068
Streptococcus pneumoniae	1.08	0.34–3.47	0.896
Other pathogen	1.00		

OR, odds ratio; CI, confidence interval.

born prior to the initiation of universal vaccination, and the two vaccinated infants had not yet received the third dose. Recent serological evidence has shown that the pentavalent vaccination in a well defined cohort of children between the ages of 7 and 93 months, demonstrated serum IgG concentrations >0.15 μg/ml.[28] These serological titers have been shown to confer protection against Hib invasive disease.[28]

Therefore, the purpose of our study was to define the leading pathogens causing community-acquired meningitis (beyond the neonatal period) in a pediatric population in a major referral pediatric hospital in Mexico City. The causative organisms found in a particular region vary with the patient's age and general health, and with the immunization status of the community. The results of our study provide some evidence that with the implementation of routine Hib vaccination in children in Mexico since 1998, the number of cases of BM due to Hib in children has decreased. With the availability of routine Hib pentavalent vaccination, cases of BM due to Hib mostly occurred among the cohort of older unvaccinated children, with only two cases occurring in previously vaccinated children in their first year of life.

Among different pediatric series, the most important causative organisms of BM are *S. pneumoniae*, *N. meningitidis*, and Hib.[5–7,23,24] *S. pneumoniae* continues as a persistent pathogen causing BM.[13,29] Universal vaccination of children <2 years of age with a conjugate pneumococcal vaccine has demonstrated three important benefits at a population level: (1) a substantial decrease in invasive disease and otitis media among vaccinees; (2) herd immunity protection in adults by decreasing the rates of invasive disease by 67% at a population level; and (3) a decrease in the circulation of antibiotic-resistant pneumococcal serotypes.[13,29] The impact of *S. pneumoniae* vaccination in children may prove to be an effective strategy to prevent the occurrence of BM. In Mexico, CONAVA, the National Immunization Council, has started to routinely vaccinate some underserved pediatric groups in some areas of the country. The impact of this program is currently under scrutiny.

Approximately 500 million people worldwide are carriers of *N. meningitidis* in their nasopharynx, but only some develop meningococcemia or meningitis syndrome.[30] Most of the burden of meningococcal meningitis occurs in Sub-Saharan Africa. In Latin America, most of the outbreaks of *N. meningitidis* have been recorded in the Southern Cone countries and in Cuba.[7,30] In Mexico, the last confirmed epidemic of *N. meningitidis* was documented in the central part of the country in 1945. Since then, the number of registered cases has persisted at a low level despite substantial increases in population density in areas of major population concentration. In our series, we confirmed the registered historically low incidence of BM due to *N. meningitidis* in children in our country. Indeed, these rates of BM due to *N. meningitidis* in Mexico have recently been confirmed by the current prospective national epidemiologic surveillance system.[7]

As our study was retrospective and hospital-based, underestimating the actual number of cases is a potential bias. We attempted to overcome this limitation by collecting data on every patient seen at our institution using multiple overlapping hospital databases in order to reduce the likelihood of omitting patients. Hospital-based epidemiologic data have been suggested to provide relevant data on vaccine effectiveness against Hib.[18] In addition, while this was a single center study, it is relevant to point out that our institution is a regional referral public hospital for a substantial area of Mexico City and neighboring Mexican states. In Mexico, the vast majority of children with BM are managed at referral public hospitals such as ours. In addition, by reviewing only the community-acquired cases of acute BM, and excluding neonatal and nosocomial meningitis cases, we attempted to indirectly evaluate what is really occurring in the larger community.[6] Since our group has previously demonstrated the impact of routine pediatric BCG vaccination as a means of reducing TB meningitis at a population-based level,[31] we also excluded cases of TB meningitis from this analysis.

In summary, our hospital-based retrospective analysis, albeit with some limitations, demonstrates that BM is a severe disease that produces significant sequelae and mortality. Since our institution is a referral center for many regions of the country, we believe that our data may be used as a surrogate marker of what is occurring in the larger community. Given the significant morbidity and mortality associated with BM despite the availability of medical therapy, we believe that most efforts should focus on preventing cases through routine vaccination programs. We conclude that our data suggest that the incidence of Hib meningitis has declined following the introduction of the Hib vaccine in our pediatric population, and *S. pneumoniae* meningitis continues to be a persistent pathogen. These data highlight the need for the implementation or the broadening of coverage for already existing vaccination programs in children against *S. pneumoniae* to prevent BM among vaccinees and to produce indirect herd immunity for other age groups.

Conflict of interest: No conflict of interest to declare.

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