Childhood Meningitis in Kuwait: Epidemiology of Etiologic Agents and the Need for Pneumococcal Disease Prevention

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Key Words

Meningitis • *Streptococcus pneumoniae* • *Haemophilus influenzae* • Type B *Neisseria meningitidis* • Heptavalent pneumococcal vaccine

Abstract

Objective: To investigate the epidemiology of the etiologic agents causing bacterial meningitis in Kuwait. **Subjects and Methods:** This is a retrospective analysis of the medical records of children 1 month to 12 years old who had cerebrospinal fluid (CSF) findings consistent with meningitis. Patients were identified from the records of the Departments of Microbiology and Communicable Diseases in six regional hospitals during 2001. They were divided into bacterial and viral infective groups. **Results:** Ninety children had CSF findings consistent with meningitis, 44 bacterial (23 culture proven, 21 probable) and 46 viral. *Streptococcus pneumoniae* and *Neisseria meningitidis* were the most frequently isolated organisms (44 and 30%, respectively). A 2-month-old child had *Haemophilus influenzae* and was the only mortality of this series. *S. pneumoniae* is the leading bacterial agent causing meningitis in children under the age of 1 year; 61% had bacterial meningitis compared to 37% with viral meningitis. Se-

quelae were encountered in 23% of bacterial cases. **Conclusion:** The results indicate that *S. pneumoniae* is the leading bacterial agent causing meningitis, indicating a need for the introduction of polyvalent pneumococcal vaccine.

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Introduction

Despite improvements in its treatment, bacterial meningitis continues to be associated with high mortality and morbidity [1]. The great majority of cases occur under the age of 5 years, and infants are particularly vulnerable [2]. During the past two decades significant changes have been observed in the epidemiology of bacterial meningitis following the introduction of *Haemophilus influenzae* type b (Hib) vaccine, with pneumococcus replacing *H. influenzae* as the leading cause of bacterial meningitis [3]. Invasive *H. influenzae* disease had been virtually eliminated before the turn of the century in many Western countries [4]. The introduction of nationwide Hib vaccination in Kuwait lagged for several years, hence *H. influenzae* continued to be the leading cause of bacterial meningitis throughout the last decade of the 20th century

[5–7]. Similar data have been reported from neighboring Saudi Arabia, where two thirds of cases were caused by *H. influenzae* [8].

Pneumococcal meningitis is associated with the highest mortality and morbidity [3]. This issue is further complicated by the increasing prevalence of antibiotic-resistant pneumococci over the past three decades [1]. A 7-valent pneumococcal polysaccharide-protein conjugate vaccine (Prevenar) has recently been licensed for use in North America, with initial efficacy of 97% [9]. After the eradication of *H. influenzae*, pneumococcal invasive disease is the next to go [4].

In this report we investigated the epidemiology of the bacterial agents causing meningitis in Kuwait after the introduction of Hib vaccine and discuss the need for the introduction of pneumococcal vaccine in the vaccination schedule in Kuwait.

Subjects and Methods

This retrospective nationwide study analyzed all cases of meningitis occurring in children 1 month to 12 years of age, who were admitted to one of the six regional hospitals in Kuwait, between January 1 and December 31, 2001. Patients were identified from the registers of the Departments of Microbiology and the offices of Communicable Diseases.

The inclusion criteria for the diagnosis and classification of meningitis were adopted from Fortnum and Davis [1] and Brook [10]. Bacterial meningitis was considered confirmed if the organism grew or was seen in the CSF, or if the blood culture was positive and CSF culture was negative but showed all of the following CSF disturbances: >10 white cells/ mm^3 , protein >0.6 g/l, glucose <2.2 mmol/l or $<40\%$ of blood glucose and $>60\%$ of white cells are polymorphs. A patient was considered to have 'probable' bacterial meningitis in CSF culture-negative cases if the CSF cell count was $\geq 100/\text{m}^3$ with $>60\%$ polymorphs with at least one of the following: positive blood culture, CSF protein >0.6 g/l, CSF glucose <2.2 mmol/l or below 40% of blood glucose. Those patients were treated with third-generation cephalosporin (cefotaxime or ceftriaxone) and dexamethasone given at a dose of 0.15 mg/kg every 6 h for the initial 48 h.

Children who did not fulfill these criteria but had evidence of CSF disturbance (white cells $>10/\text{mm}^3$) were considered to have viral meningitis. Children who were clinically suspected of having meningitis were treated empirically and were excluded from the study due to parental refusal of lumbar puncture.

Only cases with abnormal CSF findings were recorded as meningitis in the Departments of Communicable Disease and Microbiology. The clinical course of the disease, the outcome and short-term residual problems for each child were obtained from the medical records.

Table 1. Age distribution of meningitis in children up to the age of 12 years

Age group	Meningitis		
	bacterial n (%)	viral n (%)	total n (%)
1 month–1 year	27 (61)	17 (37)	44 (49)
1–5 years	3 (7)	8 (17)	11 (12)
5–12 years	14 (32)	21 (46)	35 (39)
Total	44 (100)	46 (100)	90 (100)

Table 2. Causative organisms identified in 23 children with bacterial meningitis

Organism	Children n (%)
<i>S. pneumoniae</i>	10 (44)
<i>N. meningitidis</i>	7 (30)
Group B streptococcus	2 (9)
<i>Mycobacterium tuberculosis</i>	2 (9)
<i>H. influenzae</i>	1 (4)
<i>Brucella</i>	1 (4)
Total	23 (100)

Results

There were 90 patients with CSF findings compatible with meningitis: 44 bacterial and 46 viral (table 1). Of the 44 bacterial cases, the organism was identified in 23, and the remaining 21 cases had a clinical picture and CSF findings compatible with bacterial meningitis according to the inclusion criteria. Sixty-two (69%) children were Kuwaiti nationals and 28 (31%) expatriates. This ratio is similar to that of admissions: 70 and 30%, respectively.

Sixty-one percent of the children with bacterial meningitis were under the age of 1 year, compared to 37% of cases with viral meningitis (table 1). The age distribution of probable cases of bacterial meningitis is similar to that of confirmed cases: 14 of the 23 proven cases (61%) and 13 of the 21 probable cases (62%) were under the age of 1 year. The corresponding percentage for children 1–5 years of age were 9% (confirmed) and 5% (probable), ages 5–12 years were 31% (confirmed) and 32% (probable).

The causative organism was pneumococcus in 44% and meningococcus in 30% of confirmed cases (table 2).

Table 3. Age distribution of different bacteria isolated from 23 children with bacterial meningitis

Organism	Age group			
	1 month–1 year n (%)	1–5 years n (%)	5–12 years n (%)	subtotal n (%)
<i>S. pneumoniae</i>	8 (80)	0 (0)	2 (20)	10 (100)
<i>N. meningitidis</i>	3 (43)	0 (0)	4 (57)	7 (100)
<i>H. influenzae</i>	1 (100)	0 (0)	0 (0)	1 (100)
Other organisms	2 (40)	2 (40)	1 (20)	5 (100)
Total	14 (61)	2 (9)	7 (30)	23 (100)

One child, a 2-month-old girl who had *H. influenzae*, did not receive the Hib vaccine. Other organisms were responsible for the remaining 5 cases (22%).

Eight of the 10 (80%) pneumococcal cases were encountered in children under the age of 1 year (table 3). Of the 8, 4 (50%) were in infants 1–5 months old. This age group had the highest frequency of bacterial meningitis: 4 pneumococcal, 5 other bacterial causes and 12 probable cases, a sum of 21 cases, which forms 48% of all cases of bacterial meningitis. Nine of these cases were encountered in 1- to 2-month-old infants, and 8 in 2- to 3-month-old infants. The only death in this series was the 2-month-old girl with *H. influenzae* meningitis.

The 2 children with tuberculous meningitis suffered severe spastic quadriplegia and are in a persistent vegetative state. Of the 6 children with pneumococcal meningitis (60%), 3 developed seizures, and 1 each hemiplegia, hydrocephalus and deafness, respectively. The child with brucella suffered from paraplegia. Only 1 child with culture-negative bacterial meningitis was left with abducens nerve palsy. There were no sequelae in meningococcal or viral cases.

Discussion

The small number of patients reported in this study (table 1) is primarily due to parental refusal to permit performance of lumbar puncture in their children. Clinically suspected cases, with no CSF examination, were usually empirically treated with a third-generation cephalosporin and were not recorded in the register as meningitis. Hence, a figure of 90 cases of meningitis from six regional hospitals with over 25,000 pediatric admissions annually is most probably an underestimate and the actual size of this problem is therefore difficult to determine. Despite this shortcoming, our study highlights

some important epidemiologic aspects of the disease, namely, mortality and morbidity figures.

A mortality rate of 2.2% for bacterial meningitis (1 of 44 cases) is similar to that of three previous large studies from Kuwait [5–7], where the reported mortality rates were 6 and 9% in two studies during the 1980s [5, 6] and 2.2% in the 1990s [7]. Our finding is also similar to mortality figures recently reported from industrialized countries [3, 11]. The mortality rate in developing countries is however worse, as exemplified by the mortality rate in Gambia of 17 and 37% in *H. influenzae* and pneumococcal meningitis, respectively [12]. A recent study from India reported a 50% case fatality rate for pneumococcal meningitis and an overall 25% mortality for bacterial meningitis [13].

Of the 44 bacterial meningitis patients, 10 (23%) suffered neurologic sequelae; 6 of them had pneumococcal meningitis similar to previous reports from Kuwait [5–7] and elsewhere [8, 11]. *Streptococcus pneumoniae* meningitis is associated with the highest morbidity ratios [3, 8].

Comparing our findings with previous studies in Kuwait [5–7], there is a change in the causative agents of childhood meningitis as shown in table 4. *H. influenzae* was responsible for half of the cases prior to the introduction of routine Hib vaccination in Kuwait. A few years later, pneumococcus replaced *H. influenzae* as the leading agent in causing the disease (table 4) or its sequelae. Although this change lagged by several years from that in developed countries [3, 4], it is welcome.

Although there was no mortality among children with pneumococcal meningitis, the morbidity of 60% was high. Furthermore, 80% of cases affected were infants under the age of 1 year.

The studies by Shaltout et al. [5] and Zaki et al. [6] were done in three hospitals while that by Qabazard et al. [7] was performed only in one hospital following the intro-

Table 4. Changes in the epidemiology of bacterial meningitis over two decades in six regional hospitals in Kuwait

Organism	Author [ref.], years of study			
	Shaltout et al. [5] 1981–1987	Zaki et al. [6] 1981–1987	Qabazard et al. [7] 1992–1998	Present series 2001
<i>H. influenzae</i>	42 (54%)	49 (45%)	20 (36%)	1 (4%)
<i>S. pneumoniae</i>	21 (27%)	23 (21%)	14 (25%)	10 (44%)
<i>N. meningitidis</i>	3 (4%)	14 (12%)	6 (11%)	7 (30%)
Other bacteria	12 (15%)	24 (22%)	16 (28%)	5 (22%)
Total	78 (100%)	110 (100%)	56 (100%)	23 (100%)

duction of Hib vaccination. The present study in six hospitals, in which bacterial meningitis occurred only in one 2-month-old child that had not been vaccinated, indicates the effectiveness of the vaccination program.

S. pneumoniae is now the leading causative bacterial agent for meningitis. It therefore seems that there is a need to introduce a vaccination program that can protect the children from this bacterial infection, an approach that has been effective in Western countries [14–16].

The virtual elimination of invasive *H. influenzae* disease in developed countries [3, 8] and the resurgence of pneumococcus as the main causative agent in meningitis, with the highest mortality and morbidity rates, as well as increasing prevalence of antibiotic-resistant strains [3, 9] have all provided impetus for the development of a pneumococcal vaccine that is effective in the prevention of invasive pneumococcal disease in infants and young children [3, 4, 9]. The 23-valent vaccine (PPV 23) is not effective under the age of 2 years [9], where most cases of invasive disease including meningitis are encountered.

A 7-valent pneumococcal polysaccharide-conjugate vaccine (Prevenar) has recently been licensed for use in North America [3, 9, 14]. An efficacy rate of 97% has been reported [3] and a significant reduction in otitis media has been observed [9]. Hence, there are reasons to be op-

timistic that pneumococcal invasive disease [4] might also eventually be eliminated. It is expected that by 2010, most children in industrialized countries between birth and 5 years of age will have received conjugate vaccines during infancy [14]. Despite concerns on cost-effectiveness [15], we recommended Prevenar for routine immunization in Kuwait as in the USA and other Western countries [16].

Conclusion

Currently pneumococcus is the leading cause of meningitis in children in Kuwait following the administration of Hib vaccination. The disease primarily affects infants and is associated with high morbidity. We therefore recommend the inclusion of the recently developed conjugate pneumococcal vaccine in our immunization program to prevent this disease in our infants and children.

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References

- Fortnum HM, Davis AC: Epidemiology of bacterial meningitis. *Arch Dis Child* 1993; 68:763–767.
- Parke JC Jr, Schneerson R, Robbin JB: The attack rate, age incidence, racial distribution and case fatality rate of *Hemophilus influenzae*, type b meningitis in Mecklenber County, North Carolina. *J Pediatr* 1972;81: 765–769.
- Dawson KG, Emerson JC, Burns JL: Fifteen years of experience with bacterial meningitis. *Pediatr Infect Dis J* 1999;18:816–822.
- Rappuoli R: Conjugates and reverse vaccinology to eliminate bacterial meningitis. *Vaccine* 2001;19:2319–2322.
- Shaltout AA, Auger LT, Awadallah NB, Hijazi Z, Johnny M, Hajj KE, Kandil H: Morbidity and mortality of bacterial meningitis in Arab children. *J Trop Med Hyg* 1989;92: 402–406.
- Zaki M, Daoud AS, El Saleh Q, West PWJ: Childhood bacterial meningitis in Kuwait. *J Trop Med Hyg* 1990;93:7–11.

- 7 Qabazard Z, Ben-Nakhil HA, Badawi M, Haque E, Eliwa MS, Sharma PN: Childhood bacterial meningitis in Kuwait, incidence and etiology: a seven-year review of pediatric hospital admissions. *K M J* 2000;32:132–135.
- 8 Laditan AAO, Odame I, Ogundipe O: Childhood meningitis at King Fahad Hospital, Hofuf, Saudi Arabia. *Ann Saudi Med* 1997; 17:605–608.
- 9 Garrison MW, Olds MJ: New potential in pneumococcal immunization. *Postgrad Med* 2002;112:85–96.
- 10 Brook I: The importance of lactic acid levels in body fluids in the detection of bacterial infections. *Rev Infect Dis* 1981;3:470–477.
- 11 Oostenbrink R, Maas M, Moons KGM, Moll HA: Sequelae after bacterial meningitis in childhood. *Scand J Infect Dis* 2002;34:379–382.
- 12 Palmer A, Weber M, Bojang K, McKay T, Adegbola R: Acute bacterial meningitis in the Gambia: a four-year review of paediatric hospital admissions. *J Trop Pediatr* 1999;45: 51–53.
- 13 Sahai S, Mahadevan S, Srinivasan S, Kanungo R: Childhood bacterial meningitis in Pondicherry, South India. *Indian J Pediatr* 2001;68:839–841.
- 14 Wald ER: Pneumovax (editorial). *Clin Pediatr* 2001;40:601–602.
- 15 Frayha HH, Al Mazrou YY: Vaccination against invasive pneumococcal disease in Saudi Arabia: where do we stand? *Ann Saudi Med* 2005;25:90–93.
- 16 Scheifele D, Halperin S, Pelletier L, Talbot J: Invasive pneumococcal infection in Canadian children, 1991–1998: implications for new vaccination strategies. Canadian Pediatric Society – Laboratory Centre for Disease Control Immunization Monitoring Program, Active (IMPACT). *Clin Infect Dis* 2000;31:58–64.