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## Epidemiology and drug resistance profile of acute bacterial meningitis in children in Northern India: a university hospital perspective

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#### ABSTRACT

**Objective:** To assess epidemiology, trends in etiology and the antimicrobial sensitivity pattern of the pathogens.

**Methods:** Cerebrospinal fluid was collected from 150 patients who were suspected of meningitis and processed according to standard microbiological techniques. Cerebrospinal fluid samples were tested for antigen detection by latex agglutination test (LAT). Antimicrobial sensitivity test was done by Kirby–Bauer disc diffusion method.

**Results:** Fever, abnormal movements and altered sensorium were the most common presenting features. Etiological agents were identified in 79 (53%) cases. A total of 33 (42%) samples were cultured positive while 59 (75%) were positive by LAT. *Pneumococcus* followed by Gram-negative organisms were the most common pathogens. Mortality was 28 (19%). The aminoglycosides had the best spectrum of antimicrobial activity. An alarming rise of methicillin-resistant *Staphylococcus aureus* (75%) and extended-spectrum beta-lactamase (59%) was seen. No high-level aminoglycoside resistance, AmpC or mannose-binding lectin production was observed.

**Conclusions:** *Pneumococcus* and Gram–negative pathogens were the most common organisms. High prevalence of drug resistant pathogens is seen. Inclusion of LAT for antigen detection in routine diagnosis adds a valuable adjunct in the rapid and accurate diagnosis of pyogenic meningitis especially in partially treated cases.

#### 1. Introduction

Despite the advances in vaccine development and chemoprophylaxis, bacterial meningitis remains a major cause of death and long-term neurological disabilities. Prior to the introduction of antibiotics in the 1940s, mortality for epidemic and endemic bacterial meningitis exceeded 70%<sup>[1]</sup>. Since the advent of antimicrobial agents, a profound change in the clinical course and prognosis of meningitis has been observed. Therefore, meningitis and its sequelae are best prevented by early diagnosis and appropriate treatment.

At present, it is estimated that there are 170000 deaths annually worldwide with case fatality rate up to 50% if not treated<sup>[2]</sup>. In meningitis, the microbiological laboratory plays a critical role not only in the early identification of the causative bacterium for directing antimicrobial therapy but also in the establishment of guidelines for appropriate empirical treatment. Effective empirical therapy requires knowledge of the most frequent etiological agents of meningitis in the local population and the prevalent antibiotic sensitivity patterns. Cerebrospinal fluid (CSF) latex agglutination test (LAT) is of great promise. Various authors have suggested it as be simple with superior sensitivity and specificity and unaffected by previous antibiotics thereby<sup>[3]</sup>. There are several published studies regarding epidemiology, etiology and drug resistance in meningitis from the developed countries<sup>[4,5]</sup>. However, there is scarcity of such data from the Indian Subcontinent, especially in children.

The present study was undertaken in children from Aligarh Region of North India, with the aim to analyze the

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clinical and bacteriological profile as well as antimicrobial susceptibility pattern in cases of bacterial meningitis. The emphasis of this study was on rapid diagnosis of meningitis by LAT in order to initiate prompt and accurate therapy thus reducing morbidity and mortality.

#### 2. Materials and methods

This prospective included 150 pediatric patients in the age group of 0-15 years, admitted to Jawaharlal Nehru Medical College and Hospital, Aligarh Muslim University, from September 2009 to November 2010, with the clinical suspicion of acute bacterial meningitis (ABM). It is a 1500 bedded hospital with the total number of 13217 pediatric patients admitted the last year. The inclusion criterion was based on signs and symptoms of acute pyogenic meningitis as per a predesigned proforma. The patients with clinical, radiological, or microbiological examination suggestive of tubercular/viral/fungal meningitis were excluded from the study. Nosocomial infection was defined as a positive bacterial infection not present at the time of hospital admission or clinical evidence of an infection no sooner than 48 h after admission. Otherwise, the patient was considered to have community acquired infection.

A detailed clinical history of fever, vomiting, headache, abnormal movements, head injury, immunization status, history of breast feeding, period of illness, antibiotic intake before admission were elicited. Socioeconomic status according to Kuppuswamy's socioeconomic status scales and demographic details like overcrowding, lack of proper health facilities were noted<sup>[6]</sup>. General and systemic examination was performed to assess level of consciousness, weight, pallor/icterus, papilledema, cutaneous signs like meningococcal rash, signs of meningeal irritation, and signs of raised intracranial tension like bulging anterior fontanel. Nutritional assessment was done by Gomez's classification to look for protein energy malnutrition (PEM)[7]. In this study, criteria for a definite diagnosis of bacterial meningitis were as follows: (i) identification of bacterial pathogens by culture and/or LAT; (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>2.5×10<sup>9</sup>/L and the lactate concentration of predominant polymorphonuclear cells>3.5 mmol/L, protein concentration>0.45 g/L, glucose ratio (CSF glucose/serum glucose)<0.4 mmol/L or glucose level<2.5 mmol/L[8].

After admission, 2–3 mL CSF was collected aseptically by lumbar puncture in two separate sterile test tubes. One of the two specimens from each patient was used for bacterial culture, Gram staining and LAT. The second was used for cytology and protein and sugar estimations. For bacterial analysis, each specimen was centrifuged at 1500 r/min for 5 min. The supernatant was removed aseptically into a separate tube and used for LAT for the detection of bacteriological antigens by Pastorex meningitis kit (Bio-Rad, France) for detection of soluble antigens of Neisseria meningitides A, B, C, W135 (N. meningitides), Streptococcus pneumoniae (S. pneumoniae), Streptococcus agalactiae (S. agalactiae), Escherichia coli (E. coli), Haemophilus influenzae type B (H. influenzae) as per manufacturer's instructions. The sediment was cultured using standard microbiological techniques and was also used for Gram staining[9]. All isolates were identified on the basis of their colony morphology, culture characteristics, and their biochemical reactions were identified according to standard procedures<sup>[10]</sup>. Isolates were also tested for their antibiotic sensitivity by Kirby-Bauer disc diffusion technique using Staphylococcus aureus ATCC 25923 (S. aureus) and E. coli ATCC 25922 as control strains according to the Clinical and Laboratory Standards Institute<sup>[11]</sup> using the commercially available antibiotic discs from HiMedia (Mumbai, India). The antimicrobials used for Gram-negative bacilli were gentamicin, amikacin, ceftriaxone, cefoperazone sulbactam, imipenem, cefixime, cefoperazone, cefepime, gatifloxacin, ofloxacin, piperacillin and piperacillin-tazobactam. Screening of potential extended-spectrum beta-lactamase (ESBL) production was done by using ceftriaxone (30 µg) and cefoperazone  $(75 \ \mu g)$ . Those isolates with zone diameters less than 25 mm for ceftriaxone and less than 22 mm for cefoperazone were subsequently confirmed for ESBL production. Confirmation was done by noting the potentiation of the activity of cefoperazone in the presence of cefoperazonesulbactam<sup>[12]</sup>. Detection of AmpC beta-lactamase was done on isolates resistant to ceftriaxone, cefixime, cefoperazone and cefoperazone-sulbactam. Induction of AmpC synthesis was based on the disc approximation assay using imipenem as inducer. Detection of mannose-binding lectin was done by Hodge test and double disc synergy test using ethylene diamine tetraacetic acid as described by Lee *et al*<sup>[13]</sup>.

The antibiotics used for the Gram-positive cocci were gentamicin, amikacin, ceftriaxone, erythromycin, ofloxacin, gatifloxacin, clindamycin, oxacillin, sparfloxacin, pristinomycin and vancomycin. Oxacillin (1 µg) for the detection of methicillin resistant *S. aureus* (MRSA) and 120 µg gentamycin and 300 µg streptomycin disc for the detection of high-level aminoglycoside resistance in *Enterococci* were also used[14].

Statistical analysis was performed by student's *t*-test and *Chi*-square test. Risk for mortality was also estimated by odds ratio (OR) and risk ratio with 95% confidence interval.

#### 3. Results

In this prospective study, a number of 150 clinically suspicious cases of bacterial meningitis were studied. Download English Version:

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