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Bacterial meningitis in North India: Trends over a period of eight years

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Abstract

Background: Acute bacterial meningitis is a medical emergency which warrants early diagnosis and aggressive therapy. It is important to know the regional bacterial etiology in semitropical countries like India along with their sensitivity profile to allow optimum management of such patients with least possible mortality. This study was undertaken to study the trends in etiology and the antimicrobial resistance pattern of the pathogens prevalent in North India over a period of 8 years. *Methods:* The study was performed from June 2001 to June 2009. CSF and blood samples were collected from all patients suspected of meningitis and inoculated on chocolate agar, blood agar and MacConkey agar. Antimicrobial susceptibility testing was done using Kirby Bauer disc diffusion method. Detection of methicillin resistant *Staphylococcus aureus* (MRSA), high level aminoglycoside resistance (HLAR) in *Enterococcus species*, extended spectrum β lactamases (ESBL), Amp C and metallo-betalactamases was also done. *Results:* 403 samples were positive on culture. *S. aureus* was the most common pathogen. Among the gram positive cocci as well as the gram negative bacilli, a gradual decline in the antimicrobial susceptibility was seen. The aminoglycosides had the best spectrum of antimicrobial activity. Towards the end of the study, an alarming rise of MRSA to 69.4%, HLAR among the *Enterococci* to 60% was noted. Among the *Enterobacteriaceae,* ESBL and Amp C production was found to be 16.7% and 42% respectively. No vancomycin and imipenem resistance was observed.
Conclusion: An entirely different trend in etiology in bacterial meningitis was observed in the semitropical region of North India. The high prevalence of drug resistant pathogens is a cause for worry and should be dealt with by rational use of antimicrobials. Frequent revision in drug policy may be necessitated for optimum management of patients.

INTRODUCTION

Bacterial meningitis is a life threatening illness that is prevalent worldwide. Prior to the introduction of antibiotics in the 1940s, case fatality rates for epidemic and endemic bacterial meningitis exceeded 70%. Since then, antibiotic use has reduced case fatality rates of bacterial meningitis to 25% or less. Despite advances in vaccine development and chemoprophylaxis, bacterial meningitis remains a major cause of death and long term neurological disabilities.[1] Microbiology laboratories play a critical role not only in the early identification of the causative bacterium and its antibiotic susceptibility pattern but also in providing valuable information regarding the common incriminating pathogens in that area and also which drugs to start empiric treatment with.[2]

There have been several published studies regarding meningitis conducted in hospitals in the developed countries but there is paucity of data regarding similar surveys in the developing countries like ours. Regional information regarding trends in terms of etiology and antimicrobial susceptibility are essential for correct and timely management of meningitis. This study was conducted to analyse the trends in bacterial etiology and antimicrobial resistance in meningitis in North India with emphasis on the prevalence of methicillin resistant *Staphylococcus aureus* (MRSA), high level aminoglycoside resistance (HLAR) in *Enterococcus species*, extended spectrum β lactamases (ESBL), Amp C and metallo-betalactamases (MBL).

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METHODS

This retrospective study of acute bacterial meningitis was performed at the Department of Microbiology, Jawaharlal Nehru Medical College and Hospital (JNMCH), a tertiary care centre in Aligarh, India between June 2001 and June 2009. All patients were drawn from paediatrics and medicine wards and were classified as hospital acquired and community acquired infections. Nosocomial infection was defined as a positive bacterial infection not present at the time of hospital admission, clinical evidence of an infection no sooner than 48 hours after admission, or clinical evidence of meningitis within one month after discharge from hospital where the patient had received an invasive procedure, especially a neurosurgical procedure. Otherwise, the patient was considered to have community acquired infection. Clinical details were recorded along with history of vaccination (*Hemophilus influenzae* b). In children assessment for nutritional status was done according to the Gomez classification.[3] In this study criteria for a definite diagnosis of bacterial meningitis were as follows: (i) a positive culture of bacterial pathogen(s), (ii) clinical features of meningitis including fever, consciousness disturbance, seizure or signs of meningeal irritation and (iii) purulent CSF feature including at least one of the following: leukocytosis with a leukocyte count >2.5x10^9/L and predominant polymorphonuclear cells, lactate concentration >3.5mmol/L, protein concentration >0.45g/L, glucose ratio (CSF glucose/ serum glucose) <0.4 or glucose level <2.5mmol/L if no simultaneous blood glucose level was determined. Cerebrospinal fluid (CSF) and blood samples were collected for culture from all consecutive patients suspected for meningitis.

After the naked eye examination for the presence of turbidity, microscopic examination was done by Gram's staining of the centrifuged deposit of CSF. Immediately after centrifugation of CSF, culture was done on a plate of chocolate agar, 5% sheep blood agar, Mac Conkey and a tube of brain heart infusion broth. These plates were incubated for 24-48 hours in humid air plus 5-10% CO_2 at 37°C. Any sample showing growth was tested using standard biochemicals to identify the pathogen.[4] Blood culture was performed in all the cases.

Antibiotic susceptibility testing: Sensitivity to relevant antibiotics was determined by the Kirby Bauer Disc diffusion method as per the Clinical and Laboratory Standards Institute (CLSI) guidelines[5], using the commercially available antibiotic discs from HiMedia (Mumbai, India). The antimicrobials used for gram negative bacilli were gentamicin (10μg), amikacin (30μg), tobramycin (10μg), amoxicillin (20μg), cotrimoxazole (trimethoprim/sulphamethoxazole 1.25/23.75μg), ceftriaxone (30μg), cefotaxime (30μg), cefoperazone sulbactum (75/75μg), ciprofloxacin (5μg) and imipenem (10μg). In 2005 netilmicin (30μg), ceftazidime (30μg), cefixime (15μg), cefoperazone (75μg), cefepime (30μg), gatifloxacin (5μg), ofloxacin (5μg) were also added along with pipercillin (100μg), pipercillin-tazobactum (100/10μg), ceftazidime-clavulanic acid (30/ 10 μg)and imipenem (10μg) as the second line drugs. Screening of possible ESBL production was done by using ceftriaxone (30μg) and cefoperazone (75μg). Those isolates with zone diameters less than 25mm for ceftriaxone and less than 22mm for cefoperazone were subsequently confirmed for ESBL production. Confirmation was done by noting the potentiation of the activity of cefoperazone in the presence of cefoperazone sulbactum.[6] Detection of AmpC betalactamase was done on isolates resistant to ceftriaxone (30μg), cefixime (15μg), cefoperazone (75μg) and cefoperazone sulbactum (75/75μg). Induction of AmpC synthesis was based on the disc approximation assay using imipenem as inducer.[6] Detection of MBL was done by Hodge test and Double Disc synergy test using EDTA. The method was as described by Lee *et al*.[7]

The antibiotics used for the gram positive cocci were gentamicin (10μg), amikacin (30μg), tobramycin (10μg), ampicillin (10μg), cotrimoxazole (trimetoprim/sulphamethoxazole 1.25/23.75μg), cefotaxime (30μg), ciprofloxacin (5μg), erythromycin (15 μg), ofloxacin (5μg), gatiofloxacin (5μg), clindamycin (2μg) erythromycin (15 μg), cefaclor (30μg), oxacillin (1 μg) and vancomycin (30μg) for the *Staphylococcus species* and gentamicin (10μg), amikacin (30μg), tetracycline (30μg), ampicillin (10μg), ciprofloxacin (5μg) and erythromycin (15 μg), gentamycin (120μg) and streptomycin (300μg) and vancomycin (30μg) for the *Streptococcus species*. Oxacillin (1μg) for the detection of MRSA and 120μg gentamycin and 300μg streptomycin disc for detection of HLAR in Enterococci.[8]

Over the study period, intravenous administration of ceftriaxone/cefotaxime and amikacin were the initial empiric antibiotics used in the treatment of patients with clinical evidence of meningitis in our hospital. Further antibiotic

adjustment was guided by the results of pathogenic identification and antibiotic susceptibility tests.

RESULTS

During the 8 year study period 5,859 CSF samples were collected from patients admitted in various wards of JNMCH, Aligarh, India. Out of these a total of 403 patients were confirmed as cases of bacterial meningitis on Gram's staining and culture. The presenting complaints in adult patients were fever (96%), headache (33%), neck stiffness (51%), altered sensorium or unconsciousness (62%). However, the symptoms in most of the children were vague like excessive crying, altered sensorium and fever. Around 78% of the patients had already taken treatment from private practitioners or quacks when they presented to the outpatient department or the emergency. Seventy cases out of 403 turned out to be fatal with a case fatality rate of 17.4%. Less than 1% of the patients gave history of immunization for *H. influenzae b.*

Majority of the patients 336 (83.8%) were up to 12 years of age, out of which the maximum 147 (36.7%) were infants. Table 1 describes the etiologies in different age groups. Among infants, most cases 78 (53.6%) belonged to the three months to one year age group. Most (97%) of children were suffering from protein energy malnutrition (PEM), with most of them in PEM grade II (55%). 27% were in PEM grade III and 15% were in PEM grade I. The remaining 3% were not suffering from protein energy malnutrition.

More than half of these were community acquired (279, 69.2%), whereas 124 (30.8%) were hospital acquired (Table 2). It was also noted that community acquired cases of meningitis were more common among the patients between the 20-50 year age bracket, whereas hospital acquired cases of meningitis were seen more commonly at the extremes of age. Among the adult patients with hospital acquired infection, 10 had underlying diseases/ malignancies, 19 had undergone neurosurgical procedures and 7 were immunocompromised. All the children with hospital acquired infection were in PEM grade III and 2 of them had hydrocephalus. Eight children had undergone neurosurgical procedure and 5 had other underlying disorders.

Most of the patients were from rural background (67%) and just a quarter of them (23%) were from urban or semi urban areas.

Etiology

Gram positive bacteria were responsible for a majority of cases of meningitis (240, 59.6%). The most common pathogen isolated in this study was *Staphylococcus aureus (152,* 37.7%) which predominated across all age groups. *Streptococcus species* (35, 8.7%) and *Enterococcus faecalis* (18, 4.5%) were the other gram positive organisms isolated. *Streptococcus pneumoniae* was isolated in 33 (8.2%) cases. Among the gram negative bacteria, the *Enterobacteriaceae* family predominated (82, 20.3%) with *Esherichia coli* accounting for 45 (11.2%) cases followed by *Klebsiella pneumoniae* (19, 4.7%) with *Proteus mirabilis* and *Citrobacter koseri* accounting for 9 (2.2%) cases each. Among the nil-fermenters, *Pseudomonas aeruginosa* and *Acinetobacter species* were isolated in 49(12.2%) and 8 (2.0%) cases respectively (Table 1). Overall among gram negative bacilli, Pseudomonas sp accounted for a majority of cases of meningitis. The usual pathogens of meningitis like *Neisseria meningitides, H. influenzae* and *Listeria monocytogenes* were isolated in only 10 (2.5%), 6 (1.5%) and 6 (1.5%) cases. One isolate each of *Rhodococcus equi Stomatococcus mucilaginosus* and *Corynebacterium aquaticum* were also isolated in the study all of which were isolated in children of less than five years of age.

Overall *S. aureus* predominated in all the eight years accounting for a total of almost 38% of all isolates followed by *Pseudomonas species* which were way behind at 12% and *E. coli* at 11% (Table 3). *Streptococcus species* and *S. pneumoniae* were associated with 8.7% and 8.2% cases of meningitis respectively which was unusual. *C. koseri* and *P. mirabilis* were increasingly isolated in the later years (2007-09).

Majority of cases (26%) occurred in June 2008- May 2009, followed by 22% in 2001-02. In the remaining years the number of isolates ranged from 6.2% to 13.7%.

Across all age groups, *S. aureus, E. coli, K. pneumoniae, Pseudomonas aeruginosa, Streptococcus species* and *E. faecalis* were most commonly isolated. *Streptococcus pneumoniae* was isolated in patients up to 20 years of age, and the incidence decreased with an increase in age. However, it was isolated in 2 patients more than 50 years of age. In neonates, *S. aureus, E. coli, K. pneumoniae* predominated while a few cases were due to *Listeria monocytogenes, Neisseria meningitides* and *Streptococcus agalactiae*. In infants *S. aureus, E. coli*, *Pseudomonas aeruginosa*

Table 1: Distribution of pathogens causing bacterial meningitis in different age groups

Age	E.coli	Klebsiella species	Proteus species	Citrobacter species	Acinetobacter species	Pseudomonas species	S. aureus	S. pneumoniae	Streptococcus species	E. faecalis	Neisseria meningitidis	Listeria monosytogenes	H. influenzae	Others	Total
0-1 month	9	6	1	2	1	5	16	1	2	1	2	2	–	–	**47 (11.7)**
1-3 month	2	1	1	0	1	0	10	–	1	1	2	2	–	1	**23 (5.7)**
3 month -1 yr.	10	4	1	3	1	12	25	8	7	6	1	2	1	–	**78 (19.4)**
1-3 year	4	2	4	2	1	14	26	5	5	2	3	–	3	1	**69 (17.1)**
3-5 year	6	–	1	–	1	6	19	6	5	2	–	–	–	1	**47 (11.7)**
5-12 year	6	2	1	1	–	8	37	6	5	2	2	–	2	–	**74 (18.4)**
12-20 year	2	1	–	–	–	2	8	5	2	1	–	–	–	–	**21 (5.2)**
21-30 year	2	–	–	–	2	1	3	–	3	1	–	–	–	–	**12 (3.0)**
31-40 year	1	2	–	–	1	1	5	–	2	1	–	–	–	–	**13 (3.2)**
41-50 year	1	–	–	–	–	–	2	–	–	–	–	–	–	–	**3 (0.7)**
51-60 year	2	1	–	–	–	1	–	2	2	1	–	–	–	–	**10 (2.5)**
61-70 year	–	–	–	–	–	–	1	–	–	–	–	–	–	–	**2 (0.5)**
Total	**45 (11.2)**	**19 (4.7)**	**9 (2.2)**	**9 (2.2)**	**8 (2.0)**	**49 (12.2)**	**152 (37.7)**	**33 (8.2)**	**35 (8.7)**	**18 (4.4)**	**10 (2.5)**	**6 (1.5)**	**6 (1.5)**	**3 (0.7)**	**403 (100)**

Table 2: Pathogens causing bacterial meningitis over a period of 8 years

Pathogen	Nosocomial		Community		Total
	No. of episodes	Fatal	No. of episodes	Fatal	
S. aureus	70 (46.1)	9	82 (54.0)	15	152
Streptococcus sp	2 (5.7)	0	33 (94.9)	5	35
St. pneumoniae	0	0	33 (100)	0	33
E. fecalis	2 (11.1)	0	16 (88.9)	5	18
E.coli	6 (13.3)	2	39 (86.7)	8	45
Klebseilla sp.	9 (47.4)	3	10 (52.6)	4	19
Proteus sp.	1 (11.1)	0	8 (88.9)	2	9
Citrobacter sp.	1 (11.1)	1	8 (88.9)	3	9
Acinetobacter sp.	4 (50.0)	0	4 (50)	2	8
Pseudomonas sp.	29 (59.2)	6	20(40.8)	5	49
N. meningitidis	0	0	10 (100)	0	10
H. influenza	0	0	12 (100)	0	12
Others	0	0	3 (100)	0	3
Total	**124 (30.8)**	**21**	**279 (69.2)**	**49**	**403**

and *Streptococcus pneumoniae* were isolated most commonly. In the one to three year age group, *S. aureus* and *Pseudomonas aeruginosa* were agents most commonly isolated. *Haemophilus influenzae* and *Neisseria meningitides* were also isolated in this age group but in fewer numbers.

S. aureus (70, 56.5%) and *Pseudomonas* species (29, 23.4%) were the predominant pathogens among the hospital acquired cases of meningitis. Among the community acquired cases again *S. aureus* (82, 45.8%) was the commonest pathogen followed by *E. coli* (39, 14.0%) and *Streptococcus pneumoniae* (33, 11.8%).

Antibiotic resistance profile

Gram positive cocci

Antimicrobial susceptibility pattern to different groups of antimicrobials is given in Figure 1.

Aminoglycosides were found to have the best spectrum of activity (between 80-90%) throughout the 8 year study period. At the start of the study the susceptibility of aminoglycosides (84.8%) was followed by flouroquinolones (75.7%), cephalosporins (54.5%), penicillins (51.5%) and the macrolides (48.5%). However during the study a gradual dip in sensitivity was noted to all group of drugs except macrolides where initially an improvement in sensitivity was seen (from 48.5% to 76.8%). The steepest decline was noted for the β lactam group of antibiotics and the sensitivity to penicillin dipped to 30.6% for penicillin group and to 42.2% for cephalosporins. Most marked was the increase in the prevalence of MRSA causing meningitis from 44.4% in 2005 to 69.4%in 2008-9. Among the *E. faecalis* isolates an increase in HLAR was noticed from 52.9% in 2005 to 60% in 2008-9. However all the isolates were sensitive to the glycopeptides and no vancomycin-resistant enterococcus (VRE) or vancomycin-resistant *Staphylococcus aureus* (VRSA) was detected in our study.

Gram negative bacilli

Antimicrobial susceptibility pattern to different groups of antimicrobials is given in Figure 2.

Similar to gram positive cocci, among the gram negative bacilli initially the aminoglycosides were found to have the best sensitivity (75%) followed by cephalosporins (68.7% to cefotaxime, 60% to cefoperazone-sulbactum), flouroquinolones (62.5%), and cotrimoxazole (52.3%). However, as seen in gram positive cocci, with time a gradual dip in sensitivity was noted to all the group of

Table 3: Distribution of pathogens causing bacterial meningitis over the 8 years study period

Years	E.coli	Klebsiella species	Proteus species	Citrobacter species	Acinetobacter species	Pseudomonas species	S. aureus	S. pneumoniae	Streptococcus species	E. faecalis	Neisseria meningitidis	Listeria monosytogenes	H. influenzae	Others	Total
Jun 2001 – May 02	16 (17.9)	5 (5.6)	0	0	2 (2.2)	13 (15)	33 (37)	7 (7.8)	6 (6.7)	3 (3.3)	2 (2.2)	2 (2.2)	0	0	**89 (22.1)**
Jun 2002 – May 03	3 (10.3)	1 (3.4)	1 (3.4)	1 (3.4)	1 (3.4)	4 (13.8)	9 (31)	3 (10.3)	4 (13.8)	2 (6.8)	0	0	0	0	**29 (7.2)**
Jun 2003 – May 04	7 (16.2)	3 (6.9)	0	0	2 (4.7)	4 (9.3)	14 (32.4)	4 (9.3)	3 (6.9)	1 (2.3)	2 (4.7)	0	3 (6.9)	0	**43 (10.7)**
Jun 2004 – May 05	2 (7.1)	1 (3.6)	1 (3.6)	2 (7.1)	0	2 (7.1)	8 (28.6)	3 (10.7)	5 (17.9)	2 (7.1)	0	0	1 (3.6)	0	**28 (6.9)**
Jun 2005 – May 06	2 (7.7)	2 (7.7)	2 (7.7)	0	1 (3.8)	2 (7.7)	9 (34.6)	2 (7.7)	2 (7.7)	3 (11.5)	0	0	0	1 (3.8)	**26 (6.4)**
Jun 2006 – May 07	7 (12.7)	3 (5.4)	0	0	1 (1.8)	4 (7.2)	30 (54.5)	4 (7.2)	4 (7.2)	1 (1.8)	1 (1.8)	0	0	0	**55 (13.6)**
Jun 2007 – May 08	2 (6.8)	0	1 (3.4)	1 (3.4)	0	1 (3.4)	10 (43)	3 (10.2)	5 (17)	1 (3.4)	1 (3.4)	0	1 (3.4)	2 (6.8)	**29 (7.2)**
Jun 2008 – May 09	6 (5.7)	4 (3.8)	4 (3.8)	5 (5.7)	1 (0.9)	19 (18)	38 (36)	7 (6.6)	6 (5.7)	5 (4.7)	4 (3.8)	4 (3.8)	1 (0.9)	0	**105 (26)**
Total	**45 (11.2)**	**19 (4.7)**	**9 (2.2)**	**9 (2.2)**	**8 (2.0)**	**49 (12.2)**	**152 (37.7)**	**33 (8.2)**	**35 (8.7)**	**18 (4.4)**	**10 (2.5)**	**6 (1.5)**	**6 (1.5)**	**3 (0.7)**	**403 (100)**

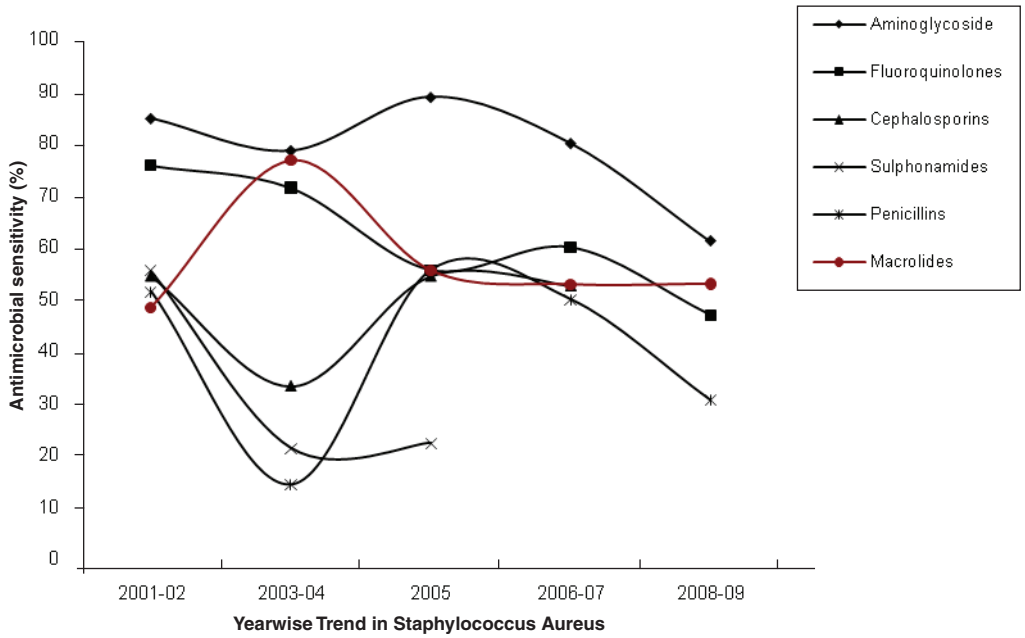

Figure 1. Yearly trend of antimicrobial sensitivity to Staphylococcus Aureus

drugs. During 2009 again aminoglycosides had the best activity against gram negative bacilli (50%) with minimum decline in sensitivity. Here the sharpest decline was seen for flouroquinolones (from 62.5% to 16.7%) and cephalosporins (68.7% to 16.7%). An alarming rise in ESBL production was noted from 10% in 2005 to 16.67% in 2009and also a sudden rise was seen for Amp C production from nil in 2005 to 42% (11 isolates) in 2009. However no MBL was detected during the entire study with 100% sensitivity to imipenem.

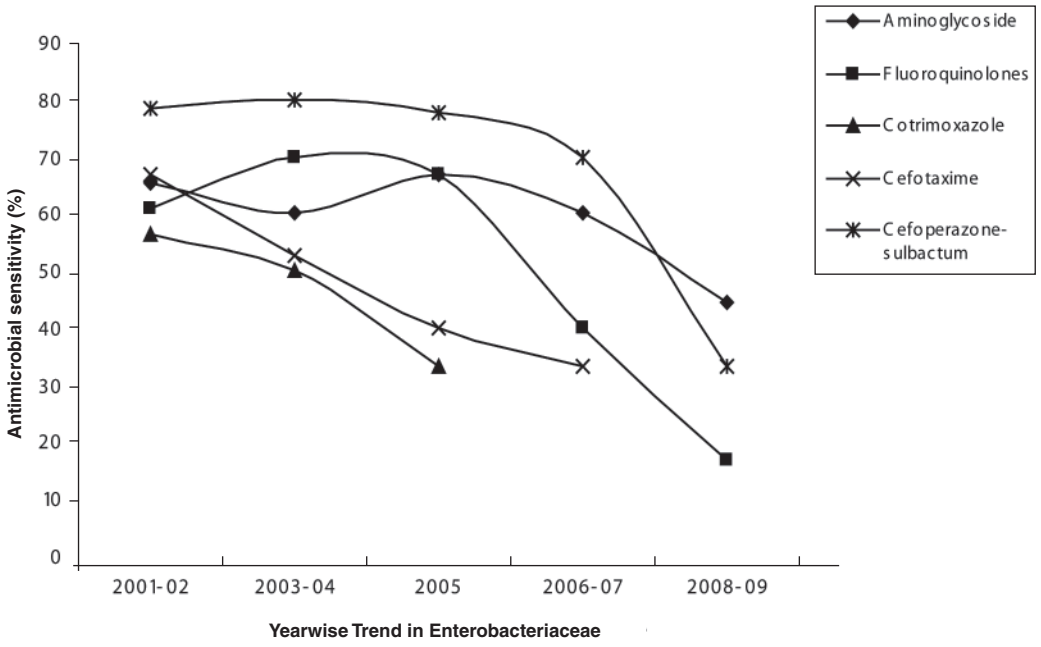

Figure 2. Yearly trend of antimicrobial sensitivity to Enterobacteriaceae

DISCUSSION

Acute bacterial meningitis is a medical emergency which warrants early diagnosis and aggressive therapy. Most often therapy for bacterial meningitis has to be started before the etiology is known. 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*[9] *and Listeria monocytogenes*[10], the relative incidence of meningitis caused by these agents is less in South East Asia.[11] However, in developed countries with effective vaccination programmes, the incidence of *H. influenzae* and *N. meningitidis* showed decreased trends.[12,13] There is a need for a periodic review of bacterial meningitis worldwide, since the pathogens responsible for infection vary with time, geography and patient age.[11] More data from systematic studies all over India in the coming years needs to be analysed to comment whether meningitis caused by Gram negative bacilli is on the increase, reflecting a trend similar to other countries.[14]

In our study we observed that *S. aureus* has emerged as the most common community as well as hospital acquired pathogen causing acute bacterial meningitis in all age groups followed by gram negative bacilli. The other important pathogens for the community acquired cases of meningitis were *E. coli* and *Streptococcus pneumoniae* whereas *Pseudomonas* was the second most important pathogen for the nosocomial cases of acute bacterial meningitis after *S. aureus*. 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 bacterial meningitis in their hospital.[11,15] Hospital acquired infections were found more commonly among the patients with extremes of age, in patients with some underlying disease and those who underwent some neurosurgical procedures. In children hospital acquired infection was seen in those who were malnourished (PEM grade III) and in those who had undergone neurosurgery. Poor nutritional status, extremes of age, underlying diseases and malignancies are predisposing factors for immunosuppression which is again a risk factor for hospital acquired infections. The presence of post-neurosurgical state is a known cause of staphylococcal acute bacterial meningitis[16-18], which was the commonest pathogen for hospital acquired cases of meningitis in our study.

In the neonates *S. aureus, E. coli* and *Klebsiella species* predominated. *H. influenzae, N. meningitidis, S. pneumoniae, S. agalactiae* and *Listeria monocytogenes* were isolated in a few cases. There are regional variations in etiology even in close geographical locales and races. In a study Meningococcal meningitis was seen only in Vietnamese children and in none of the indigenous Hong Kong Chinese children. In the same study *H. influenzae* showed an annual incidence of only 1.1/100,000 even in the absence of an effective vaccination programme.[11] In a study from Singapore, spanning over 11 years from 1994-2003, incidence of *H. influenzae* was reported to be as high as 4.4/100,000. They suggested that *Hemophilus influenzae* b vaccine should be introduced in universal infant immunization in Singapore.[19] Moreover *Citrobacter* and *Proteus species* were increasingly isolated in the later years suggesting an insidious emergence of these pathogens in causing meningitis. The usual causes of meningitis- *H. influenzae*, *Streptococcus pneumoniae* and *Neisseria meningitides* are important, however in parts of Asia, especially parts of East and Southeast Asia, a variety of gram negative bacilli are proportionately more important.[12] However, *Streptococcus suis*, a gram positive cocci is being increasingly reported from not just South east Asia but also from Northern Europe.[13,20] Three uncommon bacteria were also isolated during the course of the study namely *S. mucilaginosus, R. equii* and *C. aquaticum*. Few cases of meningitis caused by *R. equii* and *C. aquaticum* have been reported.[21,22] Although *R.equi* is considered to be an opportunistic pathogen causing meningitis in immunocompromised individuals, there are reports of cases of meningitis due to *R.equi* in immunocompetent individuals as well.[22,23]

The difference in etiology 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 and low birth weight leading to protein energy malnutrition gives an opportunity for the uncommon pathogens like

Streptococcus species to cause meningitis. Finally, unfortunately 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. These results highlight the very different etiological profile in India in comparison to that of the West, pointing to the fact that Asian epidemiology is distinctly different from the West.

The case fatality rate was 17.4% despite treatment. Although lower mortality rates have been reported from the Western countries (2.6%)[24], higher rates had been reported in some developing countries(20-30%).[25,26] In a study from India case fatality rate of 21.8% had been reported[27], which is slightly higher than ours.

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. It is particularly useful for the clinicians to possess the susceptibility data on Gram positive and Gram negative bacteria rather than for particular organisms only. 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. This can be attributed to the general tendency of the Indian populace to prefer private practitioners or quacks who do not follow proper antibiotic prescription norms. Along with a perceptible deterioration in the susceptibility to the various antibiotics, an increase in ESBL production to 17% and Amp C production to a high of 42% was noticed. Aminoglycosides maintained the best sensitivity profile at 44.4%.

As observed with the gram negative bacilli, a similar pattern of increasing drug resistance was seen among the *Staphylococcal species* and the *Enterococcus* while *Streptococcus species* maintained a uniform sensitivity throughout the study period. A significant increase in the incidence of MRSA was noted from 44.4% in 2005 to 69.4% in 2009 and in HLAR among the *Enterococci* from 52.9% in 2005 to 60% in 2009. However fortunately no vancomycin resistance was detected in *S. aureus* or *Enterococcus species*.

As in Gram negative bacilli, aminoglycosides were the most effective antimicrobials in Gram positive cocci as well. Thus aminoglycosides emerged as the most effective group barring glycopeptides (vancomycin) and carbepenems (imipenem) against gram positive cocci and the gram negative bacilli respectively. Currently aminoglycosides and cephalosporins are being used empirically in our hospital. However seeing the predominance of gram positive cocci particularly Staphylococcus aureus with alarming rates of methicillin resistance, we suggest that vancomycin should be given along with aminoglycoside for empirical treatment where aminoglycoside will cover both gram positive cocci and gram negative bacilli.

Stress should be given on the restrained and rationale use of antimicrobials both in and outside the hospital. This study also indicates the urgent need for more of such studies in the patients of meningitis vis a vis aetiology and drug resistance along with the need for the in-house review of drug policy within hospitals at least once in every five years. There is also an urgent need to develop institutional programs to enhance antimicrobial stewardship thus minimizing the emergence and spread of antimicrobial resistance.

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