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RESEARCH ARTICLE

EMERGING PATHOGEN, BACTERIAL PROFILE AND SENSITIVITY PATTERN OF ACUTE BACTERIAL MENINGITIS IN A TERTIARY CARE CENTRE, NEW DELHI, INDIA

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ABSTRACT

The irritation or inflammation of the meninges, the covering of brain and spinal cord, is known as meningitis. Acute bacterial meningitis (ABM) is a medical emergency. The emergence of antimicrobial resistance has added to this problem. The aim of the present study was to analyze the emerging pathogen, bacterial profiles and antimicrobial susceptibility patterns of the isolates which were obtained from CSF of patients with ABM in the given area. In our study Gram's stain provides 35% positivity for pus cells and 15% positivity for bacteria. In our study the culture positivity rate was 22%. *Staphylococcus aureus* was the most common pathogen in adult population. For paediatric population Staphylococcus aureus and *Acinetobacter baumannii* is the most common isolated pathogen. There was no isolation of *Haemophilus influenzae* and *Neissaria meningitides* in both group of population. The MRSA is 287(75%) of total isolated *Staphylococcus aureus* (382) species while 95(25%) were MSSA. In our study we observed that *S. aureus* and *A. bowmanii* has been emerged as the most common pathogen causing ABM in all age groups. All Gram negative organisms were showing 91% sensitivity to cefoperazone+salbactum. No vancomycin and chloramphenicol resistance were detected. Stress should be given on the restrained and rationale use of antimicrobials both in and outside the hospital.

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INTRODUCTION

The irritation or inflammation of the meninges, the covering of brain and spinal cord, is known as meningitis. Acute bacterial meningitis (ABM) is a medical emergency, which needs an early diagnosis and an aggressive management. ABM remains a major cause of mortality and long-term neurological sequelae worldwide. Despite the availability of potent newer antibiotics, the mortality rate due to ABM remains significantly high in India and other developing countries, ranging from 16-32% (Kabra *et al.,* 1991, Tang *et al*., 1999, Ayaz *et al*., 2004, Chinchankar *et al.*, 2002). Most often, therapy for ABM has to be initiated before the aetiology is known.

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The emergence of antimicrobial resistance has added to this problem, and current recommendations are to identify targets for immunization, formulate preventive strategies and to carry out a rational empirical treatment (Mani *et al.*, 2007, Schuchat *et al.*, 1995, Werger *et al.*, 1996, Das *et al.*, 2003, Madhumita *et al.,* 2011). Among neonates, Group B and non-Group B *Streptococcus* species (49%), *Escherichia coli* (18%) and *Listeria monocytogenes* (7%) are the most common pathogens which are seen. The meningitis-causing pathogens which are found in infant and child age groups are *Haemophilus influenzae* (40-60%), *Neisseria meningitidis* (25-40%) and *Streptococcus pneumoniae* (10-20%). The common pathogens which are encountered in adult meningitis are *Streptococcus pneumoniae* (30-50%), *Neisseria meningitidis* (10-35%), *Staphylococci* (5-15%), other *Streptococcus* species, *Haemophilus influenzae* (1-3%), Gram negative bacilli (1-10%) and *Listeria* monocytogenes (Chandramukhi *et al.*, 1989,

Table 1. Correlation of pus cells in Gram's stain and culture in bacterial meningitis

Culture (+)	Smear (-) for pus cell	Smear (+) for pus cells
1320	858(65%)	462(35%)

Table 2. Correlation of bacteria in Gram's stain and culture in bacterial meningitis

Culture (+)	Smear (+) for bacteria	Smear (-) for bacteria
1320	1122 (85%)	198(15%)

Sonavane *et al*., 2008, Khan *et al.*, 2011, van de Beek *et al.*, 2006, Forbes *et al.*, 2002). A delay in diagnosis and initiation of antimicrobial therapy can result in a poor outcome of the disease. The aim of the present study was to analyze the emerging pathogen, bacterial profiles and antimicrobial susceptibility patterns of the isolates which were obtained from CSF of patients with ABM in the given area.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Microbiology, VMMC & Safdarjung Hospital, New Delhi, during the period of 3 years from june2012-june2015. Six thousands suspected cases of ABM, who were admitted to various wards of our hospital, were included in this study. All cerebrospinal (CSF) fluid was send to the department of microbiology. Criteria used for inclusion of cases in the study were the presence of a positive CSF culture for bacterial pathogens and/or a positive latex agglutination test for antigen detection.

Macroscopic examination

All CSF samples were macroscopically examined for turbidity, haemorrhagic csf and cobweb appearance for suspected case of bacterial etiology, traumatic injury to spinal cord and tubercular meningitis respectively.

Cell counts, smear and culture

All CSF samples received at the microbiology department were processed immediately. Direct microscopy by doing Gram's stain was done for pus cells, red blood cells and micro-organisms. Culture was put on chocolate agar, blood agar and Mac Conkey agar in the candle jar for 48 hours. The rest samples were incubated in the brain heart infusion (BHI) broth for 48 hours. A battery of biochemical tests were done for identification of the organism (CLSI, 2010).

Antigen detection

Detection of soluble antigens of *H. influenzae* (type b), *S. pneumoniae* and *N. meningitidis* in CSF was performed by latex agglutination tests (LAT), using commercial kits Tulip Diagnostics Pvt. Ltd, India. Antimicrobial sensitivity test was performed on Mueller Hinton agar by the Kirby Bauer disk diffusion method (Schlech W F *et al.,* 1978). The antibiotics which were used like ampicillin (AMP) (10 µg), cefoxitin (Cx) (30 µg), ceftazidime (CTZ) (30 µg), amikacin (AK) (10 µg), ciprofloxacin (CIP) (30 µg), erythromycin (ERY) (30 µg), penicillin G (P)(10 units), piperacillin + tazobactam (PIT) (100/10 µg), cefoperazone+salbactum (CFS) (75/30 µg), imipenem (IMP) (10 µg), meropemen (MER) (10 µg), chloramphenicol (C) (30µg), and vancomycin (VAN) (30 µg), optochin (Opt) (5 µg), which were obtained from Hi Media Laboratories, Mumbai, India. The results were interpreted as per NCCLS-2000 recommendations (CLSI, 2010).

RESULTS

Of the total enrolled population of patients (6000), 1320 were fulfilled the inclusion criteria of this retrospective study as 1320 (22%) were culture and /or antigen confirmed cases of bacterial meningitis (Figure 1). Nine hundred and ninety were male (75%) and 330 (25%) were female (Figure 2). Two sixty four (20%) patients belonged to the paediatric age group (less than 12 years) while 1056 (80%) were adults (Figure 3). Pus cells could be demonstrated by the Gram stain in the CSF samples of 462/1320 (35%) patients, while 858/1320(65%) were Gram stain negative for pus cells. All smear positive for pus cells were also culture positive culture for bacteria (Table 1).

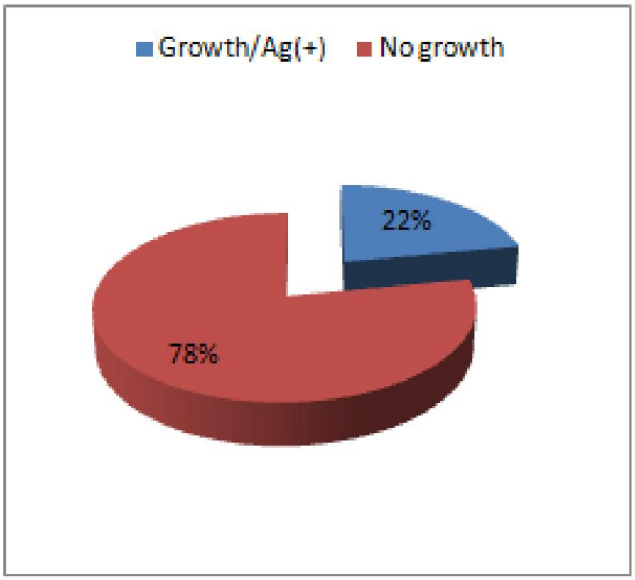

Figure 1: Percentage wise distribution of culture positive cases (1320/6000)

The bacterial pathogen could be demonstrated by the Gram stain in the CSF samples of 198/1320 (15%) patients, while 1122/1320(85%) were Gram stain negative for bacterial pathogen. All smear positive for bacteria were also culture positive culture (Table 2).

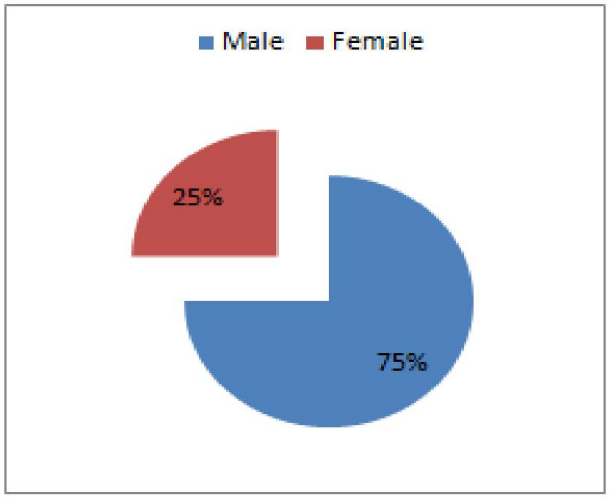

Figure 2: Percentage distribution of patients of ABM based on sex (Total patients= 1320)

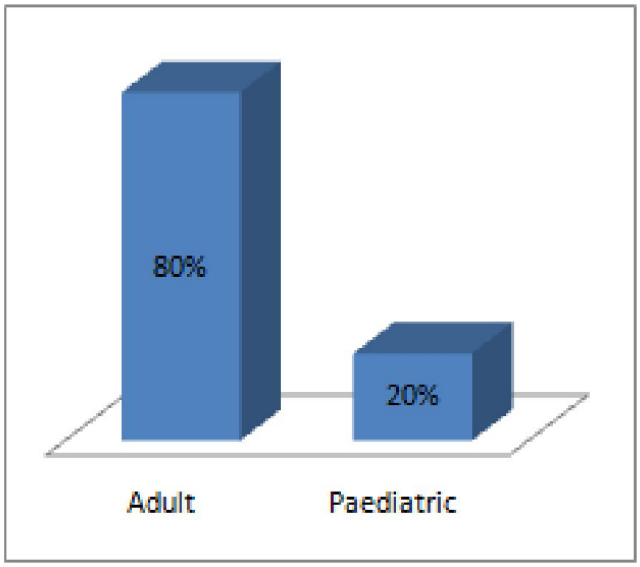

Figure 3. Percentage distribution of patients of ABM based on age (Total patients= 1320)

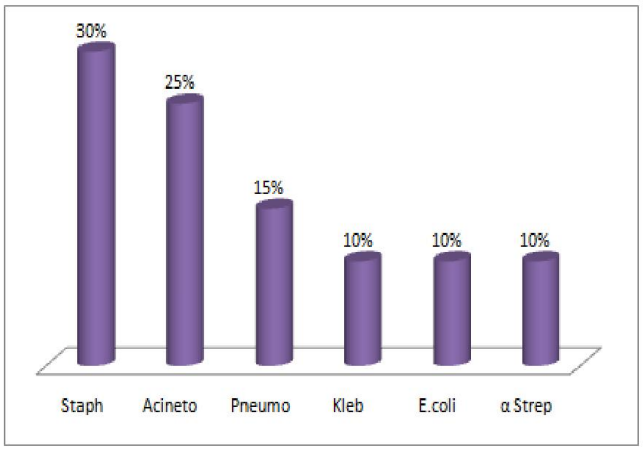

Figure 4. Distribution of organisms in adult bacterial meningitis cases

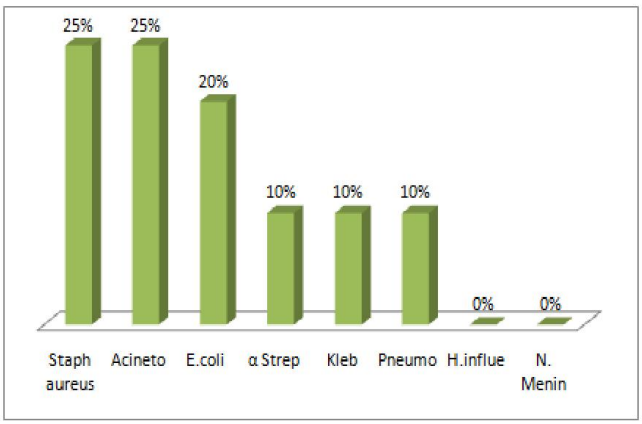

Figure 5. Distribution of organisms in paediatric bacterial meningitis cases

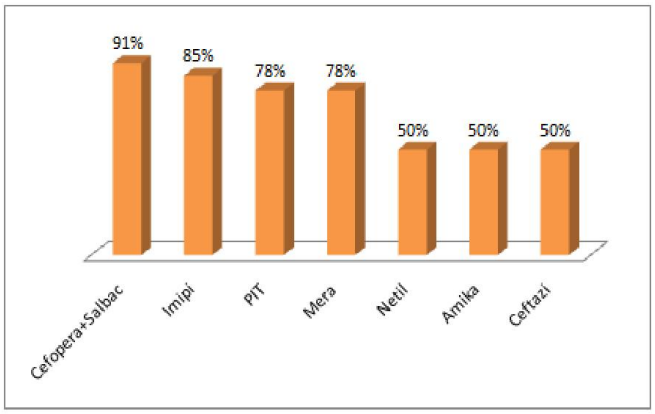

Figure 6. Showing sensitivity pattern of Gram negative organisms

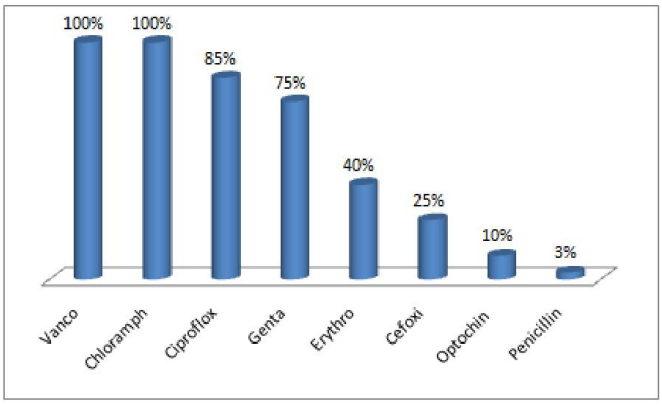

Figure 7. Showing sensitivity pattern of Gram positive organisms

Staphylococcus aureus was the most common pathogen in adult population (1056) which was isolated in 316 (30%) culture positive cases, followed by *Acinetobacter baumanii* which was isolated in 264 (25%) of patients further followed by *Pneumococcus pneumoniae* (15%), *Klebseilla pneumoniae* (10%), E. Coli(10%) and α Streptococci (10%). There was no isolation of *Haemophilus influenzae* and *Neissaria meningitides* (Figure–4). For paediatric population Staphylococcus aureus and *Acinetobacter baumannii* is the most common isolated pathogen 66(25%) followed by E.coli (20%), *Pneumococcus pneumoniae* (10%), *Klebsiella pneumoniae* (10%) and α Streptococci (10%).

There was no isolation of *Haemophilus influenzae* and *Neissaria meningitides* (Figure 5). The methicillin resistant *Staphylococcus aureus* (MRSA) is 287(75%) of total isolated *Staphylococcus aureus* (382) species while 95(25%) were methicillin sensitive *Staphylococcus aureus* (MSSA). All Gram negative organisms was showing 91% sensitivity to cefoperazone+Salbactum combination followed by imipenem (85%), piperacillin+salbactum(78%), meropenem (78%), netilimicin (50%), amikacin (50%) and ceftazidime (50%) as shown in figure 6. For Gram positive organisms all were sensitive to vancomycin and chloramphenicol followed by ciprofloxacin (85%), gentamicin (75%), erythromicin (40%), cefoxitin (25%), optochin (10%) and penicillin only (3%) as shown in Figure 7.

DISCUSSION

Meningitis can be broadly classified as pyogenic, granulomatous, and lymphocytic. Acute bacterial or pyogenic meningitis is a potentially life threatening disease that consists of inflammation of the meninges and the underlying subarachnoid CSF. ABM is a medical emergency, which warrants early diagnosis and aggressive therapy. The choice of antimicrobial therapy is based on the most common pathogen prevalent in a particular geographical area and age group and their antibiotic susceptibility pattern. Though the common pathogens associated with bacterial meningitis in the west are *H. influenzae, N. meningitidis, S. pneumoniae and Listeria monocytogenes* (Schlech W F *et al*,1985, Schuchat A *et al.,* 1997, Chong H T *et al.,* 2005, Tang L M *et al.,* 1999). However, in developed countries with effective vaccination programmes, the incidence of *H. influenzae* and *N. meningitidis* showed decreased trends (Chan *et al.*, 2002, Khan *et al.*, 2011). In our study the culture confirmed and/or antigen positive cases were 1320 ie only 22% of total study population (6000) showed growth and rest were sterile for any bacterial pathogen. The male:female ratio is 4:1. This male preponderance which is seen with this disease has also been reported in several previous studies (Tang *et al.*, 1999, Pfister *et al.*, 1993, Chinchanker *et al.*, 2002). In our study Gram's stain provides 35% positivity for pus cells and 15% positivity for bacteria. A simple Gram stained smear can offer immediate clues to aid a diagnosis of pyogenic meningitis. Some studies have reported a CSF Gram stain sensitivity of 60-90% and a high specificity city of >97%, stressing its importance in the rapid and accurate diagnosis of the causative bacteria (van de Beek *et al.,* 2004, Das *et al.,* 2003).

The yield of bacteria on a Gram stain depends on several factors like the number of organism present, prior use of antibiotics, technique used for smear preparation (centrifuged deposit, cytospin, direct smear etc.), staining techniques and the observer's skill and experience. Despite low Gram stain smear positivity from CSF samples and the fact that a negative Gram stain does not rule out infection, the importance of a positive smear cannot be over-emphasized, especially in developing countries where financial constraints limit the use of other rapid diagnostic tests to diagnose this potentially fatal infection. Most Indian studies report only culture findings or low smear positivity (Kabra *et al.*, 1991). In our study the culture positivity rate was 22% (1320/6000). Various studies report culture negative cases of meningitis or a low CSF culture positivity, ranging from 6 to 50% (Kabra *et al.*, 1991, van de Beek *et al.*, 2004, Tang *et al.*, 1999). Various reasons cited in the literature for a low yield of bacteria on culture are prior antibiotic therapy, delay in transport of specimens to the laboratory, non availability of special media for specific pathogens, presence of autolysis enzymes in CSF and lack of a 24 hour facility for processing CSF samples. *S. aureus* was the most common pathogen in adult population (1056) which was isolated in 316 (30%) culture positive cases, followed by *A. baumanii* which was isolated in 264(25%) of patients further followed by *P. pneumoniae* (15%), *K. pneumoniae* (10%), *E. Coli* (10%) and α *Streptococci* (10%).

There was no isolation of *H. influenzae and Neissaria* meningitides. For paediatric population *Staphylococcus aureus* and *Acinetobacter baumannii* is the most common isolated pathogen 66(25%) followed by *E.coli* (20%), *Pneumococcus pneumoniae* (10%), *Klebsiella pneumoniae* (10%) and α *Streptococci* (10%). There was no isolation of *Haemophilus influenzae and Neissaria meningitides.* The MRSA is 287(75%) of total isolated staphylococcus aureus (382) species while 95(25%) were MSSA. In our study we observed that *S. aureus* and *Acinetobacter bowmanii* has been emerged as the most common pathogen causing ABM in all both group followed by other gram positive and gram negative bacilli. A study in Taiwan showed an increase in the incidence of staphylococcal infection which rose from 15% to 23% and a decrease in the incidence of *Streptococcus pneumoniae* which fell from 10.6% to 3.6%. Staphylococcal strains replaced *S. pneumoniae*, becoming the most common Gram positive pathogen of acute ABM in their hospital (Liu C C *et al.,* 1993, Fournier *et al.*, 2006). In our study *Acinetobacter bowmanii* emerged as an emerging pathogen in both age group (Adult: Paediatric /30%:25%). Multidrug-resistant *A. baumannii* is a rapidly emerging pathogen in the health care setting, where it causes infections that include bacteraemia, pneumonia, meningitis, urinary tract infection, and wound infection. The organism's ability to survive under a wide range of environmental conditions and to persist for extended periods of time on surfaces make it a frequent cause of outbreaks of infection and an endemic, health care–associated pathogen (Jawad *et al.,* 1996, Huttova *et al.,* 2007). In many studies *Acinetobacter baumannii* has been reported as a cause of meningitis as hospital acquired infection or acquired after neurosurgical procedures (Meton *et al.,* 2007, Rodriguen *et al.,* 2008, Chen S F *et al.,* 2005, Denton M *et al.,* 2005, Yang M *et al.,* 2012).

All Gram negative organisms showing 91% sensitivity to cefoperazone+salbactum combination followed by imipenem (85%), piperacillin+salbactum(78%), meropenem (78%), netilimicin (50%), amikacin (50%) and ceftazidime (50%). For Gram positive organisms all were sensitive to vancomycin and chloramphenicol followed by ciprofloxacin (85%), gentamicin (75%), erythromicin (40%), cefoxitin (25%), optochin (10%) and penicillin only (3%). These results signify the varying levels of drug resistance amongst the gram positive and the gram negative microbes, and the need to control the spread of these resistant strains before they reach the alarming levels in this region. Among the gram negative bacilli a general decline

in the sensitivities to all groups of drugs was noticed. The simultaneous decline in sensitivities to different group of drugs can be correlated to the rampant indiscriminate use of antibiotics leading to a large scale drug resistance. As observed with the gram negative bacilli, a similar pattern of increasing drug resistance was seen among the *Staphylococcal species, Streptococcus species.* However, fortunately no vancomycin and chloramphenicol resistance were detected. As in Gram negative bacilli, cefoperazone+salbactum combination and carbapenems had very good sensitivity but they have side effects also. However seeing the predominance of gram positive cocci particularly *Staphylococcus aureus* with alarming rates of methicillin resistance (75%), suitable antibiotics should be given after sensitivity report. Stress should be given on the restrained and rationale use of antimicrobials both in and outside the hospital.

Conclusion

The spectrum of organisms which cause acute bacterial meningitis varies with time, geography and patients' ages. Since clinical signs of meningitis are not always reliable, a laboratory support is imperative, to achieve an early diagnosis and proper treatment. The emergence of antimicrobial resistance has added to this problem, and current recommendations are to identify targets for immunization, formulate preventive strategies and to carry out rational empirical treatment, especially for potentially fatal bacterial meningitis. Antimicrobial resistance is increasing, likely as a result both of the emergence of resistance in the context of antimicrobial pressure and of health care–associated transmission of drug-resistant strains. *Acinetobacter* infection poses a formidable threat to patients and is an emerging pathogen for meningitis in this study.

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