Original Research Article

Clinical profile and outcome of pediatric bacterial meningitis: a prospective study from tertiary institute in Northern India

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ABSTRACT

Background: Meningitis is one of the fatal infections occurring in infants and older children. In acute bacterial meningitis (ABM), inflammation of the leptomeninges is triggered by bacteria present in the subarachnoid space. ABM is associated with a high rate of acute complications and long-term morbidity. Aim of our study was to determine the incidence, etiological profile and complications of acute bacterial meningitis amongst children belonging to one month to five years of age.

Methods: The present study was conducted over a period of one year and diagnosis of meningitis was made on basis of history, examination and laboratory investigations. Clinical features were recorded on case sheet. Lumbar puncture was done, and CSF was sent for biochemical analysis, cell counts, staining, culture and latex agglutination test (LAT).

Results: Out of total 1560 admitted cases (1 month to 5 years age group), 160 cases were suspected with meningitis while 57 cases were confirmed to have ABM. Most (59.6%) cases belonged to 3 months to 1-year age group and males outnumbered the females by a ratio of 2:1. Group B Streptococcus (45.6%) was most common pathogen in 45.6% cases followed by Streptococcus pneumoniae (21%) and Hemophilus influenzae (10.52%). Seizures (45%) and increased ICP (28%) were main acute complications observed during hospitalization while hemiparesis 9.6%, monoparesis 4.8%, seizures 38%, vision and hearing deficits were the sequelae observed on follow up examination. These complications were predominantly contributed by S. pneumoniae and H. Influenzae.

Conclusions: The incidence of ABM is still high and Group B streptococcus is main pathogen even in post neonatal period. The complications of ABM are markedly higher in cases of S. pneumoniae, H. Influenzae meningitis in comparison to Group B streptococcus meningitis. Formulating standard protocols for management of ABM and rational antibiotic use to prevent resistance is the need of hour.

Keywords: Bacterial, Complications, Hemophilus, Meningitis

INTRODUCTION

Brain is normally a sterile organ that is protected from outside by bony skull and from inside by blood brain barrier. Vulnerability of the brain to infections is related to breach in BBB and deficient host defenses leading to multiplication of pathogens. Further altered cerebral blood flow, increased intracranial pressure (ICP), brain tissue inflammatory process and limited repair mechanism of neuronal tissue manifest into complications and late sequelae.¹ Acute bacterial meningitis (ABM) is an inflammation of the leptomeninges triggered by bacteria present in the subarachnoid space.¹ The community prevalence of ABM is between 3/100,000 in USA, 16/100,000 in UK to 45.8/100,000 in Brazil. According to Indian records 0.5 to 2.6% of hospital admissions are of ABM. In developed countries (with best available facilities), the cases fatality
rate is 10% while it is 16-30% in India and other developing countries.2

Most common pathogens during first two months of life are Groups B and D streptococci, gram-negative enteric bacilli and Listeria monocytogenes. While 2 months to 12 years children are primarily infected by S. pneumoniae, N. meningitidis, or H. influenzae type b.3 Prior to immunization, Pneumococcal and H. influenzae meningitis was common.4 Pneumococcal conjugate vaccination and H. influenza type b vaccination in developed countries has declined this rate drastically.5 But in India and other developing countries these pathogens are still the major cause for ABM.5

For early diagnosis, clinical signs and symptoms are of utmost important. In infants, these features may be subtle, variable, nonspecific or even absent. Infants usually present with fever, lethargy, irritability, poor feeding, vomiting, diarrhea, respiratory distress, seizures and bulging fontanel. In older children; fever, headaches, photophobia, nausea, vomiting, confusion, lethargy, seizures or irritability are key symptoms. Kernig sign, Brudzinski sign, focal neurological signs and increased intracranial pressure are various signs found on examination. The constellation of systemic hypertension, bradycardia and respiratory depression (Cushing’s triad) are late signs of increased intracranial pressure.6

Diagnosis of ABM is established by analysis of cerebrospinal fluid (CSF), which reveals microorganisms on gram stain/culture, neutrophilic pleocytosis on wet mount examinations, elevated proteins and reduced glucose concentration on biochemistry. CSF culture is gold standard, but it requires 18-24 hours for bacterial growth hence delaying the etiological diagnosis. Moreover, not all cultures yield positive growth due to various reasons. Gram staining demonstrates the organisms in only 25-30% of the cases whereas the blood culture is positive in about 80-90% of cases.7

Bacterial meningitis requires early diagnosis and empirical antibiotic treatment. In recent years various rapid antigen detection techniques have been developed including latex particle agglutination, electrophoresis, radioimmunoassay and enzyme linked immunosorbant assay. These tests detect the presence of bacterial antigens present consistently in the CSF. Latex agglutination test is the most popular and widely used one.3 Diagnosis of ABM is based primarily on clinical and CSF findings. Neuroimaging (CT or MRI) is useful for detecting and monitoring the complications of meningitis. Various complications are hydrocephalus, brain abscess, cerebritis, cranial nerve palsy, thrombosis, infarct, ventriculitis, vasculopathy and extra-axial collection.9

Prompt diagnosis and adequate treatment of ABM in children remains a major challenge, as reflected by the continued high morbidity and case fatality rates of the disease worldwide. Antibiotics should be bactericidal against the common organisms, capable of penetrating blood brain barrier and should be effective in the milieu of subarachnoid space.10 Further bactericidal concentration should reach 10-30 times higher than the minimal bactericidal concentration for maximum effectivity. So appropriate use of antibiotics, along with adjunctive therapies, such as dexamethasone has proved beneficial to minimize the risk of severe morbidity and mortality besides reducing the emergence of multi drug resistant organisms.11

Severe neurodevelopmental sequelae occur in 10-20% of patients recovering from bacterial meningitis and as many as 50% may have some neurobehavioral morbidities. The most common neurological sequelae include hearing loss, behavioural problems and learning disabilities.2 Numerous studies have been done on the sequelae of bacterial meningitis in children but very few are from developing nations.3

METHODS

The aim of our study was to determine the incidence, etiological profile and complications of acute bacterial meningitis amongst the hospitalized children in the age group of 1 month to 5 years. The proposed study was conducted in the Department of Pediatrics, Indira Gandhi Medical College Shimla over a period of one year from November 2012 to October 2013.

Well informed consent was taken from the parent/guardian prior to proceeding for study. The diagnosis of meningitis was made on the basis of clinical history, examination and laboratory investigations. The clinical features suggestive of presumptive meningitis were: Fever of any duration, temperature >38.5°C, one or more of the following symptoms or signs: hypothermia, lethargy, irritability, poor feeding, vomiting, bulging fontanels, altered sensorium varying from drowsiness to coma, headache, vomiting, prostrations, history of convulsions (focal or generalized), meningeal signs, papilloedema, cranial nerve palsy and motor weakness of the limbs. CSF samples were obtained in sterile test tubes/ screw capped bottles and sent for biochemistry, cytology, latex agglutination test, gram staining, AFB staining, culture sensitivity. Lumber puncture was done for CSF analysis in all clinically suspected cases of ABM. CSF parameters showing 1) polymorphonuclear pleocytosis (>100 leucocytes permm3 with predominantly polymorphonuclear cells) with or without 2) CSF biochemistry suggestive of ABM (CSF glucose <40 mg/dl or <50% of the serum glucose levels and CSF proteins >100mg/dl) were taken as diagnostic parameters. In partially treated cases or in those cases where above parameters were not fulfilled, CSF was sent for gram staining and antigen detection by Latex agglutination test. Further, culture of pyogenic organism was done on CSF and blood sample to confirm the diagnosis of ABM in such cases. Old cases of meningitis treated outside the
hospital before referral, children suffering from chronic illness or malignancy and children on immunosuppressive drugs, post-operative and post lumbar puncture cases were excluded out from the study.

RESULTS

A total of 1560 children (1-59 months) were admitted in Pediatric ward during study period, 160 were suspected to be suffering from meningitis while 57 cases were diagnosed as ABM. Maximum cases (59.6%) were in the age group of 3 months to 12 months (Figure 1). Males outnumbered the females by a ratio of 2:1 (Figure 2).

LAT showed maximum positivity in 47(82.45%) cases followed by CSF biochemistry which was positive in 36 (63%) cases. Gram staining was positive in 5 (8.7%) cases while bacteria were grown in CSF culture only in 2 (3.5%) cases (Figure 3). Blood cultures were sent in 45 cases and growth of organism was found in 17.5% cases of ABM (Figure 4).

Among etiological agents most [n=26 (45.6%)] cases were caused by Group B streptococci followed by Streptococcus pneumoniae [n=12 (21%)] and H. influenza [n=6 (10.52%)]. Less common pathogens were also found as shown in the figure 5 but in 9 (15.78%) cases, pathogen couldn’t be isolated.

In hospitalized cases seizures were observed in 26 (45.62%) cases followed by raised intracranial pressure in 16 (28%) cases and coma in 6 (10.5%) cases (Figure 6).
Other complications were infarct on imaging [4 (7%)], hydrocephalus [2 (3.5%)] and subdural effusions [3 (5.26%)]. Out of 57 cases of ABM, 89.5% got discharged and 6 (10.5%) died thus showing a high case fatality rate of 10.5% (Figure 7) although this was statistically insignificant.

On examination various complications were encountered among these patients. Seizures, cranial nerve palsies and developmental delay were main sequelae observed in 38%, 31% and 26.2% cases respectively. Other complications were vision impairment, hearing deficit, hemiparesis and monoparesis as shown in Figure 8.

In all followed up patients etiological profile was reviewed parallel to various complications. It was found that 2 cases of hemiparesis had underlying Streptococcus pneumoniae infection, 1 case had Hemophilus influenza infection while 1 remained with unidentified etiology. In monoparesis patients (n=2), one case was secondary to Streptococcus pneumonia and second was associated with Group B streptococcus. Statistical difference was not significant 5 (0.24) in both monoparesis and hemiparesis etiology.

Streptococcus pneumonia was underlying agent in all patients (n=2) of extrapyramidal movements with statistically insignificant results of 5 (p=0.24). While studying etiological profile of seizures patients (n=16), it was found that 3 out of 13 Group B streptococci cases, 5 out of 6 H. influenza cases and 7 out of 10 Streptococcus pneumoniae cases developed seizures on follow up examination. The statistical difference was found significant (5) with p value of 0.01. Amongst hearing deficit cases (n=4), underlying pathogens were mainly H. influenzae (3/6) and Streptococcus pneumonia (1/10) carrying a significant statistically difference value of 5(p=0.01). Streptococcus pneumoniae (4/10) and H. influenzae (2/6) were found as main underlying pathogens responsible for vision impairments in 6 (14.3%) cases. The statistical difference (5) was found significant with p value of 0.04.

On follow up examination, 13(31%) patients had one or other cranial nerve palsies. On reviewing the underlying causative pathogens it was found that most cases were secondary to Streptococcus pneumoniae [(5)11.5%] and H. influenzae [(2) 4.8%].

Group B streptococci, Klebsiella and E. coli were other less commonly found pathogens. Developmental delay was found in 11 (26.2%) patients of ABM and etiological profile revealed that 6/10 streptococcus pneumoniae cases and 3/6 H. Influenza cases and 2 patients of unknown origin meningitis were having developmental delay on follow up. This finding was statistically significant with a p value of 0.01.

### Table 1: Follow up of ABM.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Done</td>
<td>42</td>
<td>73.68</td>
</tr>
<tr>
<td>Not done</td>
<td>15</td>
<td>26.31</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Three monthly follow up visits were advised to patients to look for long term sequelae of ABM. 42 (73.68%) patients revisited our institute while 15 (26.31%) cases were lost on follow up examination (Table 1). Out of these 42 cases, 22 (52.38%) cases presented/revisited within 3 months after discharge, while 14 (33.33%) patients showed back between 3 to 6 months after discharge and only 6 (14.29%) cases came after 6 months of discharge.
**DISCUSSION**

In developed countries incidence of pyogenic meningitis has declined after pneumococcal and *H. influenzae* vaccination. Since vaccination against *H. influenzae, S. pneumoniae* and *N. meningitidis* is not done in developing countries so a higher incidence of ABM is still there. In our study, ABM constituted 3.6% of hospital admissions in the age group of 1 month to 5 years. Incidence rate between 0.5-3.5% has been reported in other studies also.12,13

In our study, prevalence of ABM was more (59.6%) in the age group of 2 months to 12 months of age in accordance with study by Mani et al.14 Prevalence rate amongst below one-year age group has been reported as 77%, 65% and 75% and 61% by various authors.2,15-17 Males outnumbered the females by a ratio of 2:1 indicating male preponderance of ABM in our study in accordance with other studies.12,14,16 Relative resistances to infection in females is related to certain factors regulating the synthesis of gamma globulin on X chromosome, thus explaining the preponderance for meningitis and septicemia amongst males. In our study, bacterial agents (*S. pneumoniae, H. influenzae type b, Klebsiella pneumoniae*) were found only in 5 (8.7%) cases on grams staining. While, Bhat et al and Surinder et al demonstrated bacteria on grams staining in 53%, 36% and 16.9% cases respectively.19,20 CSF culture sensitivity was positive only in two out of 57 cases. Prior use of antibiotics (in most cases), poor method of sample collection, poor transportation and poor quality of culture media in our setup were assumed the reasons for poor results of our study in comparison to other studies.

Most cases [n=26 Group B Streptococcus, n=5 *H.influenzae type b, n=10 S. pneumoniae, n=1 N. meningitides and n=1 Klebsiella pneumonia)] were diagnosed by latex antigen detection tests. Das et al and Chinchankar et al detected meningitis by LAT in 83% and 66% respectively in accordance to our study.21,2 The etiological agents were identified as GBS [n=26(45.6%)], *H. Influenzae* [6(10.52%)], *S. Pneumoniae* [12(21%)], *Klebsiella, Staphylococcus aureus, N. Meningitidis* and *E. coli* [1(1.75%)] for each in 46 cases while in 9(15.78%) cases, organism couldn’t be identified. In above mentioned studies *S. pneumoniae* was commonest pathogen while in our study it was Group B Streptococcus in 26 (45.6%) cases.19,20 Although GBS is a common cause of ABM in neonates, but it can also infect children in postneonatal period.8 Florindo et al, Dwivedi reported, 60, 27 and 5(17%) cases of Group B streptococcus meningitis in post neonatal period.12,23 It is worth noticing that out of 26 cases of GBS meningitis 23, were diagnosed purely on the basis of LAT while only three (11%) had CSF findings suggestive of ABM in addition to LAT. Baker et al, also documented LAT to have high sensitivity for GBS as compared to culture.24 In our study, only one case of *N. Meningitidis* was detected indicating its low prevalence except during epidemics as stated in various Indian studies by Mani et al and Chinchankar et al.11,2

Bacteria reach meninges through hematogenous route further bacteremia has been reported in patients of ABM. This has been documented by Kabra et al and Mani et al in their studies.13,14 In the present study, blood culture could be sent only in 45 (61.40%) cases. The blood culture positivity was found in 10 (17.54%) cases for the agent found positive on LAT. Only in one case *staphylococcus aureus* and in another case *E. coli* was grown on culture alone with negative LAT positivity, CSF biochemistry and cytology. Chinchankar et al, also established the diagnosis of ABM in 2 cases from blood
culture with sterile CSF report.\textsuperscript{2} The reason for bacterial positivity in blood but not in CSF can be explained by the fact that in early stage bacteria are more in blood than in CSF. Thirty-five blood cultures were sterile in the laboratory and this can be explained by the fact that most of the patients were already on antibiotics on arrival to the hospital. These findings correlate with those observed by Backer et al.\textsuperscript{24} The complication rate of ABM is too high in spite of aggressive management of hospitalized patients. In our study almost 45\% of patients had one or more acute complications including seizures, increased ICP, hydrocephalus, infarct and subdural effusion. Similar rate of acute complications was reported by Chinchankar et al, Bhat et al and Goetghebeur et al.\textsuperscript{2,19,25}

Out of total 57 cases of ABM 51 (89.7\%) were discharged and 6 (10.5\%) cases died inspite of best available treatment. The case fatality rate in developing nations including India has been reported between 10-30\% by various authors.\textsuperscript{19} Approximately one third mortalities occurred during first 48 hours reflecting the critical condition of the patients at admission. Even in developed nations with best available facilities case fatality rate is around 10 \%.\textsuperscript{27}

Out of 57 cases, only 42 (73.68\%) patients could be followed up, rest 15 (26.31\%) were lost on follow up examination (not statistically significant). Amongst them 22 (52.38\%) were followed up at a gap of less than 3 months after discharge, 14 (33.33\%) patients between 3 to 6 months after discharge and only 6 (14.29\%) could be followed up after 6 months of discharge. The time of follow up was very early in comparison to the studies by Sighi et al and Chinchankar et al where time ranged between 27.2 and 1-3 yrs respectively.\textsuperscript{3,2} The compulsion to complete follow up within a stipulated time of thesis submission was the major factor to determine the complication rate on follow up. The reported worldwide frequency of neurological sequelae has varied from 10-50\%, but from the developed world it is around 10-20\%.\textsuperscript{28-30}

We could complete follow-up examination in 42 patients, out of them 4 (9.6\%) patients had hemi paresis. Chinchankar et al found hemiparesis in four (7.4\%) patients initially which decreased to two patients on follow up at 1-3 years. The rate of hemiparesis in another study done by Singh et al, was 25\% among affected patients that reduced to 8 (10\%) on follow up examination.\textsuperscript{3} The rate of hemiparesis in our study is 9.6\% in accordance with above mentioned studies. The rate of monoparesis was 2 (4.8\%) on follow up in our study, these both findings were statistically insignificant. 16 (38\%) patients had seizure disorders on follow up examination. As per etiology 3/13 of GBS, 5/6 H. Influenza patients and 7/10 patients of streptococcus pneumoniae cases developed seizures on follow up. This finding was statistically significant with \textit{p} value of 0.01. It can be inferred that streptococcus pneumoniae was main pathogen complicating into seizures. This fact was supported by meta-analysis done by Bedford et al, Oostenbrink et al.\textsuperscript{30,31} The rate of hearing deficit has been described between 9%-30\% in various studies and we found in 4 (9.20\%) cases.\textsuperscript{2,3} H. Influenza (3/6) and (1/10) streptococcus pneumoniae were found as key pathogens with statistically significant \textit{p} value (0.01). This finding reiterates the known fact of increased predisposition for hearing loss in \textit{H. influenzae} meningitis as suggested by Prober et al.\textsuperscript{11} Six patients (14.3\%) had some form of vision impairment with statistically significant \textit{p} value (0.04). Singh et al found vision impairment in 2 (6.3\%) cases which was less than in our study.\textsuperscript{3} This discrepancy can be explained on the basis of time of follow up which was in weeks to months in our study while in years in other studies.

In our study 13 (31\%) patients were having one or other cranial nerve palsy is on follow up examination. Amongst them 5/10 had \textit{Streptococcus pneumoniae}, 2/6 \textit{H. Influenza} and each one had GBS, \textit{Klebsiella} and \textit{E. coli} as underlying causative agents. The statistical difference was found significant with \textit{p} value of 0.05. This shows that rate of complications including cranial nerve palsy are more with \textit{Streptococcus pneumoniae} and this fact is further supported by meta-analysis done by Bedford et al, and Oostenbrink et al.\textsuperscript{30,31} Our 2 (4.8\%) patients developed extrapyramidal movements in accordance with study by Singh et al, who found this complication in 3.1\% of patients.\textsuperscript{2} Developmental delay was found in 11 (26.2\%) patients on follow up and this observation was statistically significant with a \textit{p} value of 0.01. Our results are in accordance with other studies showing developmental delay in 23\% and 31\%.\textsuperscript{3,5}

**CONCLUSION**

We conclude that the incidence of meningitis is still high probably due to low practice of vaccination against common causative agents such as \textit{S. pneumoniae}, \textit{H. Influenza}. Group B streptococcus has strongly emerged as a causative agent of ABM even in post neonatal period. Diagnosis of ABM can be best established by CSF Latex agglutination test, biochemistry, cytology. Early diagnosis and aggressive management is essential to prevent complications. The complications of ABM are markedly higher in cases of \textit{S. pneumoniae}, \textit{H. Influenzae} meningitis in comparison to Group B \textit{streptococcus meningitis}. The rate of hearing deficit is conspicuously higher with \textit{H. influenzae} meningitis.

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**REFERENCES**
