ORIGINAL ARTICLE

Childhood Acute Bacterial Meningitis: Clinical Spectrum, Bacteriological Profile and Outcome

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ABSTRACT

Objective: To determine the disease pattern, etiological agents and outcome of childhood acute bacterial meningitis.
Study Design: A descriptive study.
Place and Duration of Study: Department of Paediatric Medicine, The Children's Hospital, Lahore, from January to December 2012.
Methodology: A total of 199 children between the ages of 1 month and 5 years, admitted with the diagnosis of meningitis on the basis of clinical findings and positive cerebrospinal fluid (CSF), were included. In all patients, complete blood count (CBC), CSF culture sensitivity, and blood culture sensitivity were performed. Data was analysed using SPSS version 20.
Results: Out of 199 children, 127 (63.8%) were males with M:F ratio of 1.7:1. Mean age was 11.33 ±12 months. Maximum numbers of children were < 1 year of age, 136 (68.3%). Only 90 (45.2%) children were fully vaccinated according to Expanded Program of Immunisation (EPI) schedule. Presentations with refusal to take feed (p=0.008) and with impaired conscious state were independent predictors of death (p=0.002). Complications were noted in 34 (17%) and were significantly associated with severe malnutrition (p=0.006) and altered conscious level at presentation (p < 0.001). The common pathogens identified on CSF culture were *coagulase negative staphylococci* (CoNS) in 11 (5.5%) and *streptococcus pneumoniae* in 5 (2.5%). Overall mortality was 10.1%. The commonest pathogen isolated from children who died was *streptococcus pneumoniae* (p=0.039).
Conclusion: Acute bacterial meningitis mostly affected children under the age of 1 year. CSF culture revealed both Gram-positive and Gram-negative bacteria. The most common pathogen in children who died was streptococcus pneumoniae.

Key Words: *Bacterial meningitis. Vaccination. Gram-positive bacteria. Lumbar tap. Cerebrospinal fluid.*

INTRODUCTION

Acute bacterial meningitis (ABM) is a life threatening illness that is prevalent worldwide. It is a medical emergency that needs early diagnosis and aggressive therapy. Despite advances in management and vaccination, bacterial meningitis remains a severe infection with high rate of mortality and long term neurological disabilities. Therefore accurate diagnosis is necessary regarding the important etiological agents to ensure appropriate management.[1] In children, the pathogens responsible for the most cases of meningitis in developing countries are *streptococcus pneumoniae* and *haemophilus influenzae* type b (Hib).[2,3] To minimise complications and adverse outcomes, early clinical suspicion and implementation of appropriate anti-microbial therapy are critical.[4] The gold standard test for diagnosing meningitis is cerebrospinal fluid (CSF) analysis. Bacteria can be isolated in 50 to 80% of cases in Gram staining and the highest CSF culture positivity is 80%.[5] The sensitivity of either tests is less than 50% in patients who are already on antibiotic treatment. CSF leukocyte count and concentration of protein and glucose lack specificity and sensitivity for the diagnosis of meningitis.[6] The exact etiological diagnosis is often not possible, because of prior antibiotic therapy, low bacterial load and delay in plating for culture.

In the last few years, numerous public health interventions have been introduced in Pakistan, including *haemophilus influenzae* type b (Hib) vaccination. There is considerable improvement in under-5 childhood mortality in Pakistan. However, it is less certain how this intervention has affected the burden of ABM. We have taken advantage of this consistently collected data of one year to analyse ABM in children. We, therefore, conducted the study with the aim to describe disease pattern, diagnostic features, bacteriological profile, complications and mortality of ABM in children over a period of one year.

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METHODOLOGY

This was a prospective hospital-based descriptive study, conducted at The Children's Hospital and The Institute of Child Health, Lahore. This was a longitudinal study conducted over a period of one year from January to December 2012. Children between the ages of 1 month and 5 years, admitted with the diagnosis of meningitis on the basis of clinical findings and positive CSF, were included. Inclusion criteria for suspected meningitis were all the admitted cases during the study period, 1 months to 5 years of age with the history of sudden onset of fever and the presence of one or more of the followings, such as, seizures, excessive crying, poor feeding, neck stiffness, altered consciousness, bulging fontanelle (in children aged < 12 months), signs of meningeal irritation and positive CSF with > 10 cell count/mm3. Children with comorbidities like meningomyelocele, prior central nervous system diseases, seizure disorders, hydrocephalus, history of recurrent meningitis, and acute head trauma were excluded from the study. A detailed history and thorough clinical examination was undertaken for each patient. Their clinical features were noted focusing mainly on age, gender, presenting symptoms, examination findings, total hospital stay, and complications. Information regarding vaccination and history of previous treatments were also obtained. In all patients, relevant laboratory data including complete blood count (CBC), CSF cell count with differential, protein, glucose, Gram staining with CSF culture sensitivity (C/S), and blood culture sensitivity (C/S) were performed. The patients were managed with intravenous antibiotics along with supportive treatment. Antibiotic treatment was continued for a minimum of 10 days. Antibiotics were changed to second line according to blood C/S or CSF C/S report. All patients were examined daily for acute neurological complications. Acute neurological complications such as seizures after fourth day of admission, persistent altered state of sensorium, cranial nerve palsy or any neurological deficit were checked during daily examination. CT scan of brain was done in patients having neurological deficit to detect acute complications of meningitis like, subdural effusion, hydrocephalus or brain abscess. Outcomes of patients were noted in the form of discharged, died, left against medical advice (LAMA) or shifted to other ward. Information recorded in a pre-designed proforma and data was analysed.

The data was analysed using Statistical Package for Social Sciences (SPSS) version 20 software. Variables were summarised using frequencies and percentages for categorical variables, median, and range for continuous variables. The Chi-square test/Fisher's exact test was used for statistical analysis. A p-value of < 0.05 was considered statistically significant.

RESULTS

During this one year study period, 199 patients were hospitalised with ABM. Males 127 (63.8%) out numbered the females 72 (36.2%), with a male to female ratio of 1.7:1. The mean age of children was 11.33 ±12 months. Most patients (68.3%, n=136) were < 1 year of age. For all patients at the time of admission, the mean duration of illness was 3 ±2 days and (74.4%, n=148) children presented within first 7 days of symptoms. Average length of hospital stay (LOS) was 8.98 ±4 days. The patients with stable clinical condition were discharged on parent's request on intravenous antibiotics before complete 10 days of recommended treatment for meningitis. Only (45.2%, n=90) children were fully vaccinated according to EPI schedule and (23%, n=46) were severely malnourished according to WHO - z Scoring Charts. Twenty of 199 patients (10.1%) died (Table I).

The most common presenting symptom was fever (n=190) 95%, (n=174) 87% had seizures, (n=50) 25% presented with poor feeding, and (n=46) 23% had impaired consciousness. Presentations with refusal to take feed (p=0.008) and with impaired conscious state were independent predictors of death (p=0.002). CSF culture positivity, severe malnutrition and development of complications also had statistically significant p-values of 0.039, 0.037 and < 0.001, respectively (Table II).

CT scan of brain was done in 34 (17%) patients who showed no improvement in sensorium or developed acute neurological complications during hospital stay (Table III). Uneventful course was present in 165 (83%) (Table II). More than two complications were noted in 20 (10%) children. Complications were significantly

Table I: Demographics and outcomes of 199 children with acute bacterial meningitis.

Category	Total n = 199 (100%)
Age	
Mean age in months	11.33 ±12
Median age in months	6 (1-60)
< 1 year	136 (68.3%)
1 year-3 years	53 (26.6%)
3.1 years-5 years	10 (5.0%)
Sex (M:F)	1.7:1
Male	127 (63.8%)
Female	72 (36.2%)
Duration of hospital stay	
Mean duration of stay	8.98 ± 4 days
< 7 days	27 (13.6%)
7-10 days	72 (36.2%)
11-14 days	65 (32.6%)
> 14 days	35 (17.6%)
Treatment taken before coming to hospital	
Yes	23 (11.6%)
No	176 (88.4%)
Vaccination status	
Vaccinated according to EPI	90 (45.2%)
Un-vaccinated	96 (48.2%)
Partially vaccinated	13 (6.6%)
Severe malnutrition	
Present	46 (23.1%)
Absent	153 (76.9%)
Outcome	
Discharged	165 (82.9%)
Died	20 (10.1%)
Left against medical advice (LAMA)	12 (6.0%)
Shifted to neurosurgery ward	02 (1%)

Table II: Factors associated with outcomes of children with acute bacterial meningitis.

	Outcomes				p-value
	Discharged n=165	Died n=20	LAMA n=12	Shifted n=2	
Altered mental status					
Yes	30 (18%)	11 (55%)	4 (33%)	1 (50%)	0.002
No	135 (82%)	9 (45%)	8 (67%)	1 (50%)	
Poor feeding					
Yes	34 (21%)	8 (40%)	7 (58%)	1 (50%)	0.008
No	131 (79%)	12 (60%)	5 (42%)	1 (50%)	
Severe malnutrition					
Yes	34 (21%)	6 (30%)	4 (33.3%)	2 (100%)	0.037
No	131 (79%)	14 (70%)	8 (66.7%)	0	
Complications					
No	148 (90%)	9 (45%)	8 (66.7%)	0	< 0.001
Motor loss	5 (3%)	4 (20%)	0	0	
Seizures	12 (7%)	6 (30%)	4 (33.3%)	0	
Subdural effusion	0	1 (5%)	0	0	
Hydrocephalus	0	0	0	2 (100%)	
Age					
<1 year	114 (69%)	11 (55%)	9 (75%)	2 (100%)	0.728
1-3 year	43 (26%)	8 (40%)	2 (17%)	0	
> 3 year	8 (5%)	1 (5%)	1 (8%)	0	
Duration of symptoms					
1-2 days	73 (44%)	10 (50%)	3 (25%)	0	
3-7 days	50 (30%)	7 (35%)	5 (42%)	0	
> 7 days	42 (26%)	3 (5%)	4 (33%)	2 (100%)	
Treatment in past					
Yes	18 (11%)	4 (20%)	1 (8%)	0	0.605
No	147 (89%)	16 (80%)	11 (92%)	2 (100%)	
Vaccination					
Yes	80 (48.5%)	6 (30%)	4 (33.4%)	0	0.313
No	76 (46%)	11 (55%)	7 (58.3%)	2 (100%)	
Incomplete	9 (5.5%)	3 (15%)	1 (8.3%)	0	
CSF culture					
No organism	148 (90%)	15 (75%)	10 (83.3%)	2 (100%)	0.039
CoNS	10 (6%)	1 (5%)	0	0	
S. pneumoniae	2 (1.1%)	2 (10%)	1 (8.3%)	0	
H. influenzae	2 (1.1%)	0	0	0	
Staph aureus	0	1 (5%)	0	0	
Gm -ve rods	1 (0.6%)	0	0	0	
E. coli	0	0	1 (8.3%)	0	
Klebsiella	1 (0.6%)	0	0	0	
S. pyogenes	1 (0.6%)	1 (5%)	0	0	

Table III: Neuro-imaging (n=34).

CT scan brain reporting	n (%)
Normal	14 (41%)
Basal meningeal enhancement	7 (20%)
Infarct	5 (14.7%)
Prominent ventricular system	5 (14.7%)
Hydrocephalus	2 (5.8%)
Subdural effusion	1 (2.8%)

associated with severe malnutrition (p=0.006), prolonged duration of symptoms (p=0.047) and altered conscious level at presentation (p= < 0.001).

The CSF appearance was turbid in 19 (9.5%), bloody in 9 (4.5%), and clear in 171 (86%). Gram staining was

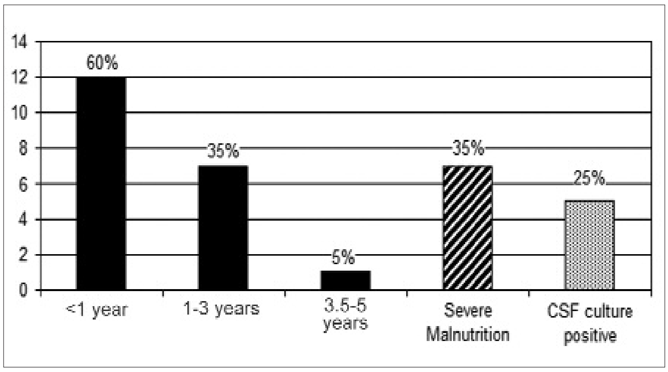

Figure 1: Deaths in children with acute bacterial meningitis in correlation with age, nutritional status and CSF culture positivity (n=20).

Table IV: Microbiological diagnosis based on Positive CSF cultures, according to age.

Age (years)	Positive CSF cultures n=24								
	CoNS	S.pneumoniae	H.influenzae	S.pyogenes	E. coli	G-ve rods	S. aureus	Klebsiella	Total
< 1 year	10	3	1	1	1	1	1	1	9
1-3 years	1	1	1	1	0	0	0	0	4
3.1-5 years	0	1	0	0	0	0	0	0	1
Total number	11	5	2	2	1	1	1	1	24
Percentage	5.5%	2.5%	1%	1%	0.5%	0.5%	0.5%	0.5%	12%

positive in 15 patients and showed both Gram-positive and Gram-negative organisms. CSF cell count was less than 1000 in 185 (93%), and only 14 (7%) showed cell count > 1000. CSF sugar level was < 40 mg/dl in 48 (24%), and 40 - 60 mg/dl in 99 (49.7%). CSF protein level was < 45 mg.dl in 39 (19.6%), 46-100 mg/dl in 73 (36.7%) and > 100 mg/dl in 87 (43.7%). The blood culture and CSF culture positivity was 12.6% and 12%, respectively. The common etiology beyond the neonatal period based on CSF culture is shown in (Table IV).

Majority blood culture 174 (87.4%) showed no growth. *coagulase negative staphylococci* (CoNS) was the predominating organism 16 (8%) isolated on blood culture followed by *pseudomomas* 3 (1.5%), *streptococcus pneumoniae* 2 (1%), *acinetobacter* 2 (1%), *klebsiella* and *staphylococcus aureus* 1 (0.5%) each.

Out of 199 patients, 20 (10.1%) patients died and 2 (1%) patients were shifted to neurosurgery ward for shunt surgery (Table I). The commonest pathogen isolated from CSF in children who died was *S. pneumoniae* (p=0.039) (Table II).

DISCUSSION

ABM is an important cause of mortality and morbidity in children. It carries a risk of fatal outcome or severe neurological deficit, especially when the diagnosis and the antibiotic administration are delayed.[1,2] The incidence of this disease is about 10 times greater in poor-resource countries, than that in well-resource countries.[7] The mortality rate caused by ABM remains significantly high and ranges from 16 - 32% in India and other developing countries.[8,9] Most often treatment for ABM has to be started before the etiology is known.

The disease pattern and bacteriology associated with acute bacterial meningitis were investigated in this study. The demographic analysis shows a high proportion of patients having male gender 127 (63.8%). A preponderance of males 1.8:1 was noted in an Indian study done by Dhrubajjoti *et al*., and a study from Pakistan (80% male).[10,11] A study by Qazi *et al*. also showed higher positivity in male children (60%).[12] This may signify the male dominance and sex discrimination in South-East Asia.

In this study, (68.3%) of our patients (n=136) were below 1 year of age, confirming that meningitis is more likely to occur in young children than in older children. Meningitis incidence is most strongly and consistently associated with young age as shown in a study by Iregbu *et al*., in which majority of children were under the age of 2 years.[13] This study is also consistent with study by Naz *et al*. in which (76%) were infants less than 12 months of age; but in a study conducted by Dhrubajjoti *et al*., only 46.8% of hospitalised children with meningitis were < 1 year of age.[10,11] Our 23.1% children were severely malnourished comparable with the results published by Khan *et al*., which showed grade III malnutrition in 27%.[14]

In this study, the microbial diagnosis of meningitis with CSF culture was confirmed in only 24 patients (12%). Our results were comparable with a study done by Guarav *et al*., in which CSF culture was positive in 13.94% cases.[15] A much higher percentage of 62.7% CSF culture positivity is reported in another study published by Kuti *et al*.[16] In our study, a high proportion (88%) of all meningitis cases grew no bacterial pathogen. This finding is consistent with a number of previous studies, suggesting that the negative cultures are not the result of limitations in routine microbiology laboratory procedures.[13,15] The negative cultures more likely are due to the widespread use of antibiotics (including inappropriately chosen or dosed antibiotics).

The pathogen spectrum identified on CSF culture according to age group is shown in Table IV. This study identified culture positivity in 24/199 patients (12%) and CoNS was the most common organism isolated, followed by *streptococcus pneumoniae* 5, *H. influenzae* and *streptococcus pyogenes*. Maximum number of CSF cultures positive for CoNS may be due to skin contamination and improper sterilization technique used at the time of lumbar tap. In this study, second commonest pathogen isolated was *streptococcus pneumoniae;* and this was consistent with a Korean study, in which *streptococcus pneumoniae* was the commonest pathogen isolated in post-neonatal age group.[17] Pneumococcal Conjugate Vaccine (PCV) was included in Pakistan National Immunisation Program by the end of 2012. Majority of children in whom *streptococcus pneumoniae* was isolated were either unvaccinated or only had partial vaccination 60%. A study by Raj *et al*. showed *streptococcus pneumoniae* as the commonest organism followed by *klebsiella*.[18] Reports from Third World communities of Asian sub-continent have described a greater etiologic role of *staphylococcus aureus*.[13-15] Previous literature reviews describing bacterial organisms isolated from children with meningitis, suggest that Gram-positive as well as Gram-negative organisms may invade the CNS.[14-16,18]

Acute neurological complications were noted in 34 patients (17%). Similar results were seen with 20% complications rate in a study published by Cho *et al*.[17] Multiple studies demonstrated a much higher percentage of complications as compared to our study; (43%, 35%, 42%) patients developed acute neurological complications during the hospital course.[1,11,16]

The case-fatality rate in our study was 10.1%, close to that (9.5%) reported in a Korean study, yet much lower than that detected (19%) by Khan and Kuti *et al*., in which 27.2% children died.[14,16,17]

CONCLUSION

The present study found that ABM is a serious disease resulting in neurological complications and mostly affecting children < 1 year of age with a male preponderance. CSF culture revealed both Gram-positive and Gram-negative bacteria. CoNS and *streptococcus pneumoniae* were the most common pathogens. There is an increased risk of acute complications in patients with severe malnutrition, prolonged duration of symptoms, and altered mental status at presentation. The mortality due to ABM was observed mostly under one year of age and the commonest bacterial pathogen isolated in these cases was *streptococcus pneumoniae*.

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