BACTERIOLOGICAL PROFILE OF PATIENTS WITH ACUTE PYOGENIC MENINGITIS - A HOSPITAL BASED STUDY

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ABSTRACT

BACKGROUND

Pyogenic meningitis is one of the most common infectious disease emergencies involving the central nervous system with higher incidence in developing countries than developed nations. Despite the large number of pathogens that have been reported to cause acute pyogenic meningitis, certain microorganisms are isolated with higher frequency depending on patient's age, immune status and geography.

Present study was aimed to determine the trends in aetiology and spectrum of the bacteriological profile in adult patients with suspected pyogenic meningitis in North-East India.

MATERIALS

50 CSF samples from as many patients of Acute Bacterial Meningitis over a period of one year were processed for cell counts, biochemical analysis, gram staining, culture, antigen detection by latex agglutination test and antibiotic susceptibility tests, as per standard techniques.

OBSERVATION

CSF cell counts showed neutrophilic predominance in all cases along with high protein and low sugar levels. 44% of the cases were culture positive and latex agglutination test was positive in 46.4% of the cases where culture was negative. S. pneumonia was the predominant pathogen identified in the present study in 12(24%) cases, followed by Pseudomonas and E. coli in 5(10%) cases each. Gram stain indicated the causative organisms in 68.2% of the culture positive cases. Among the culture negative patients gram stain indicated the causative organism in 3(10.7%) cases and these three cases were positive by LAT also.

CONCLUSION

Simple, rapid, inexpensive tests like gram staining remain significant means for diagnosis of acute pyogenic meningitis in developing countries. LAT goes a long way in identifying the organisms where the cultures are negative. This study thus paves the way for larger studies in this region for better recognition of the predominant organisms and the empirical antibiotic regimens.

KEYWORDS

Cell count, Emergencies, E. coli, Bacterial meningitis, Gram staining.

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INTRODUCTION: Acute infections of the nervous system are among the most important problems in medicine because early recognition, efficient decision-making, and rapid institution of therapy can be lifesaving. These distinct clinical syndromes include acute bacterial meningitis, viral meningitis, encephalitis, focal infections such as brain abscess and subdural empyema, and infectious thrombophlebitis.[1] Key goals of early management are to emergently distinguish between these conditions, identify the responsible pathogen, and initiate appropriate antimicrobial therapy.[2] Bacterial meningitis is an acute purulent infection within the sub-arachnoid space associated with a CNS inflammatory reaction that may result in decreased consciousness, seizures, raised intracranial pressure (ICP), and stroke. The meninges, the subarachnoid space and the brain parenchyma are all frequently involved in the inflammatory reaction (meningoencephalitis). Acute bacterial meningitis (ABM) is at least ten times more common in developing countries than in the rest of the world.[3,4] Despite advances in vaccine development and chemoprophylaxis, bacterial meningitis remains a major cause of death and long-term neurological disabilities in India as well as other developing countries. Variation in etiological profile is noted with time and geography.

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Increase in awareness, availability of vaccines may also reflect a change in the epidemiological pattern of these pathogens. The etiological agents of community acquired meningitis may differ from hospital acquired meningitis. Thus, there is a need for a periodic review of bacteriological profile of acute pyogenic meningitis worldwide, and regionally.

This study was therefore aimed to know the trends in aetiology and the spectrum of the bacteriological profile in adult patients with suspected pyogenic meningitis admitted in Medicine department of a tertiary care teaching hospital of North-Eastern India.

MATERIALS AND METHODS: The present study, which was approved by our Institutional Ethics Committee, was a hospital based prospective observational study conducted from 1st June 2014 to 31st May 2015.

The patients were assessed for acute meningitis, based on the following clinical signs and symptoms: headache (not relieved by analgesics), nausea or projectile vomiting (not relieved by antiemetics), low or high-grade fever of acute onset which lasted for several days, delirium or altered consciousness, mental apathy, neck rigidity, a positive Kernig's sign, opisthotonos, etc.

Inclusion Criteria: Patients aged > 13 years with clinical signs and symptoms compatible with a diagnosis of meningitis attending OPD and emergency department of Medicine; and Cerebrospinal fluid (CSF) with neutrophilic pleocytosis of at least 100 neutrophils/mm^3; and/or a positive CSF culture for bacterial pathogens and/or a positive Latex agglutination test (LAT) for antigen detection.

Exclusion Criteria: Post-traumatic meningitis, meningitis developing after cranial surgery and cases of nosocomial meningitis.

Lumbar puncture was performed aseptically on the patients and cerebrospinal fluid (CSF) was collected in sterile screw capped containers and subjected to the following tests: - Macroscopic examination, Cytological examination, Gram staining of CSF smear, CSF Culture and LAT for antigen detection.

In the present study criteria for a definite diagnosis of pyogenic meningitis were as follows:

1. A positive culture of bacterial pathogen(s), or
2. A positive LAT for antigen detection, or
3. Clinical features of meningitis including fever, consciousness disturbance, seizures or signs of meningeal irritation and
4. Purulent CSF feature including at least one of the following:
   - Polymorphonuclear (PMN) leucocytosis (>100 cells/microL),
   - Protein concentration [>0.45 g/L (>45 mg/dL)],
   - Decreased glucose concentration [CSF/serum glucose ratio of <0.4 and/or CSF glucose <2.5 mmol/L (<40 mg/dL) if no simultaneous blood glucose level was determined].

50 cases after fulfilling the inclusion and exclusion criteria were included in the study and analysed.

Data were analysed by SPSS version 17.0 software and p value <0.05 were considered as statistical significance.

RESULTS AND OBSERVATIONS: In the present study, 50 patients fulfilling the inclusion and exclusion criteria within the study period were included in the study group. The age of the study group ranged from 15 - 70 years with a mean of 35.46±7.39 years (Table 1). Maximum number of cases were in 31–50 years (62%) age group followed by the elderly (>60 years) age group (14%) with male: female ratio of 2.33: 1(Fig 1). Most of the patients were of low socio-economic strata (76%) (Fig. 2).

Age group (years)	No. of patients	Percentage
12-20	3	6%
21-30	4	8%
31-40	21	42%
41-50	10	20%
51-60	5	10%
>60	7	14%
Mean±	35.46±7.39	

Table 1: Distribution of ABM patients based on age groups

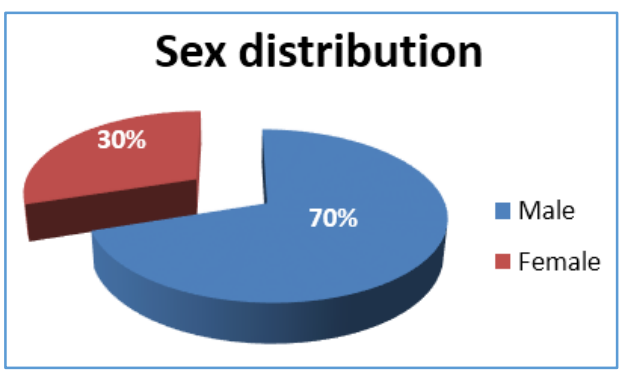

Fig. 1: Percentage distribution of patients of ABM based on sex

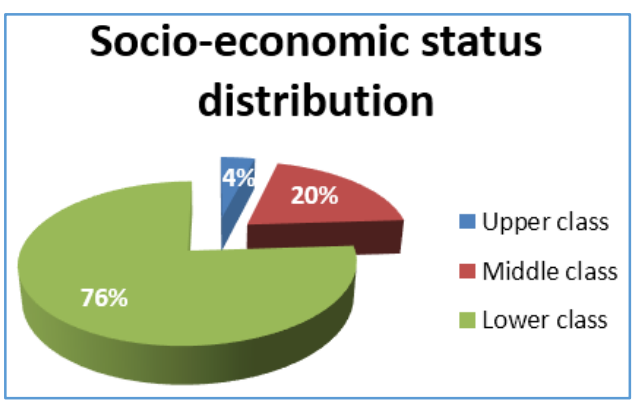

Fig. 2: Socio-economic distribution of the patients

Fever (98%), headache (96%), neck stiffness (90%), nausea (94%) and vomiting (94%) were the common clinical features. 10 patients (20%) had altered sensorium while 7 patients had seizures (14%). Hypotension was noted in 6

patients (12%). Skin rash was seen in 5 (10%) of the cases. Presence of skin rash in 4 (80%, n=5) patients of meningitis correlated with a diagnosis of N. meningitidis (by LAT) (p<0.05).

Evidence for the presence of microbial activity could be detected in 50% cases by LAT, whereas a direct microbiological confirmation could be seen in only 22 cases (44%). CSF culture isolated Streptococcus pneumoniae in 8 (36.36%, n=22) cases, followed by Pseudomonas aeruginosa in 5 (22%), Klebsiella pneumoniae in 04 (18.18%) and E. coli in 03 (13.63%) cases. Other bacterial isolates were Staphylococcus aureus and H. influenza, 01 (4.55%) case each (Fig. 3). Culture positivity in the series was 80% (20, n=25) in the cases without prior exposure to any broad spectrum antibiotic (p<0.01) [Table 2]. LAT was positive in all cases of the present series which were picked up by the gold standard, CSF culture while among the culture negative cases LAT was positive in 46.4% (n=28). Among the culture negative cases, LAT identified Pneumococcus antigen in 4 cases, N. meningitidis A in 4 cases, H. influenza type b and E. coli in 2 cases each, and, another case of Gr. B Streptococcus was LAT positive (Fig 4). CSF LAT was more sensitive than serum LAT in concurrently drawn serum samples (Fig. 5).

	Culture +	Culture -	Total	
Prior antibiotics	5	20	25	P<0.05
No. prior antibiotics	17	8	25	
Total	22	28	50	

Table 2: Culture positivity according to prior use of antibiotic

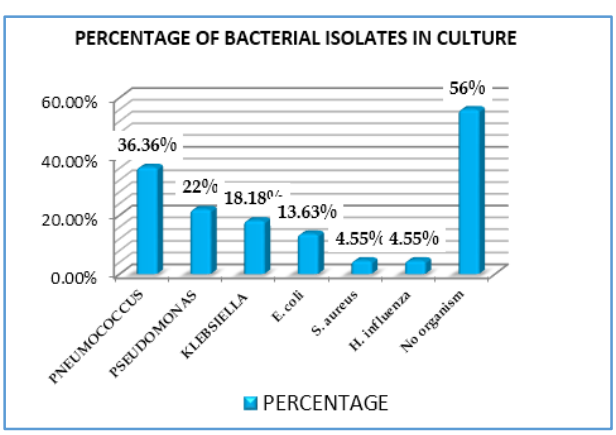

Fig. 3: Etiological agents isolated in culture positive CSF samples (n=22)

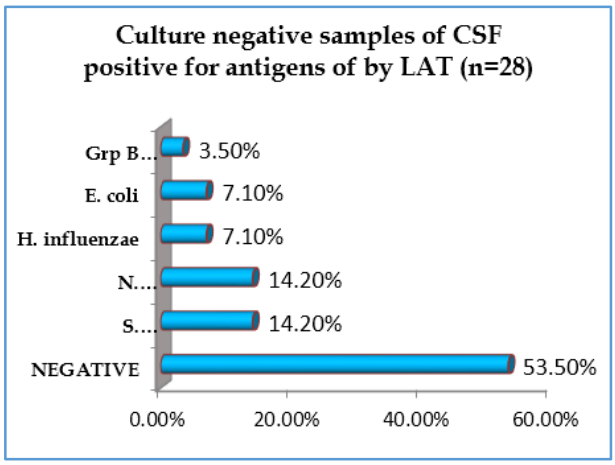

Fig. 4: Culture negative samples of CSF positive for antigens of by LAT (n=28)

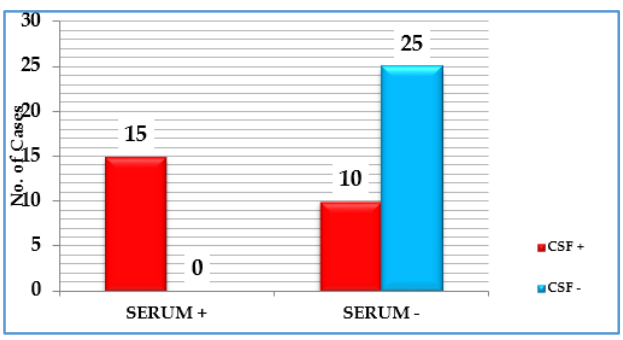

Fig. 5: Comparative analysis of CSF LAT vs. Serum LAT for antigen detection

Gram stain indicated the causative organisms in 68.2% of the culture positive cases (p<0.001). Among the culture negative patients gram stain indicated the causative organism in 3(10.7%) cases and these three cases were also positive by LAT (Table 3).

	Culture +	Culture -	Total	
Smear $_+$	15	3	18	P<0.05
Smear -	07	25	32	
Total	22	28	50	

Table 3: Correlation of smear and culture findings in ABM

Majority of the isolates (68.18%) displayed a cell count ranging from 1001 to 5000/mm^3.

S. pneumonia was the predominant pathogen identified in the present study in 12(24%) cases, followed by Pseudomonas and E. coli in 5(10%) cases each, Klebsiella and Neisseria in 4(8%) cases each, H. influenza in 3(6%) cases and S. aureus and other Grp B Streptococcus in 1(2%) case each. Neither of the cases with Neisseria meningitidis yielded growth in culture but all were positive by LAT.

56% (28) of the patients had one or more predisposing factors identified in the study. Alcoholism was present in 40% (20) followed by Diabetes mellitus in 30% (15) of the cases. Other risk factors identified were Pneumonia (10%), Chronic otitis media (8%), Endocarditis (4%) and altered immune state (4%). Two patients with altered immune

status in the present study were a case of HIV+ status and a Chronic liver disease patient, respectively.

A cranial CT was performed in 40 (80%) patients of which 25% (10) had abnormalities related to meningitis or its complications – ventriculomegaly or hydrocephalus (1 patient), cerebral oedema (3 patients), meningeal enhancement (3 patients), cerebral infarct (2 patients) and subdural empyema (1 patient). Infarct that was not apparent on the admission CT scan was seen on later CT scan (72 hours after admission) in one patient.

5(10%) patients expired during the course of the study. Causative organism couldn't be identified in any of these cases. Out of these five patients 4 (80%) were above 60 years of age, 3 (60%) of these patients had seizures within 24-hr of admission, all of these patients were obtunded on admission and were known alcoholic.

DISCUSSION: Acute bacterial meningitis is a medical emergency, which warrants early diagnosis and aggressive therapy. Mostly, therapy for bacterial meningitis has to be initiated before the aetiology is known. The choice of initial antibiotics therapy is based on the most common pathogens prevalent in geographical area, age group and antibiotic susceptibility pattern.

As it is a hospital based study, true prevalence and incidence of acute bacterial meningitis are difficult to define in general population. This is probably due to the fact that most of the cases give history of prior use of broad spectrum antibiotics before reaching a tertiary health care centre thus resulting in lesser culture isolates or gram stain positivity. Delay in transport of specimens to the laboratory, non-availability of special media for specific pathogens in the emergency setting, autolysis of enzymes in CSF, fastidious nature of pathogen are the other reasons for poor microbial isolation.[5,6]

50 patients were found to have acute pyogenic meningitis in this period. Maximum number of cases was in 31 – 50 years (62%) age group followed by the elderly (>60 years) age group (14%). These two age groups had the maximum prevalence of the predisposing factors for acute pyogenic meningitis viz. Diabetes mellitus, alcoholism, etc. and this was comparable to various studies.[6,7] Males in this study group suffered 2.33 times more frequently than that of the females and this male preponderance has been reported in various previous studies.[7,8,9] The disease was more prevalent in low socioeconomic families of the society (76%) and this correlated with other previous studies.[10]

Presence of microbial activity could be detected in 50% cases by LAT, whereas a direct microbiological confirmation by CSF culture could be seen in only 22 cases i.e. 44%. This was comparable to various studies done previously.[9,11] The relatively high positivity of LAT in our study was probably because a sizeable proportion of the patients in this series received prior antibiotic which was also seen in various other studies.[11,12] Several studies from India report a low CSF culture positivity, ranging from 6–50%.[13,14] Most of the patients turn to the tertiary care centre after taking treatment from local practitioners which may lead not only to culture negative results but also to lower isolation of H. influenzae, N. meningitidis, S. pneumoniae, S. agalactiae and Listeria monocytogenes which have not developed significant resistance to the usual antimicrobials. LAT was positive in all the cases in our study which were picked up by the gold standard, CSF culture which was comparable to various studies where they reported 100% correlation between the culture positive cases and the LAT results.[6,15] LAT was positive in 46.4% of the culture negative cases which was comparable with various Indian studies.[6,8,11] The correlation between gram stain positive results and culture positivity was 68.2%. Similar correlation was also reported in other studies.[5,9,11,16,17] The chances of recovery of bacteria in CSF goes up to 100-fold, if the CSF sample can be intensified by replacing conventional centrifugation with cytospin centrifugation[11,18] and this was used in the present study. Majority of the isolates (68.18%) displayed a cell count ranging from 1001 to 5000/mm^3. This finding was consistent with various studies.[6,9,13] Thus in developing countries like India, where there is a widespread hindrance to the possibility of culture isolation because of delay in transportation, prior antibiotic(s) use, limitations in culture isolation facilities including lack of special media and techniques, simple and rapid tests like gram staining, CSF pleocytosis and antigen detection tests would serve a greater purpose in identifying the disease and early administration of specific treatment.

S. pneumonia was the predominant pathogen identified in the present study, followed by Pseudomonas and E. coli. Klebsiella and Neisseria were identified in 4(8%) cases each, H. influenza in 3(6%) cases, S. aureus and other Grp B Streptococcus were identified in 1(2%) case each. Neither of the cases with Neisseria meningitidis yielded growth in culture but all were positive by LAT. Although S. pneumonia was the predominant pathogen individually in our study but an increasing prevalence of gram negative bacilli altogether (14 cases, 28%) was seen in this series. This was in contrary to the studies of the west where the most common pathogens causing ABM were Haemophilus influenzae, Neisseria Meningitides, Listeria spp. and Streptococcus respectively.[19,20] Although, the recent incidence of H. influenza meningitis in the west is in a decreasing trend after the introduction of the Hib vaccine.[21] The findings in our study are comparable to that of the studies by L M. Tang et al.[7] 1999, A Sonavane et al[13] 2008 and Rajesh Bareja et al[14] 2013, all of which reported an increasing prevalence of gram negative bacilli than that of other studies like Syamal Modi et al.[12] 2013, R Mani et al.[9] 2007 and Madhumita P. et al[6] 2011. The later studies reported predominance of organisms like S. pneumonia, H. influenza and Neisseria spp. predominantly in their study group. The difference in aetiology from the temperate West may be due to the fact that India is a semitropical country, where hardy bacteria like S. aureus and gram negative bacilli flourish, and the relatively more fragile bacteria like H. influenzae, N. meningitidis, S. pneumoniae, S. agalactiae and Listeria monocytogenes in comparison do not have a survival advantage. Secondly the predominance of patients from low

socio-economic status with poor hygiene, poor nutrition, alcoholism and thus decreased immunity gives an opportunity for these organisms to cause infection.

56% of the cases had one or more predisposing factors identified in this series. Alcoholism was most predominant followed by diabetes mellitus, pneumonia, chronic otitis media, endocarditis and altered immune status. These findings are consistent with the findings of other studies, probably explaining the basis for the increasing trend of prevalence of gram negative bacilli in these studies.[7,21]

Abnormalities related to meningitis or its complications were seen in 20% of the patients in CT Scan. 6 of 7 patients with seizures had evident CT scan abnormality related to meningitis whereas only 3 patients with no focal findings had such abnormality ($p<0.001$). These findings correlate with the CT findings of other studies.[21]

5(10%) patients expired during the study period. Causative organism couldn't be identified in any of these cases. This posed a dilemma of an aggressive infection in the setting of an unconfirmed pathogen, and was associated with a much higher mortality rate. Out of these five patients 4(80%) were above 60 years of age, 3 (60%) of these patients had seizures within 24-hr of admission, all of these patients were obtunded on admission and were known alcoholic. Deaths in similar profile of patients had been reported in other studies.[21,22] No relation with any isolated pathogens in this series could be traced which were successfully ascertained in two studies by Madhumita P. et al[6] 2014 and Moumita Adhikary et al.[16] 2013. CSF specimen from such patients in those studies maximally yielded L. monocytogenes in culture but the provisions for isolation of this microorganism was not available in our set up. The studies of Madhumita P. et al[6] 2014 and Moumita Adhikary et al[16]. 2013 reported maximum mortality in their series with Neisseria meningitidis infection. Mortality was ascribed predominantly to gram negative (pseudomonas, E. coli and klebsiella) bacilli in the study by M. A. Rabbani et al.[22] 2003.

CONCLUSION: Despite developments in microbiologic diagnostic techniques and advances in antibiotics, bacterial meningitis remains a serious disease with substantial mortality and morbidity.

The management of bacterial meningitis is particularly difficult in resource poor settings because of factors such as late presentation of the disease, a wide differential diagnosis, and the limited range of diagnostic facilities and therapeutic options.

The disease is mostly prevalent in the low socio-economic strata of the society. 31-50 years age group of patients and the elderly people constitute the most commonly suffering population. Most of the patients in these age groups have one or the other predisposing factors for ABM.

Diabetes, alcoholism and chronic ear infections are the most common predisposing factors for ABM.

Fever and headache are the dominant clinical features. Altered sensorium and seizures are associated with a poor outcome. Skin rash in patients with ABM correlates mostly with a diagnosis of meningococcal meningitis.

Culture isolation of organisms in developing countries has many limitations. Simple and rapid tests like antigen detection by LAT, gram stain and CSF cytological tests will serve a greater purpose in identifying the disease and early administration of specific treatment. LAT can be used in the peripheral set up to promptly identify the organism and start specific therapy.

Though S. pneumoniae is the predominant pathogen across all age groups there is increasing prevalence of gram negative bacilli other than N. meningitidis viz. Pseudomonas, Klebsiella and E. coli in our patients. Poor hygiene, poor nutrition, alcoholism and low socio-economic status of the people at large in India give an added opportunity for these organisms to cause infection.

Though the scope of this study is very vast and this study provides a lot of information on this important subject, there is need of more detailed studies with much larger group of population over a prolonged period of time with advanced culture isolation facilities catering to a wider group of causative organisms. This would more clearly establish the bacteriological profile of the patients with ABM in this part of the country and lay down a more authentic empirical antibiotic regimen for such patients.

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