CHILDHOOD MENINGITIS AT KING FAHAD HOSPITAL, HOFUF, SAUDI ARABIA

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The medical records of 132 children with meningitis treated at King Fahad Hospital, Hofuf, Saudi Arabia, between June 1994 and May 1996, were reviewed with a view to defining the incidence, types of meningitis, their management and clinical outcome. Subjects were classified into three groups: bacterial, partially treated, and viral meningitis. There were 37 patients (28%) in period I (1994/95) and 95 (72%) in period II (1995/96). The higher incidence in period II was accounted for by a sharply increased incidence of viral meningitis in the latter half of the period. Of the 132 patients, 36 (27.3%) had bacterial meningitis, 45 (34.1%) had partially treated meningitis and 51 (38.6%) had viral meningitis. The most common CSF isolate was *Haemophilus influenzae* type B (HIB) from 24 (66.7%) of the 36 bacterial meningitis cases. About half of the cases of HIB meningitis occurred in infants under the age of 12 months. *Ann Saudi Med 1997;17(6):605-608.*

Childhood meningitis is a major cause of morbidity and mortality in many parts of the world.[1,2] Rapid diagnosis and immediate initiation of treatment are critical in order to reduce the likelihood of neurological sequelae and death.[3]

Although there have been several reports on childhood meningitis from almost every region of Saudi Arabia, most have been on pyogenic (bacterial) meningitis.[4-8] Apart from bacterial meningitis, there are other types whose causative agents may not be identified and for which empirical treatments must be administered.[9] Such cases are classified as either partially treated or viral meningitis. Causative agents are known to vary in different areas of the world[10] and to be seasonally related so that epidemics occur at certain intervals.[11] Data published by the Ministry of Health indicated a seasonal outbreak of aseptic meningitis in early 1996 in Saudi Arabia.[12]

In early 1996 (late 1416H), it was observed that a large number of children were admitted in relatively quick succession with a diagnosis of meningitis at King Fahad Hofuf Hospital (KFHH), Al-Hassa, Saudi Arabia. The impression was one of either an epidemic outbreak of meningitis, or probable increase in its incidence over the previous year. This observation prompted us to review all the cases of children who were admitted between June 1994 and May 1995 (period I), and between June 1995 and May 1996 (period II). The aim of this study was to document our experience, ascertain whether there was an increased incidence, determine the type of meningitis that gave the high value, and offer a possible explanation for our observation.

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Materials and Methods

During the two-year study period, the medical records of all children up to 12 years of age with diagnosis of meningitis who were admitted to KFHH, Al-Hassa, were retrospectively reviewed. Information collected included age, sex, nationality, presenting complaints, clinical findings on admission, laboratory data, treatment and outcome.

Lumbar puncture was done under aseptic condition and cerebrospinal fluid (CSF) was immediately sent to the laboratory for analysis. Gram's staining and latex agglutination tests were done using the Wellcogen Bacterial Antigen kits for the detection of antigen from *Haemophilus influenzae* type B, *Streptococcus* group B, *Streptococcus pneumoniae, Neisseria meningitidis* and *Escherichia coli* K1. A portion of the CSF was cultured for bacteria by direct inoculation of blood, chocolate and MacConkey agar, as well as 24-hour incubation in Brain-Heart infusion broth, followed by subculture in agar plates. Antibiotic sensitivity was determined by the comparative disc diffusion method. Another portion of the CSF was used for cytology, while the rest was examined for estimation of glucose, protein and chloride contents. Other investigations carried out included CBC, blood sugar and blood culture by routine methods.

Classification of our subjects into cases of bacterial, partially treated bacterial, and viral meningitis was based

TABLE 1. *Age and sex distribution of 132 children with meningitis.*

	Age (months)					
Sex	<1	1-12	13-24	25-72	>72	Total
Male	3	16	8	28	17	72
Female	3	12	7	19	19	60
	6	28	15	47	36	132

TABLE 2. *Presenting complaints.*

Complaints	No. of patients (%)
Fever	121 (91.7)
Vomiting	103 (78)
Headache	72 (54.5)
Convulsions	12 (9.1)
Lethargy	12 (9.1)
Poor or reluctant feeding	11 (8.3)
Irritability/excessive crying	2 (1.5)
Purpuric skin rash	2 (1.5)

on the method of classification used by El-Amin et al. in a previous study.[8] In that study, bacterial meningitis was defined as the presence of an organism in the CSF demonstrated by culture, Gram's staining or latex agglutination tests. Partially treated bacterial meningitis was diagnosed if the patient had received antibiotic treatment prior to admission, and/or no organism could be seen in the CSF, but the CSF cell count exceeded 60% polymorphs, and the CSF/blood glucose ratio was under 60%. On the other hand, viral meningitis was the presumed diagnosis if no organisms were found in the CSF, and the cell count was under 60% polymorphs with a CSF/blood glucose ratio of greater than 60%.

Results

One hundred and thirty-two patients with meningitis based on our diagnostic criteria were identified during the two-year study period. All of them were Saudi citizens and comprised 72 males and 60 females, a male-to-female ratio of 1.2 to 1. The mean age ($\pm$SD) of the 132 patients was 50.9 ($\pm$39.5) months, with a range of <1 to 132 months. Table 1 shows the age and sex distribution of the 132 patients, with 90 of them (68.2%) occurring between the age of one month and six years.

The frequency of presenting complaints is shown in Table 2. Of the 132 patients, 121 (91.7%) presented with fever, and this, together with vomiting (78.0%) and headache (54.5%), constituted the most common presenting complaints. Two of the three patients with meningococcal meningitis presented with purpuric skin rash on admission.

The duration of illness before presentation in our emergency room (ER) ranged from a few hours to three days in 108 patients (81.8%), four to seven days in 21 (15.9%), and over one week in three patients (2.3%). The mode of referral was by direct presentation at the ER (self-referral) in 99 of the patients (75%), while the remaining 33 patients were either referred from a private clinic (16), Primary Health Center (PHC) (14) or a smaller hospital (3).

Antibiotic administration prior to presentation was not uncommon, in that 46 (34.8%) of the subjects had received antibiotic therapy before admission. Of the 46, 12 were among those with proven bacterial meningitis, another 12 belonged to the partially treated cases, while the remaining 22 were cases of viral meningitis.

The seasonal incidence of meningitis in our series is shown by the fact that there were 37 cases (28%) in period I and 95 (72%) in period II. While admissions during period I were nearly uniform throughout the year, except for October 1995 and May 1996, there was a steep rise in admission frequency during the latter half of period II, when 75 (78.9%) of the 95 patients were admitted. The higher proportion of admissions in period II was due to a higher incidence of non-bacterial meningitis. The latter half of this period corresponded to the winter months. There was no difference in the actual number of cases of bacterial meningitis between periods I and II, however, bacterial meningitis accounted for 45.9% and 20% of all the cases respectively. Table 3 displays the different types of meningitis according to age. There were 36 cases of bacterial meningitis (27.3%), 45 of partially treated meningitis (34.1%), and 51 of viral meningitis (38.6%). The most common organism isolated in our study was *Haemophilus influenzae* type B (HIB), which was isolated in 24 (66.7%) of the 36 bacterial meningitis cases. Although almost all the HIB cases occurred between the ages of one month and six years, the peak was under the age of 12 months. Table 4 illustrates the CSF cell count, sugar and protein level for all three types of meningitis. The values are expressed in median with their range in parentheses. Table 5 displays the results of positive Gram's stain, latex agglutination test and culture in 36 patients with bacterial meningitis. Latex agglutination test was positive in 54.5% of cases with bacterial meningitis who had sterile CSF culture, while Gram's stain was positive in 55.6%. In 13.9% of the patients, CSF culture was positive despite negative Gram's staining. Blood cultures were positive in 36% of patients with bacterial meningitis.

The management of our patients consisted of general, therapeutic and preventive measures. The general supportive measures included rehydration, lowering of fever, and control of convulsions with the use of parenteral

diazepam. Therapeutically, antibiotics were administered in the combination of either crystalline penicillin/ampicillin with chloramphenicol, or ceftriaxone alone, or ceftriaxone in combination with ampicillin. The choice of antibiotics used was based on what was available at the time. The most common combination used in the present study was ceftriaxone/cefotaxime with ampicillin in 80 (60.6%) of the patients, while the remaining 52 (39.4%) received crystalline penicillin/ampicillin with chloramphenicol. Treatment lasted between 10 and 14 days. The prophylactic measures undertaken against the bacterial meningitis cases comprised isolation on admission for four to five days, and administration of dexamethasone in a dose of 0.15 mg/kg/dose for 16 doses for those who had received no antibiotics prior to admission. Those patients with HIB and meningococcal meningitis, as well as their families, received rifampicin at the appropriate doses.

There was no mortality in this study. The early complications encountered were among the 36 bacterial meningitis cases, of whom two had transient hemiparesis, three developed syndrome of inappropriate ADH secretion (SIADHS), hearing defect and delayed milestones, while five had subdural effusions and hydrocephalus.

TABLE 3. *Type of meningitis according to age.*

Type of meningitis	Age (months) <1	1-12	13-24	25-72	>72	Total
Bacterial						
H. influenzae type B	–	12	3	7	2	24
Strept. pneumoniae	1	1	2	1	1	6
Meningococcal	–	–	–	2	1	3
E. coli	1	1	–	–	–	2
Klebsiella	–	–	–	1	–	1
Partially treated meningitis	2	5	5	16	17	45
Viral meningitis	2	9	5	20	15	51
	6	28	15	47	36	132

TABLE 4. *CSF cell count, sugar and protein level for all three types of meningitis.*

Types of meningitis	Variables: WBC ($x10^6$/L)	Polymorphs (%)	CSF/blood glucose ratio (%)	Protein (g/L)
Bacterial	298 (8-11,840)	74 (31-98)	41 (2.1-159)	1.0 (0.21-5.68)
Partially treated	113 (8-1200)	81 (4-100)	58 (13.9-137)	0.44 (0.24-2)
Viral	43 (6-480)	33 (4-95)	71 (37-200)	0.27 (0.10-1.19)

The data are expressed in median with their range in bracket.

Discussion

In the two-year period of this study, 27.3% of all the cases of meningitis were bacterial, accounting for 45.9% in period I and only 20% in period II. The higher incidence of meningitis in period II (95 as against 37 in period I) was due to a sharply increased incidence of aseptic meningitis during the last four months of that period (Figure 1). What is striking is a seasonal peak incidence of aseptic meningitis during period II, an event which did not occur in the preceding year. Although many reports have been published on the incidence of bacterial meningitis in Saudi Arabia,[4-8] much less is known about aseptic meningitis. Epidemiological and virus isolation studies in several centers have shown that viruses are the most common identifiable cause of aseptic meningitis. These have the tendency to occur in seasonal outbreaks, and although not usually associated with long-term sequelae, they may nonetheless cause short-term morbidity in a significant number of individuals.[13,14] Further studies of the trends of aseptic meningitis in Al-Hassa and other parts of Saudi Arabia would help to uncover any cyclical patterns of aseptic meningitis epidemics. This information would be useful in predicting such epidemics and facilitate the allocation of resources to cope with them.

The most common causative organisms of bacterial meningitis in the present study were *Haemophilus influenzae* (66.7%), *Streptococcus pneumoniae* (16.6%) and *Neisseria meningitidis* (8.4%). This observation compares with 41.9%, 23.8% and 11.4%, respectively, in a previous study from the Eastern Province of Saudi Arabia.[6] About half of the cases of HIB meningitis occurred in infants who were less than one year old. This underscores the importance of incorporating HIB vaccination into immunization programs as a preventive measure. Although earlier HIB vaccines were poorly immunogenic in children less than two years old, the emergence of conjugate vaccines of proven efficacy in infancy makes it possible now to protect younger children from HIB meningitis.[15] The importance of HIB vaccine is emphasized by the recommendations of the American Academy of Pediatrics for its incorporation into the schedule of primary immunization of all healthy infants, as well as children not immunized in the first year of life.[16]

During the study period, no resistant strains of HIB or *Streptococcus pneumoniae* were identified in CSF culture isolates. Although Abomelha et al. identified 14% ampicillin resistance in HIB CSF isolates, chloramphenicol resistance was demonstrated in only one case.[6] Azubuike reported that 7% of HIB meningitis cases from Tabuk were resistant to both ampicillin and chloramphenicol.[7] This, however, was not our experience, and a combination of ampicillin and chloramphenicol

TABLE 5. *Positive CSF results for gram staining, latex agglutination tests and culture in 36 patients with bacterial meningitis.*

Tests	HIB	*Strept. pneumoniae*	*Meningo-coccal*	*E. coli*	*Klebsiella*	Total
Gram's stain	21	5	2	1	–	29
Latex agglutination	21	5	1	1	–	28
Culture	9	3	–	2	1	15

remains an efficacious first-line therapy for bacterial meningitis beyond the neonatal age group in Al-Hassa. Continuous surveillance for the emergence of resistant strains, however, cannot be overemphasized.

Significant morbidity resulted from cases of bacterial meningitis. Hydrocephalus occurred in 14%, subdural effusion in another 14%, hearing impairment in 8.3% (not all patients have been tested yet), delayed milestones in 8% and hemiparesis in 5.5%. There was far less morbidity associated with the cases of aseptic meningitis. The relatively better prognosis of aseptic meningitis would explain the absence of any mortality during this period of study. It is worth noting, however, that mortalities have occurred in our center during periods outside the scope of this study.

On the whole, patients reported early to the hospital (81.8% within three days), but there was a significantly high rate of antibiotic therapy prior to presentation in 34.8% of the patients. This compares with the value of 39.6% reported from Riyadh.[17]

Meningitis in childhood remains a significant cause of morbidity and mortality despite early diagnosis, effective antibiotic and supportive therapy. Preventive measures by the administration of vaccines deserve greater attention in order to cope with this problem. Viral meningitis ocurring in epidemic proportions can place profound strains on available resources, as was our experience in Al-Hassa.

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