Original Research Article

Clinical profile, bacterial profile and outcomes of acute bacterial meningitis in a tertiary care hospital– one year study

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ABSTRACT

Background: Bacterial meningitis is still one of the major causes of mortality and morbidity among all groups in developing countries. The mortality and prevalence of common pathogens has reduced in developing countries with implementation of successful vaccination against the pathogens. Laboratory surveillance of pathogens is crucial in formulating the empirical treatment guidelines and to identify the targets of immunization. The present study was undertaken to evaluate the clinical profile, bacterial pathogens and their antibiotic sensitivity pattern of the pathogens. The outcome of the cases was recorded and followed for six months to detect any neurological sequelae.

Methods: A one year prospective cross sectional study was done and all suspected cases of acute bacterial meningitis (ABM) were screened and confirmed by diagnostic criteria. Clinical features were recorded and entered into the case sheet. CSF culture was done and biochemical analysis and cell counts were performed. All the data was entered in Microsoft excel and analysed.

Results: A total of 547 cases were screened and 282 confirmed with 164 males and 116 females. 282 pathogens were isolated with 266 bacterial and 12 fungal isolates. Gram negative bacterial pathogens were predominant than gram positive. *Streptococcus pneumoniae* was the common isolate in the study followed by others like *S. aureus*, Coagulase negative *staphylococci* and *Acinetobacter* sp., *Escherichia coli*, *Klebsiella pneumoniae* and *meningococci*. *Candida albicans* and *Cryptococcus* sp. were fungal pathogens. Community acquired meningitis was commonest cause and seen in 51-60 years of age. Gram positive pathogens exhibited maximum sensitivity to vancomycin and linezolid whereas Gram negative pathogens to carbapenems.

Conclusions: There is an overwhelming need to formulate policies in the management of cases of ABM. The rationale use of antibiotics is necessary to prevent the development of antibiotic resistance. Hence minimizing the emergence of antibiotic resistance and its spread is necessary, which can be achieved by regular prevalence and antibiotic susceptibility studies.

Keywords: *Acinetobacter* sp., Acute bacterial meningitis, Antibiotic resistance, Cerebro spinal fluid, *Streptococcus pneumoniae*

INTRODUCTION

Acute bacterial meningitis (ABM) is one of the leading health conditions causing morbidity and mortality in all age groups. It is usually caused by bacteria, virus, fungi, and parasites. Knowing the etiological agent early helps in appropriate intervention and management with good prognosis and absence of defects. In developing countries like India despite significant advances in management and intervention, the mortality remains 16-34%.[1,2] Pathogens responsible for ABM varies from region, time and patient age. Awareness, availability and vaccination coverage influences the prevalence and epidemiological pattern of pathogens of ABM.[3] Studies globally have

reported *Streptococcus pneumoniae*, *Meningococci*, and *Haemophilus influenza* as the most common pathogens.[4] However, by the implementation of successful vaccination against the pathogens, the incidence of meningitis by these pathogens has reduced in developed countries. Clinical manifestations and outcome of patients with meningitis are variable depending upon the pathogen. Hence a thorough knowledge about the prevalent pathogen and its prognosis and complication are a must to the physician in management. Laboratory support is imperative in knowing the pathogen. Laboratory surveillance of isolates is essential to identify targets for immunization, to develop strategies and formulate national policies for potential bacterial pathogens. Since the development of antimicrobial resistance is observed it becomes more necessary in the management of meningitis.

The present study was done to evaluate the bacterial pathogens of meningitis in adults and to determine their antibiogram. The outcome and prognosis of the patients were also evaluated

METHODS

A prospective cross-sectional study was conducted in Department of General Medicine at Narayana Medical College and Hospital, a tertiary care hospital. All the subjects suspected with acute bacterial meningitis (ABM), attending the casualty or OPD were included in the study. The study was done for a period of one year from August 2014 to July 2015. Informed consent was obtained from all the participants or from guardians after explaining the study. The clinical profile, socio-demographic data was collected by interviewing and examining the participants and entered into case sheet. The study was approved by the Institutional ethical and hospital research committee. The outcomes of all the included patients were noted as favourable (recovery) and unfavourable which included any neurological defects or other clinical morbidities and mortality.

Diagnostic criteria for acute bacterial meningitis

- Positive culture with or without a positive gram stain.
- CSF cell count >10 cells/mm^3 with predominant polymorphonuclear Neutrophils.
- CSF protein >45mg%.
- CSF glucose <40mg%.

Inclusion criteria

Patients above 18 years of age with symptom and signs of meningitis (fever, severe headache, vomiting, altered mental status, photophobia, neck stiffness, and Kerning's, Brudziniski signs) were included in the study. The CSF sample was collected from the patients by lumbar puncture under aseptic conditions and transported to the clinical microbiology laboratory for processing in a sterile leak-proof container. The specimen was processed immediately.

The macroscopic appearance of CSF sample was noted, hemorrhagic and inadequate sample (<2ml) was not processed. The sample was divided into three portions and one was centrifuged at 1000 rpm for 15 minutes and deposit used for, Gram staining, Zn staining and negative staining with Indian ink. The 2nd portion was inoculated on sheep blood agar, MacConkey agar, and chocolate agar, also on Sabourads dextrose agar for fungal growth. All the culture plates were incubated in CO_2 incubator at 37°C with 5% Co_2. All the media were inspected for growth up to 72 hours. Routine CSF cell count, glucose, and protein estimation were done on 3rd portion. Growth on media plates was identified by standard biochemical tests and antibiotic susceptibility test was done by modified Kirby-Bauer disk diffusion method and interpreted in accordance with CLISI guidelines.[5] Antibiotics used for gram-positive organisms were penicillin (10 units), oxacillin (1µg), cefoxitin (30µg), ceftriaxone (30µg), vancomycin (30µg) and linezolid (30µg). For gram-negative pathogens, gentamicin (10µg), amikacin (30µg), ceftriaxone (30µg), ceftazidime (30µg), cefixime (30µg), piperacillin (100µg), amoxycillin+ clavulanic acid (20/10µg), piperacillin/tazobactam (100µg/10µg), meropenem (10µg) imipenem (10µg) and polymyxin-B (300U) were used. For quality control-*Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used.

Exclusion criteria

All the cases which were culture negative and not fulfilling the criteria of meningitis by CSF cell counts or other parameters (raised protein, hypoglycorrhachia) were excluded from the study.

RESULTS

During the study period of one year, a total of 547 cases suspected with bacterial meningitis were screened. Out of 547 cases, only 282 cases were diagnosed as ABM based on inclusion criteria. Out of 282, 164 (58.16%) were males and 118 (41.84%) were females. The most common age group in the study was 51-60 years (25.18%) followed in order by 61-70 years (22.34%), 41-50 years (18.79%), >70 years (14.18%) and least among 20-30 years (6.38%). Most of the cases (50.35%) were community acquired whereas others post-surgical (17.02%), traumatic (21.28%) and nosocomial (11.35%). Table 2 explains the distribution of cause of meningitis among different age groups. Community-acquired and nosocomial were more common at 51-60 years and traumatic and post-surgical were common at 61-70 years. Headache was the commonest symptom (97%) followed by fever (94%), vomiting (93%), 49% complained of photophobia, seizures in 19%, altered mental status in

43%, Neck stiffness in 39%, Kernig's sign (11%) and Brudziniski sign in 14% were observed (Figure 1).

Table 1: Clinical, socio demographic profile of cases.

Parameter	Variable	Number	%
Gender	Male	164	58.16
	Female	118	41.84
Age	20-30 years	18	6.38
	31-40 years	37	13.12
	41-50 years	53	18.79
	51-60 years	71	25.18
	61-70 years	63	22.34
	>70 years	40	14.18
Cause	Community	142	50.35
	Nosocomial	32	11.35
	Traumatic	60	21.28
	Post-surgical	48	17.02
Signs and symptoms	Fever	188	94
	Headache	194	97
	Vomiting	186	93
	Photophobia	98	49
	Seizures	38	19
	Altered mental status	86	43
	Neck stiffness	78	39
	Kernigs sign	22	11
	Brudzinski sign	28	14
Outcome of the case	Favourable	264	93.62
	Unfavourable	18	6.38
Laboratory parameters of CSF			
CSF cell count	10-100 cells/mm^3	122	43.26
	>100 cells/mm^3	160	56.74
CSF glucose	< 21-40 mg%	168	59.57
	<20mg%	114	40.43
CSF protein	45-90mg%	84	29.79
	>90 mg%	198	70.21

The patients were managed as per the guidelines and followed till recovery and further for six months for any defect or morbidity. 93.62% (264 cases) had favorable outcome without any defects and 6.38% (18 cases) had an unfavourable outcome. 6 cases expired out of which 4 were HIV positive and 2 had septicaemia with multi-

organ failure, 7 cases developed partial deafness and 5 had paresis of right upper limb (Table 1).
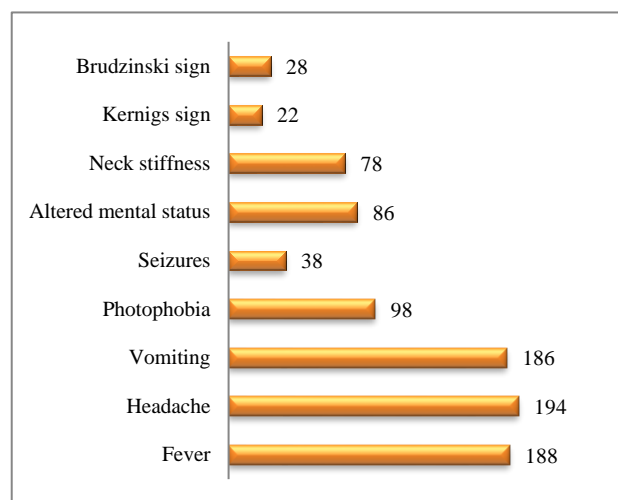

Figure 1: Clinical signs and symptoms.

Laboratory analysis of CSF parameters

43.26% of cases had cell counts with 10-100 cells/mm^3 and 56.74% had >100cells/mm^3. CSF glucose <20mg% was observed in 40.43% and 21-40mg% in 59.57%. CSF protein >90mg% in 70.21% cases and 45-90 mg% in 29.79% cases were observed (Table 1).

CSF gram stain and culture were done. Out of 282 culture positive CSF specimens, gram stain positivity was seen in 36.88% (104 cases). Gram-negative bacteria were predominant 134 (47.52%) followed by gram positive 132(46.81%) and fungi 12 (5.67%). Streptococcus pneumoniae was the major pathogen in the study (19.15%) followed by Staphylococcus aureus (16.31%), *Acinetobacter* sp. (12.06%), coagulase negative *staphylococcus* (11.35%), *Escherichia coli* and *meningococci* (9.93%) and *Pseudomonas* sp. and *Klebsiella pneumoniae* (7.8%) in the study. *Candida albicans* and *Cryptococcus* accounted for 5.67%. *Cryptococcus* was isolated from four cases of HIV positive individuals in the study (Figure 2).

Table 2: Distribution of meningitis and cause in different age groups.

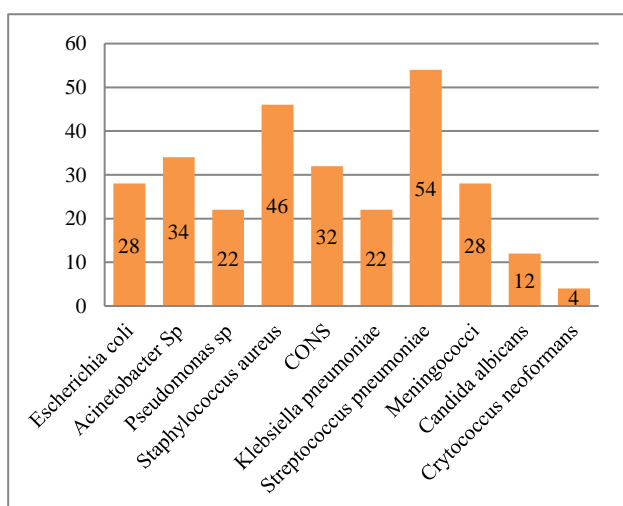|	20-30 years	31 -40 years	41-50 years	51-60 years	61-70 years	>70 years	Total
Community	8	23	38	53	10	10	142
Nosocomial	2	5	3	11	6	5	32
Traumatic	5	7	7	2	28	11	60
Post-surgical	3	2	5	5	19	14	48
Total	**18**	**37**	**53**	**71**	**63**	**40**	**282**

Table 3: Antibiotic sensitivity of gram negative bacterial isolates from CSF (%).

Antibiotic	*Escherichia coli* (n=28)	*Acinetobacter* sp. (n=34)	*Pseudomonas* sp. (n=22)	*Klebsiella pneumoniae* (n=22)	*Meningococci* (n=28)
Pencillin	NT	NT	NT	NT	94
Piperacillin	NT	NT	82	NT	NT
Gentamycin	88	86	84	88	86
Amikacin	90	88	88	88	92
Ceftriaxone	82	86	NT	90	88
Cefotaxim	78	88	NT	92	NT
Cefixime	88	92	88	88	NT
Ceftazidime	82	90	84	88	NT
Amoxycillin + clavulanic acid	88	NT	NT	82	92
Piperacillin+ tazobactam	NT	88	94	NT	NT
Imipenem	98	100	100	100	100
Meropenem	100	100	100	100	100
Polymyxin-B	91	90	98	90	NT

*NT- Not tested.

Table 4: Antibiotic sensitivity of Gram positive bacterial isolates from CSF (%).

Antibiotics	*Streptococcus pneumoniae* (n=54)	*Staphylococcus aureus* (n=46)	*CONS* (n=32)
Pencillin	100	68	76
Oxacillin	NT	88	92
Cefoxitin	94	92	88
Ceftriaxone	94	86	84
Vancomycin	100	100	100
Linezolid	100	100	100

Figure 2: Isolates from the CSF.

Antibiotic sensitivity was done by Modified Kirby-Bauer disk diffusion method and results were interpreted. Gram-negative isolates exhibited resistance towards commonly used antibiotics and maximum sensitivity was seen to imipenem, meropenem, and piperacillin + tazobactam.

Among gram-positive bacteria maximum sensitivity was observed to vancomycin and linezolid (Table 3 and 4).

DISCUSSION

Bacterial meningitis is an inflammation of the meninges and the underlying subarachnoid CSF. Acute bacterial meningitis is a medical emergency requiring immediate management. The choice of antibiotic depends on the isolate prevalent in the region, its antimicrobial susceptibility pattern and the age of the patient.[6] Laboratory investigations of CSF specimens are extremely important in diagnosing and management of patients.

Most studies reported Grams staining as an appropriate single test for identifying bacteria in CSF specimens. In present study, the CSF positivity by gram staining was 36.88%. However, various studies reported a gram stain sensitivity ranging from 30-60% and high specificity of >97%.[7,8] In present study the overall culture positivity from suspected cases of ABM was 51.55% (282/547) which was low when compared with findings in studies of Modi S et al, (65.07%) and Farag HM et al (65.16%).[9,10]

However culture positivity of CSF in a study of Madhumitha P et al, was <26% and Kahn F et al were <34%. The reasons for low CSF culture positivity may be attributed to delay in transport and processing of specimens in the laboratory, autolysis of enzymes in CSF, lack of appropriate media for culture and prior antibiotic treatment.[11,12]

In present study, ABM was more in males than females and the male to female ratio was 1.4:1. This finding is in par with findings of studies of Singh AK et al, Manjiyil IJ et al.[13,14] The most common age group observed in the study was 51-60 years, and community-acquired was the commonest cause of meningitis in present study. This is variable from place to place based on the age, prevalent predominant pathogen, and multiple factors. In present study, an exceptional finding was the traumatic cause of ABM was most common in 61-70 years age group. The reason could not be explained.

Headache was the most common symptom followed by fever, vomiting, and photophobia. Episodes of seizures were seen in 19% of cases, many studies reported less incidence of seizures in adults when compared to pediatric age. Findings of Sudharshan Reddy RC et al, Bareja et al reported a high incidence of seizures >38% in children and adults.[15,16] Altered mental status, neck stiffness and Neurological signs Kernings sign and Brudzniski's sign were observed and found similar with other studies.[17] Laboratory parameters were on par with many studies with neutrophilic pleocytosis in all cases of ABM, raised protein and reduced glucose levels.

In present study, *Streptococcus pneumoniae* was the commonest isolate (19.15%) in all age groups as described by many studies in India. Most studies globally and in India reported a high incidence of pneumococcal meningitis.[18,19] The predominance of *Streptococcus pneumoniae* as the causative agent of community-acquired and nosocomial meningitis following CSF leak has been reported by Marlene LD et al and Kirsten SA et al.[20, 21] No penicillin resistance was detected in our study, however, some studies from India reported prevalence of 1-12% resistant strains.[22,23] Other gram positive bacterial isolates in the study were *Staphylococcus aureus* and coagulase negative *staphylococci* (CONS). Methicillin resistance was not observed in present isolates. Maximum sensitivity was noted to Vancomycin and linezolid in present study. Most of the studies have reported the same findings.

Among the gram-negative pathogens, *Acinetobacter* sp. remained high and was resistant to most common antibiotics. There has been a significant increase in the number of *Acinetobacter* as a major pathogen in immunocompromised conditions. Carbapenems exhibited maximum sensitivity towards a majority of gram-negative pathogens in the study. Cephalosporins tested exhibited second best activity against gram-negative pathogens and Piperacillin/tazobactam exhibited good sensitivity to *Pseudomonas* sp.

CONCLUSION

To conclude, there is an overwhelming need to formulate policies in the management of cases of ABM. The rationale use of antibiotics is necessary to prevent the development of antibiotic resistance. Hence minimizing the emergence of antibiotic resistance and its spread is necessary, which can be achieved by Regular prevalence and antibiotic susceptibility studies. This would also be helpful for clinicians choosing an appropriate empirical antimicrobial rationale.

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