ORIGINAL ARTICLE

A 2-YEAR PROSPECTIVE STUDY ON CHILDHOOD ACUTE BACTERIAL MENINGITIS IN TENGKU AMPUAN AFZAN HOSPITAL, KUANTAN, PAHANG

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Abstract

During a 24-month period, 21 children with acute bacterial meningitis were identified and studied. The majority of the children was from low socio-economic group and the male:female sex ratio was equal. Seventeen children (81%) were aged twelve months or below. In 15 (71.5%) of the children. *Haemophilus influenzae* type b was recovered, while *Streptococcus pneumoniae* was isolated from 4 children. *Neisseria* spp and *Salmonella* spp were identified respectively in each of the other two cases. The case fatality was four (19.0%) with nine others (42%) exhibiting neurological sequelae. Except for the *Salmonella* spp strain that was resistant to the cephalosporin, the rest of the bacterial species were sensitive to the commonly used antibiotics. As *Haemophilus influenzae* type b is still the most prevalent cause of acute bacterial meningitis, it is therefore strongly recommended that the national immunisation programme in this country should include the vaccine for it in our effort to minimise the mortality and morbidity caused by this organism.

Key words: *Antibiotics; bacteria; fatality; morbidity; mortality and vaccine*

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Introduction

Acute bacterial meningitis is an important cause of mortality and morbidity in children. The disease caused by *Haemophilus influenzae* type b (Hib) is recognised as one of the major causes of high morbidity and mortality in children worldwide before routine immunisation was adopted. Acute bacterial meningitis caused by *Haemophilus influenzae* type b has ceased to be important in the developed countries like North America, Northern Europe, Australia and New Zealand,[1-3] subsequent to the introduction of mass Hib vaccination. It is still a leading cause of bacterial meningitis, responsible for over 200,000 cases with more than 40,000 deaths annually in Asia and Africa.[4,5] Moreover, *Neisseria meningitides* and *Streptococcus pneumoniae* remain important pathogens even though they occur sporadically. In spite of its availability, failure to include *Haemophilus influenzae* type b conjugate vaccine into national immunisation programmes in many developing countries means that bacterial meningitis will remain a serious regional health problem.[6,7]

Up until now, most of the published reports on acute bacterial meningitis in Malaysia were based on retrospective studies.[8-13] The present

prospective study was carried out to document the epidemiology of acute bacterial meningitis in one of the referral hospitals on the east coast of Peninsular Malaysia.

Materials and methods

Hospital Tengku Ampuan Afzan, Kuantan, a tertiary hospital in the state of Pahang, is situated on the east coast of Peninsular Malaysia about 265 km from Kuala Lumpur. This hospital is currently a teaching hospital of the Kulliyyah of Medicine, International Islamic University of Malaysia.

This 2-year prospective study was carried out between January 1, 1999 and December 31, 2000 in this hospital. All children aged 1 month to 12 years admitted to this hospital with acute bacterial meningitis were enrolled. The inclusion criteria in this study were:

1. Isolation of the bacteria in the cerebrospinal fluid culture.
2. Presence of bacteria antigen in the cerebrospinal fluid in cases where bacteria could not be isolated from the cerebrospinal fluid or blood.
3. Clinical and imaging evidence of acute meningitis, plus isolation of bacteria from the blood culture. Imaging evidence included presence of cerebral oedema, effusion or abscess by either ultrasound or computerised tomography scanning. In these cases lumbar puncture could not be performed or was refused.

In cases where serotyping was done, isolates were serotyped by slide agglutination with specific antisera (Murex Diagnostics Limited, Dartford, UK). Antibiotic susceptibility testing was carried out by disc diffusion test.[14]

Demographic and clinical information such as: age, sex, race, family income, and duration of illness were obtained from the parents once the diagnosis was confirmed. The poverty line for the Peninsular Malaysia is defined as total income of RM460.00 per month in a household with 4.6 members.[15] The acute complications and outcome were documented. The antimicrobial sensitivity pattern of the bacteria was obtained from the microbiology laboratory of the hospital. The antimicrobial protocol for treatment of childhood bacterial meningitis is as follows:

1. For *Haemophilus influenzae* –
   Cefotaxime 50 mg/kg per 24 hours intravenously 6 hourly for 14 days or Chloramphenicol 20–25 mg/kg intravenously 6 hourly for 14 days.
2. For *Streptococcus pneumoniae* –
   Benzylpenicillin 2–4 mega intravenously 4 hourly for 14 days.
3. For *Neisseria meningitidis* –
   Benzylpenicillin 2–4 mega intravenously 4 hourly for 7 days
4. For *Salmonella* species –
   Chloramphenicol 75 mg/kg orally 6 hourly for 14 days or Ceftriaxone 50 mg/kg per 24 hours intravenously daily for 5 days

Data was analysed using Epi-Info v6 software.

Results

Twenty-one cases of acute bacterial meningitis were diagnosed during the 2-year study. The median age was 12.7 months with a range of 4 to 36 months. Seventeen (81%) of the children were less than 1 year of age. The ratio of male to female was 1:1. Except for two Orang Asli and one Chinese, the remaining patients were Malays. Sixteen (76%) children were from families whose income were below the poverty line. The mean duration of illness prior to admission was 7 days with a range of 2 to 14 days (Table I). The minimum duration of hospitalisation was 14 days. Organisms were identified from a total of 25 cerebrospinal fluid and blood specimens. From eight specimens of cerebrospinal fluid with positive culture, five grew *Haemophilus influenzae; Streptococcus pneumoniae* was recovered in two, and *Salmonella* spp. in one. *Haemophilus influenzae* type b antigen was detected in the cerebrospinal fluid of six cases by latex agglutination test. *Haemophilus influenzae* was also isolated in six blood cultures, *Streptococcus pneumoniae* in

three and *Neisseria* spp. and *Salmonella* spp. in one each. *Haemophilus influenzae* was detected in 15 (71.5%) of 21 children and was the most common cause of acute bacterial meningitis in this study. No organism could be isolated from five of the children. This could be due to prior antibiotic treatment by general practitioners.

Lumbar puncture was not performed in five children because of parental refusal. The clinical presentations strongly suggested that these children were suffering from acute bacterial meningitis. These children were considered as having acute bacterial meningitis following isolation of bacteria from their blood cultures (Table I).

An analysis of the antimicrobial sensitivity patterns of the isolated organisms to various antimicrobials is shown on Table II. With the exception of *Salmonella* spp that was resistant to ceftriaxone, all other isolates were sensitive to penicillin, chloramphenicol and cefotaxime.

The most frequent clinical presentation was fever with seizures (Fig. 1). Acute complications of the disease were documented in 11 children. Seven children had subdural effusion, four children were comatose and one child had cerebral abscess (Fig. 2).

Long-term complications or sequelae, were documented in nine (42%) of 17 children who survived. These were as follows: deafness in four children, mental retardation in three children

Table I. Age distribution, duration of illness prior to hospitalisation, cerebrospinal fluid and blood cultures results in 21 children with acute bacterial meningitis

Cases	Age (months)	Duration of illness (days)	CSF culture	Latex agglutination	Blood culture
1*	5	14	ND*	ND	Hib
2*	9	12	ND*	ND	Hib
3	6	4	Hib	Hib+ve	NG
4	4	2	Hib	ND	Hib
5	7	10	Hib	ND	NG
6*	12	14	Hib	ND	NG
7	24	3	Hib	ND	NG
8#	5	14	NG	Hib+ve	NG
9#	24	4	NG	Hib+ve	NG
10#	9	3	NG	Hib+ve	NG
11#	12	14	NG	Hib+ve	NG
12#	12	4	NG	Hib+ve	NG
13*	12	10	St.p	ND	NG
14	48	5	St.p	ND	St.p
15	11	6	ND*	ND	St.p
16	8	3	R	ND	Hib
17	9	4	R	ND	Hib
18	6	7	R	ND	Hib
19	12	7	R	ND	St.p
20	5	3	R	ND	Ns
21	36	7	S	ND	S

* Died; # Partially treated; * Severe cerebral oedema; S = *Salmonella;* St.p = *Streptococcus pneumoniae;* Ns = *Neisseria*; NG = No growth; ND = Not done

Table II. Type and number of organisms tested and their antibiotic sensitivity pattern

Antibiotics	Hib	Streptococcus pneumoniae	Neisseria spp.	Salmonella spp.
Penicillin	10 (S)	4 (S)	1 (S)	NT
Ampicillin	10 (S)	4 (S)	1 (S)	1 (S)
Chloramphenicol	10 (S)	4 (S)	1 (S)	1 (S)
Cefuroxime	10 (S)	4 (S)	1 (S)	1 (R)
Cefotaxime	10 (S)	4 (S)	1 (S)	1 (R)
Ceftriaxone	10 (S)	4 (S)	1 (S)	1 (R)
Cotrimoxazole	10 (S)	4 (S)	1 (S)	1 (S)
Vancomycin	NT	4 (S)	NT	1 (S)

S = Sensitive; R = Resistant; NT = Not tested

Fig. 1. Clinical presentation of 21 children with acute bacterial meningitis.

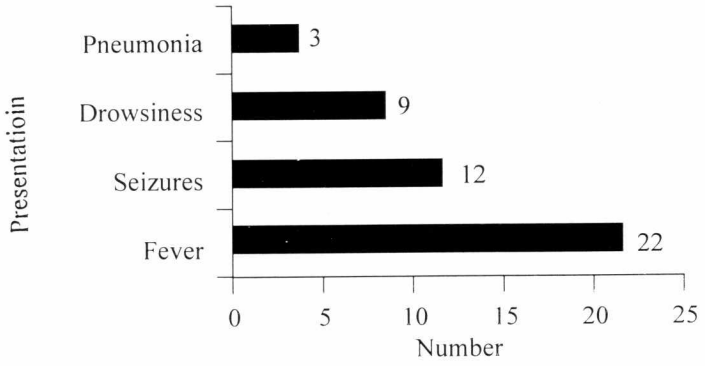


Fig. 2. Acute complications following hospitalisation in children with acute bacterial meningitis.

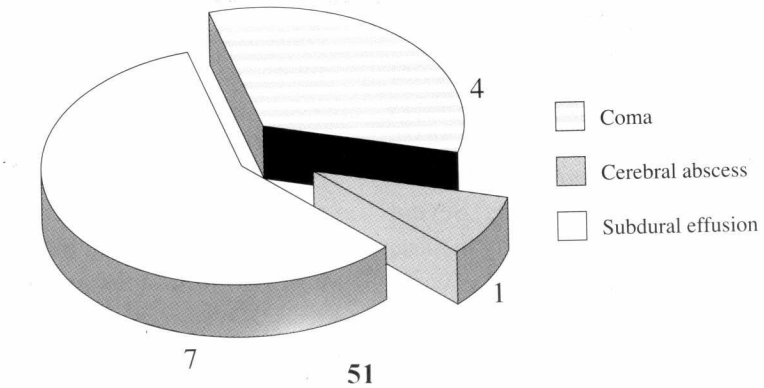


Fig. 3. Neurological sequelae of nine children with acute bacterial meningitis.

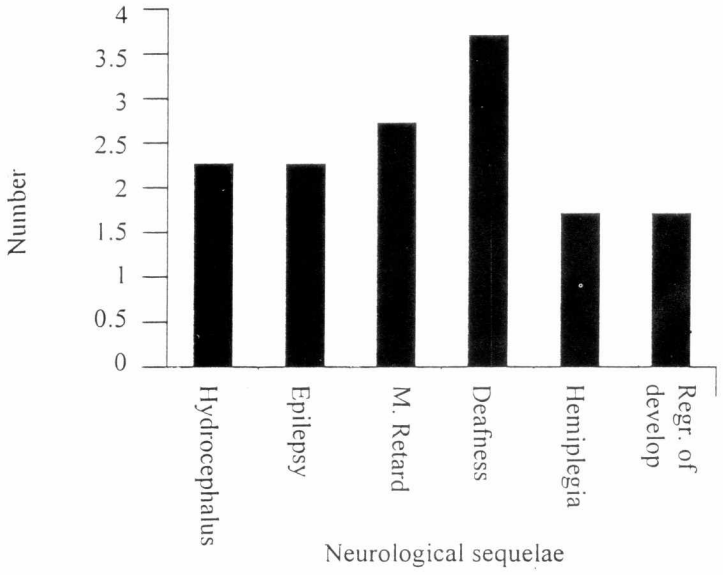
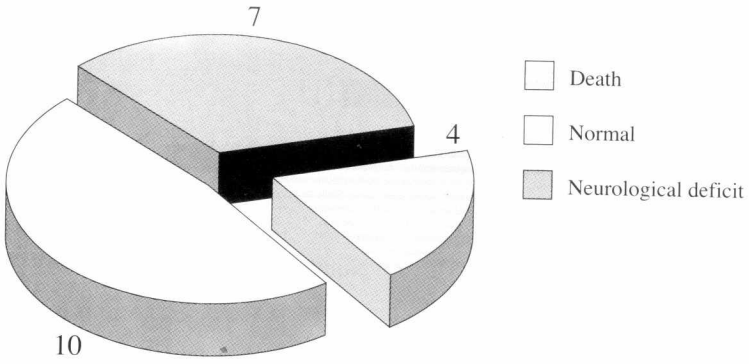


Fig. 4. Outcome of children with acutebacterial meningitis.



and two each had regression of development, hemiplegia, epilepsy and hydrocephalus respectively (Fig. 3). One child had an isolated left third cranial nerve palsy.

The case fatality rate for acute bacterial meningitis in this study was 19% (four of 21) (Fig. 4). Of the four children who died, three were caused by *Haemophilus influenzae* type b and one by *Streptococcus pneumoniae*. Severe cerebral oedema contributed to mortality in these children. Morbidity and mortality were particularly high in those that presented late: fever of more than four days duration, persistent seizure and altered levels of consciousness. All the four cases that died presented in a comatose state.

Discussion

Eighty-one percent of children who were admitted to Hospital Tengku Ampuan Afzan in this study with acute bacterial meningitis were less than 12 months of age. This conforms with

earlier studies between 1984 and 1999 by Puthucheary,[8] Choo,[9] Nik Khairulddin[10] and Ismail Hussain[13] in which they found that most children affected were aged below one year. The age distribution of our cases is also similar to that of other less industrialised populations such as Thailand and Chile.[16,17] This is in contrast to those of western countries where the percentages of children below the age of one year developing acute bacterial meningitis were much lower, i.e. 53.5% in Switzerland,[18] 54.0% in Sweden,[19] 59.0% in Finland,[20] 64.0% in the Netherlands[21] and 69.7% in the USA.[22]

In this study, the invasive *Haemophilus influenzae* is the commonest organism isolated from the cerebrospinal fluid and blood. This finding is similar to those reported by Choo,[9] Ismail Hussain[13] and previous published data from various Asian[23,24] and African countries.[25-27] This further confirms that *Haemophilus influenzae* type b is the most common organism causing bacterial meningitis in Malaysia.

The case fatality rate of 19% is consistent with the previous local studies[8-10,13] and with those from other developing countries,[15-17,23,25-27] where the range is from 12–47%. It is much higher when compared to the figure from the western countries (1–5%).[18-22,24] Similarly the morbidity rate of 42% is similar to the previously reported studies on acute childhood bacterial meningitis.[8-10,13]

Bacterial resistance to commonly used antibiotics has been reported increasingly since the late 1980s. The majority of the resistant strains was reported in Spain and developing countries such as Thailand, South Africa, Kuwait and Mexico as well as developed countries such as US, Britain and Australia.[28] In this study, almost all the isolates were sensitive to the commonly used antibiotics except for one that was resistant to ceftriaxone. The present antibiotic protocol for acute bacterial meningitis in this hospital is thus justified.

The small number of cases of bacterial meningitis encountered during this study period of 2 years is most likely an under-estimation of the real situation. The likely explanations are parental refusal of lumbar puncture procedure, antibiotic therapy before hospitalisation and death before seeking treatment in hospitals.[13,29,30] The present study suggests that acute bacterial meningitis is still an important disease, which contributes considerably to mortality and morbidity in children in this community. In spite of the availability of *Haemophilus influenzae* type b conjugate vaccine and its proven efficacy in reducing the incidence of *Haemophilus influenzae* meningitis, it is still not included in our national immunisation programme. This policy therefore, needs to be readdressed.

Conclusion

The present study shows that there have not been changes in mortality and morbidity of acute bacterial meningitis caused by *Haemophilus influenzae* in this country in the last 30 years. Ever since the introduction of *Haemophilus influenzae* type b conjugate vaccine, this disease is almost totally eliminated in the developed countries. For a country like Malaysia with a significant burden of Hib disease, this vaccine needs to be incorporated into the current immunisation programme. Only then will the mortality and morbidity caused by this micro-organism be brought under control.

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