

ORIGINAL

Acute Pyogenic Meningitis in Childhood : A 17-Year Experience in Bahrain

By I. Mannan Khan* Akbar M. Mohammad**

ABSTRACT

The aetiologic, epidemiologic and clinical aspects of 452 cases of acute pyogenic meningitis in children treated over a 17-year period, from January 1970 through December 1986, were reviewed. An aetiological agent was identified in 237 cases (52.4%). *H influenzae b* was the commonest organism isolated in the culture-positive cases. Ninety per cent (90%) of influenzal, 66% of pneumococcal and 42% of meningococcal meningitis cases were under 2 years of age. About 60% of influenzal and pneumococcal meningitis cases occurred during October through February. A male : female ratio of 2:1 in pneumococcal meningitis was consistently seen throughout the entire period of study. Gross neurological handicaps in 15% of *H influenzae b* and 14% pneumococcal meningitis were noted. Thirty per cent (30%) of the culture-proven and 59% of the culture-negative cases had received prior antibiotic treatment. Twenty-eight per cent (28%) of the cases presented with seizures and 85% of these were aged 1 year or less. Overall mortality was 9% with a marked reduction in mortality in culture-proven meningitis during the last 7 years of the study. Ampicillin-resistant *H influenzae b* was isolated from 3 cases, 2 of whom died.

Over the past several decades use of antibiotics has brought about a dramatic decline in the mortal-

ity and morbidity from infectious diseases. Bacterial meningitis, however, continues to be the cause of considerable mortality and morbidity, especially in the developing countries^{1 2 3 4}. Pyogenic meningitis beyond the neonatal period is mostly caused by three organisms, viz. *H influenzae type b*, streptococcus pneumonia and *Neisseria meningitidis*. Pathogenesis of meningitis, however, remains to be further elucidated⁵. Epidemiologic studies, it is hoped, might be useful in defining populations at risk and with rapid developments in influenzal and meningococcal vaccines, it will become possible to protect children at risk of invasive diseases caused by these organisms.

This retrospective study was carried out to assess the incidence, aetiology, clinical features and outcome of children treated for acute pyogenic meningitis.

METHODS

Medical records of all children aged 12 years and under, treated at Salmaniya Medical Centre, Bahrain, with the diagnosis of acute pyogenic meningitis from January 1970 through December 1986, were reviewed and relevant data collected. Patients were placed in one of two categories :

* Chief Resident
Salmaniya Medical Centre
State of Bahrain

** Consultant & Chairman
Department of Paediatrics
Associate Professor
College of Medicine & Medical Sciences
Arabian Gulf University

1. Culture - Positive -
 - i) Organism isolated from cerebrospinal fluid in the presence of signs and symptoms consistent with CNS infection or sepsis.
 - ii) Organism isolated from blood in the presence of pleocytosis in CSF along with signs and symptoms of CNS infection or sepsis.
2. Culture - Negative (purulent) : Clinical presentation consistent with acute infection of CNS/Sepsis, with at least one or more of the following :
 - i) CSF WBC count equal to or over 1000/mm³.
 - ii) CSF glucose level below 40 mg/dl in the presence of pleocytosis
 - iii) CSF protein level over 40 mg/dl in the presence of pleocytosis.
 - iv) CSF pleocytosis with a history of prior treatment with antibiotics.

Because of insufficient information, culture-negative (purulent) cases admitted before January 1980 were excluded from the study, except for the mortality figures which were included for comparison.

Treatment protocol consisted of therapy with Ampicillin or penicillin, in a dosage of 300 mg to 400 mg/kg/day or 300000 units to 400000 units/kg/day

respectively given intravenously in 6 divided doses for a period of 10 to 14 days. From October 1979, all patients were initially started on a combination of Ampicillin and Chloramphenicol until culture results were available. Neonatal meningitis was treated with combination of Ampicillin and Gentamicin for a minimum of 2 to 3 weeks.

RESULTS

From January 1970 through December 1986, a total of 452 cases were treated for pyogenic meningitis. An aetiological agent was identified in 237 of these cases (Table 1, 2). One hundred and sixty-one (161) culture negative, purulent meningitis cases treated prior to January 1980 were excluded from the study as stated earlier. Out of the 54 patients treated for purulent meningitis (culture-negative) from January 1980 through December 1986, 32 fulfilled our criteria and were included in the study (Table 3) :

Incidence

Culture proven meningitis accounted for 0.32% of admissions in the paediatric wards during January 1980 through December 1986. The incidence rises to 0.45% if culture-negative cases are included in the analysis.

TABLE 1
Culture-proven Cases of Pyogenic Meningitis
Total Number and Sex Distribution
1970 - 86

| Microorganism | 1970 - 79 | | | 1980 - 86 | | | 1970 - 86 Total |
|----------------------|-----------|------|--------|-----------|------|--------|--------------------|
| | No | Male | Female | No | Male | Female | |
| H influenzae b | 46 | 21 | 25 | 33 | 18 | 15 | 79 |
| Strep pneumoniae | 53 | 37 | 16 | 21 | 13 | 8 | 74 |
| Neisseria meningitis | 50 | 26 | 24 | 18 | 8 | 10 | 68 |
| Others * | 7 | 1 | 6 | - | - | - | - |

* Include salmonella species 3, pseudomonas aeruginosa 1, klebsiella 2, multiple organisms 1.

TABLE 2
Meningitis Under the Age of 2 Months

| <i>Microorganism</i> | <i>No</i> | <i>Outcome</i> |
|---------------------------------------|-----------|------------------------|
| Streptococcus group B | 2 | 1 Expired |
| Streptococcus beta haemolytic group A | 2 | |
| Streptococcus faecalis | 1 | |
| Escherichia coli | 3 | |
| Salmonella group D | 1 | Hemiplegic at 6 years. |
| Neisseria meningitidis | 2* | |

*Included in Table 1 under *Neisseria meningitidis*.

Aetiology

Strep pneumoniae (35.5%) and *Neisseria meningitidis* (33.5%) were slightly more prevalent than *H influenzae b* (30.8%) in the period between January 1970 through December 1979. *H influenzae b* was the most common cause (46%) of meningitis in children during January 1980 through December 1986 (Table 1).

Age

Fifty-five per cent (55%) of culture-proven cases and 44% of the culture-negative, purulent meningitis cases were aged 1 year or less. Ninety per cent (90%) of *H influenzae b* cases were under 2 years of age. Mean ages for the three commonest organisms were: *H influenzae b* 10.8 months, strep pneumoniae 32 months and *Neisseria meningitidis* 18 months (Fig 1).

Sex

Male : female ratio for influenzal and meningococcal meningitis was 0.97 and 1 respectively. For pneumococcal meningitis the sex ratio was 2. This male preponderance has prevailed throughout the entire 17-year study period (Table 1).

Seasonal Prevalence

Influenzal and pneumococcal meningitis were more prevalent during the cooler months (Nov, Dec, Jan and Feb). There were small epidemics of meningococcal disease in the summer of 1974 and 1975 (Table 4).

TABLE 3
Culture-Negative (Purulent) Meningitis
Total Number, Age and Sex Distribution
(1980 - 86)

| <i>Age in Months</i> | <i>No</i> | <i>Male</i> | <i>Female</i> |
|----------------------|-----------|-------------|---------------|
| 0 - 12 | 14 | 10 | 4 |
| 13 - 36 | 11 | 6 | 5 |
| Over 36 | 7 | 5 | 2 |
| Total | 32 | 21 | 11 |

Presenting Clinical Features

Fever was present in all the patients. Vomiting, signs of toxicity and change in effect were commonly present. Seizures as a presenting symptom occurred in 28% of all patients and were more common in pneumococcal meningitis (33%) than in *H influenzae b* meningitis (27%) and meningococcal meningitis (22%). All except one presenting with seizures were under 3 years of age and 85% were aged 1 year or less (Table 5).

Pre-hospital Treatment

Thirty per cent (30%) of the culture-proven cases and 59% of culture-negative, purulent meningitis cases had received antibiotics before the examination of their cerebrospinal fluids.

Cerebrospinal Fluid Findings

Total white blood cell count and the percentage of polymorphonuclear leucocytes varied widely. Mean WBC counts were, however, elevated in all cases (Table 6).

Peripheral White Blood Cell Count

Mean white blood cell counts were elevated in all types of meningitis, more in pneumococcal than in the other types. However, variation around the mean was also large in all types of meningitis (Table 7).

Morbidity

Residual neurological handicaps were present in 5 (15%) out of 33 cases of *H influenzae b* meningitis

Figure 1

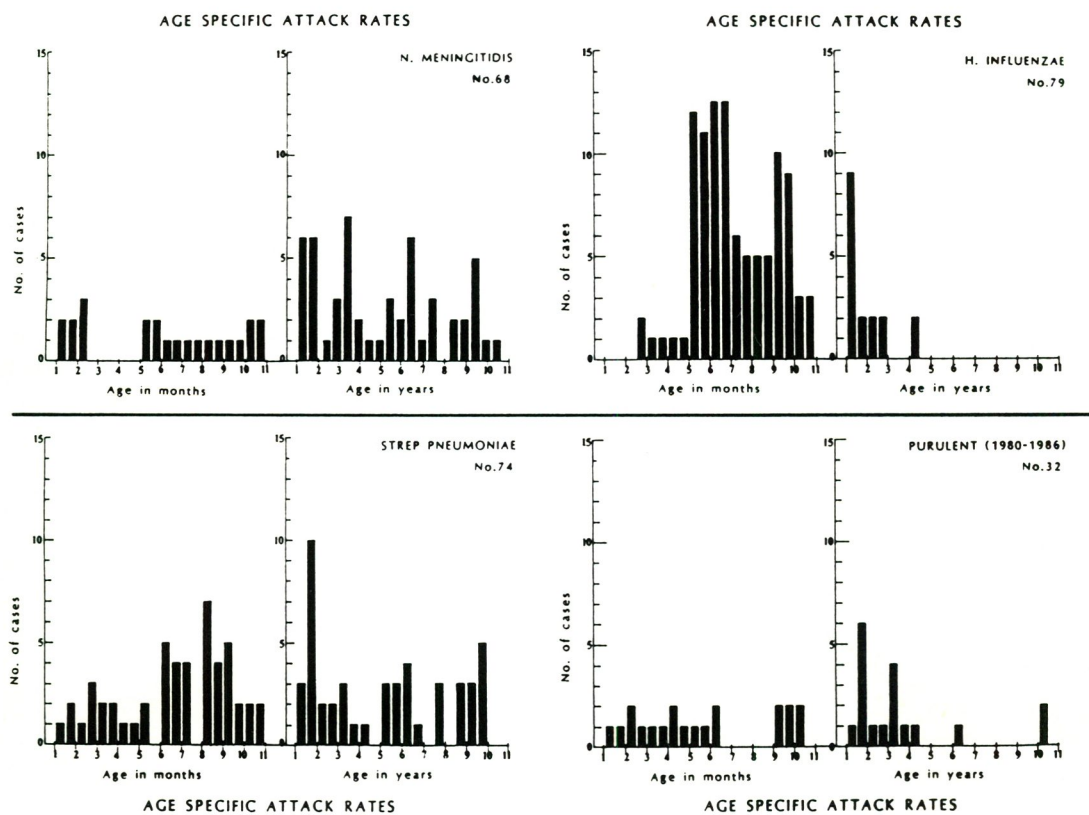


TABLE 4
Seasonal Incidence for All Types of Meningitis
Culture-Positive
(1970 - 86)

| Type | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| H influenzae b | 13 | 9 | 3 | 4 | 9 | 2 | 6 | 4 | 4 | 9 | 9 | 7 |
| Strep pneumoniae | 12 | 9 | 5 | 5 | 2 | 4 | 5 | 6 | 5 | 4 | 11 | 6 |
| Neisseria Meningitidis | 6 | 7 | 5 | 2 | 4 | 5 | 3 | 12 | 12 | 10 | 2 | 0 |

TABLE 5
Presenting Clinical Features of Meningitis (1980 – 86)

| Clinical Features | Culture-Positive | | Culture-Negative | |
|---|------------------|------------|------------------|------------|
| | 1-12 Months | >12 Months | 1-12 Months | >12 Months |
| | No 46 (%) | No 26 (%) | No 14 (%) | No 18 (%) |
| Fever | 46 (100) | 26 (100) | 14 (100) | 18 (100) |
| Vomiting | 24 (52) | 15 (57) | 8 (57) | 14 (77) |
| Irritability / excessive crying | 16 (35) | 0 (0) | 8 (57) | 3 (16) |
| Seizure | 17 (37) | 3 (11) | 6 (43) | 3 (16) |
| Toxicity | 35 (76) | 21 (80) | 8 (57) | 11 (61) |
| Altered sensorium | 31 (67) | 20 (76) | 9 (66) | 13 (72) |
| Full / bulging fontanelle | 22 (47) | 3 (11) | 8 (57) | 0 (0) |
| Neck stiffness / +ve kerning's sign | 22 (47) | 19 (73) | 6 (43) | 13 (72) |

TABLE 6
Cerebrospinal Fluid Findings
from 71 Culture-Positive Cases and 32 Culture-Negative Cases of Meningitis

| | <i>H Influenzae b</i> No 33 | <i>Strep pneumoniae</i> No 20 | <i>Neisseria</i> Meningitis No 18 | <i>Purulent</i> No 32 |
|--|--------------------------------|----------------------------------|---|--------------------------|
| CSF leucocyte count / mm ³ | | | | |
| Range | 5 – 33000 | 5 – 8200 | 50 – 18000 | 160 – 1400 |
| Mean | (4888) | (2235) | (5620) | (2627) |
| % Polymorphonuclear leucocyte | | | | |
| Range | 34 – 99 | 0 – 99 | 12 – 98 | 2 – 98 |
| Mean | (81) | (69) | (82) | (68) |
| CSF glucose mg/dl | | | | |
| Range | 2 – 189 | 3 – 86 | 1 – 94 | 7 – 126 |
| Mean | (35) | (40) | (28) | (54) |
| Protein mg/dl | | | | |
| Range | 30 – 410 | 12 – 327 | 28 – 315 | 26 – 633 |
| Mean | (168) | (151) | (163) | (133) |

TABLE 7
Peripheral Blood White Cell Count
from 72 Culture-Positive Cases and 32 Culture-Negative Cases of Meningitis

| | <i>H Influenzae b</i> (No 33) | <i>Strep Pneumoniae</i> (No 21) | <i>Neisseria Meningitis</i> (No 18) | <i>Purulent</i> (No 32) |
|--|----------------------------------|------------------------------------|--|----------------------------|
| Peripheral leucocyte count / mm ³ | | | | |
| Range | 3100-44000 | 4700-67500 | 6600-33000 | 7200-3300 |
| Mean | 15679 | 21224 | 14450 | 15416 |
| Peripheral polymorphonuclear leucocyte / mm ³ | | | | |
| Range | 11 - 80 | 21 - 86 | 28 - 82 | 24 - 87 |
| Mean | 49 | 57 | 57 | 57 |
| Bands range | 0 - 42 | 0 - 23 | 0 - 29 | 0 - 33 |
| Mean | 15 | 11 | 9 | 6 |

TABLE 8
Total No of Cases with Sequelae in Meningitis (Jan 1980 - Dec 1986)

| <i>Aetiological Agent</i> | <i>Age (Months)</i> | <i>Sex</i> | <i>Sequae</i> |
|------------------------------------|---------------------|------------|--|
| 1. <i>Haemophilus influenzae b</i> | 9 | F | Spastic paresis of left upper arm at 7 years |
| 2. " | 5 | M | Deaf |
| 3. " | 7 | M | Hydrocephalus |
| 4. " | 9 | M | Delayed milestones |
| 5. " | 15 | M | Hydrocephalus, psychomotor retardation |
| 6. " | 7 | M | Hydrocephalus |
| 7. <i>Strep pneumoniae</i> | 3 | M | Deaf mute at 6 years, delayed milestones |
| 8. " | 12 | M | Dilated ventricles recurrent seizures |
| 9. " | 9 | M | Facial palsy, mildly spastic |
| 10. <i>Neisseria meningitis</i> | 2 | M | Hemiplegic at 4 years |
| 11. <i>Salmonella</i> group D | 2 | F | Spastic hemiplegia at 6 years |
| 12. No organism (purulent) | 5 | M | Delayed walking |
| 13. " | 3 | M | Cerebral palsy at 13 months |

TABLE 9
Deaths : Organism Age and Sex Distribution
of Cases of Meningitis
(1980 - 86)

| Age (Months) | <i>H influenzae b</i> | <i>Strep</i> | <i>Neisseria</i> | <i>Purulent</i> |
|--------------|-----------------------|----------------------------|------------------------------|-----------------|
| | No 33 | <i>Pneumoniae</i> No 21 | <i>Meningitidis</i> No 18 | |
| | M/F | M/F | M/F | M/F |
| 0 - 12 | 0/1 * | 0/0 | 0/0 | 0/1 |
| 13 - 36 | 0/1 | 0/0 | 0/0 | 1/1 |
| Over 36 | 0/0 | 0/0 | 0/0 | 1/0 |
| Total | 0/2 | 0/0 | 0/0 | 2/2 |
| % | 6% | 0% | 0% | 12% |

Both haemophilus and strept pneumoniae were cultured from CSF.

TABLE 10
Deaths : Organism, Age and Sex Distribution
of Meningitis Cases
(1970 - 79)

| Age (Months) | <i>H influenzae b</i> | <i>Strep.</i> | <i>Neisseria</i> | <i>Purulent</i> |
|--------------|-----------------------|----------------------------|------------------------------|-----------------|
| | No 46 | <i>Pneumoniae</i> No 53 | <i>Meningitidis</i> No 50 | |
| | M/F | M/F | M/F | M/F |
| 0 - 12 | 2/2 | 4/0 | 0/0 | 4/9 |
| 13 - 36 | 2/0 | 0/1 | 0/0 | 3/1 |
| Over 36 | 0/0 | 2/0 | 0/1 | 1/0 |
| Total | 4/2 | 6/1 | 0/1 | 8/10 |
| % | 13% | 13% | 2% | 11% |

and in 3 (14%) of the 21 cases of pneumococcal meningitis. Overall moderate to severe neurological handicaps were noted in 9.7% of the cases (culture-proven and culture-negative, purulent meningitis). Auditory function was not evaluated routinely in all cases (Table 8).

Mortality

Out of 452 patients treated for meningitis over the 17-year period, 41 died, a mortality rate of 9%. This included 18 deaths from culture-negative, purulent meningitis between January 1970 through December 1979. Case fatality rates for H influenzae b, pneumococcal and meningococcal meningitis were 10%, 9.5% and 1.5% respectively. Four (4) deaths from meningococcaemia, without meningitis, were not included in the analysis (Table 9, 10)

Meningitis Under the Age of 2 Months

Eleven (11) infants aged 2 months and less had culture-proven meningitis between January 1980 through December 1986. *Escherichia coli* was the causative organism in three neonates in the newborn nursery. (Table 2).

Meningitis and Haemoglobinopathies

Between January 1980 and December 1986, four children with sickle cell disease (SCD) and one splenectomised beta thalassemia major case had pneumococcal meningitis. One SCD patient had influenzal meningitis, and no organism was cultured from another case of SCD and meningitis. One of the patients with SCD had received Pneumovax 2 years prior to the attack of pneumococcal meningitis. All survived except the one with culture-negative, purulent meningitis.

Ampicillin-Resistant H Influenzae b

Ampicillin-Resistant H influenzae b was isolated from 3 cases. The first case was recorded in September 1979. Two patients died.

DISCUSSION

Our study shows that during the seventies, the three organisms, viz. H influenzae b (31%), streptococci (36%) and *Neisseria meningitidis* (34%) were almost equally prevalent. In the eighties, however, H influenzae b by accounting for 46% of the cases has emerged as the most common cause of meningitis in children in Bahrain. Reports from

Riyadh³, Libya⁴ and Tehran² have shown streptococci as the commonest cause of meningitis in children in their respective countries. Our observation is in agreement with a recent report from Kuwait⁶.

Age distribution of pyogenic meningitis has important implications on immunization programmes. Ninety percent of influenzal, 66% of pneumococcal and 42% of meningococcal meningitis cases in our series were under 2 years of age. Currently available vaccines are not sufficiently immunogenic to elicit protective antibody responses in children younger than 2 years of age⁷. However, preliminary reports of trials of polysaccharide-protein conjugate vaccines are very encouraging⁸.

About 60% of influenzal and 57% of pneumococcal meningitis attacks occurred during October through February. Elzouki, et al.⁴ have reported similar observation from Libya⁴.

Early diagnosis of meningitis in infants and children is crucial for a favourable outcome. A careful physical examination, observation of the child for subtle changes in sensorium and signs of toxicity, together with a liberal policy of spinal fluid examination are, in our experience, absolutely essential for early diagnosis of meningitis.

While some investigators have observed that prior antibiotic treatment does not hamper the diagnosis of meningitis, others have noted a higher incidence of sterile CSF in pneumococcal and meningococcal meningitis cases who had received pretreatment with effective drugs⁹. It is noteworthy that in our series almost twice as many culture-negative meningitis cases (59%) as culture-positive cases (30%) had received prior treatment with antibiotic.

Seizures as presenting complaints were noted in 28% of our cases and were more common in pneumococcal (33%) than in influenzal (27%) and meningococcal (22%) meningitis cases.

Most reports indicate a higher attack rate in males for the three common organisms^{4,7}. We found a striking male predominance only in the case of pneumococcal meningitis, an observation also reported from Egypt².

In a recent large prospective study of bacterial meningitis in children, 32.8% of children had neuro-

logic abnormalities at the time of discharge from hospital; by 5 years after discharge specific deficits were noted in 11.1%⁹. Dodge et al.¹⁰ have reported sensorineural deafness in 31% of pneumococcal, 6% of influenzal and 10% of meningococcal meningitis cases. Five of our H influenzae b meningitis cases and 3 of pneumococcal meningitis cases were left with neurological handicaps. Factors responsible for the poor outcome in these as well as the others were young age, prior treatment, late presentation and the level of consciousness at the time of admission to the hospital. Six of these patients were under 1 year, 4 had been ill for over 3 days, were semi-conscious or comatose at presentation, and had received pre-hospital treatment. Auditory function was not assessed routinely in our cases.

We noted a mortality rate of 13% in influenzal and pneumococcal meningitis in the last decade. In our series of cases since January 1980 through December 1986, there were no fatalities from pneumococcal and meningococcal meningitis and mortality in influenzal meningitis had declined to 6%. Fatality rates of 16.5% to 31% have been reported in pneumococcal meningitis and a mortality rate of 6% in influenzal meningitis has recently been reported from USA⁷.

Beta haemolyticus streptococci group A was isolated from 2 neonates. This organism is rarely reported nowadays as a cause of neonatal meningitis. During the 30s and 40s it used to be the commonest cause of meningitis in USA.

The predisposition of sickle cell disease patients and splenectomised individuals to overwhelming sepsis with pneumococci and haemophilus influenzae b is well known. What is not well appreciated is that the need for vigilance is not obviated even after vaccination with the presently available polyvalent pneumococcal vaccine. In our series of 6 cases of SCD with meningitis, a 9-year-old child had received Pneumovax 2 years prior to the attack of pneumococcal meningitis. Spleen plays a major role in trapping bacteria from the blood and in the formation of specific pneumococcal opsonins. Many patients with SCD develop functional asplenia at an early age thereby becoming prone to serious infection with pneumococci and other bacteria. After recovering from meningitis the splenectomised beta thalassemia

patient in our series had two further attacks of gram-negative sepsis, the second of which he did not survive.

Ampicillin resistance was noted in 4% of H influenzae b isolated from respiratory infections in Riyadh in 1982 by Chowdhury et al.¹² and in 9.5% of H influenzae b isolated from meningitis cases in Riyadh in 1984 by Babikar et al.³ We recorded 3 cases of meningitis with Ampicillin-resistant H influenzae b. in our series of 79 cases; two patients died. Although the prevalence rates of Ampicillin-resistant H influenzae b is low in this region compared to USA (23.7%)⁷, there is need for vigilance. Higher case fatality rates (6.2%)⁷ in patients with Ampicillin-resistant infections than in those with Ampicillin-sensitive infections (3.7%) have been reported.

CONCLUSION

In this retrospective study we have highlighted the epidemiological and the clinical aspects of childhood pyogenic meningitis in Bahrain. Of the culture-positive cases, H influenzae b was the commonest aetiological agent. The majority of the influenzal and the pneumococcal, while only 42% of the meningococcal cases were under 2-year of age. A 2:1 male to female ratio was outstanding in the pneumococcal meningitis throughout the study period.

Comparison was drawn with results of some regional and international studies. The information, it is hoped, might be of help not only to practicing clinicians in the region but also provide reference background material to future prospective research on meningitis.

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