



## BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN OF NEONATAL SEPTICAEMIA IN NICU OF PATNA MEDICAL COLLEGE & HOSPITAL, PATNA

### Pediatrics

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### KEYWORDS

#### INTRODUCTION

Neonatal septicemia is responsible for approximately 25% of the neonatal deaths in the world and mostly in developing countries<sup>1,2</sup>. Increased prevalence of extended spectrum beta-lactamases (ESBLs) and methicillin-resistant *Staphylococcus aureus* (MRSA) and multiple drug resistant (MDR) strains is a cause of concern in Neonatal Intensive Care Units (NICU) worldwide<sup>3</sup>. Neonatal sepsis has been classified as early onset sepsis (EOS) and late-onset sepsis (LOS). The microorganisms most common associated with EOS include Group B *Streptococcus* (GBS), *Escherichia coli*, coagulase negative *Staphylococcus* species (CONS). *Haemophilus influenza* and *Listeria monocytogenes*. and LOS is caused by CONS, *E. coli*, *Klebsiella* spp., *Pseudomonas* spp., *Candida* spp., GBS, *Serratia* and anaerobes. The recent trends show an increase in infections due to CONS.

Although extensive research on neonatal septicemia is available worldwide and in India. However, very few studies have been conducted on neonatal septicemia in states of Bihar.

We conducted cross-sectional prospective study to investigate the causative organism of neonatal septicemia and to assess their antibiotic susceptibility pattern over the period of 1-year in NICU of PMCH, Patna.

#### MATERIALS AND METHODS

It was a cross-sectional study carried out in the NICU of a tertiary care medical College and hospital PMCH, Patna from May 2019 to April 2020. The various neonatal and maternal risk factors were also analysed. The neonatal risk factors studied were low birth weight (LBW, birth asphyxia, meconium staining, congenital anomalies, prematurity, central venous catheterization >10 days, nasal cannula usage, and continuous positive airway pressure use.

The maternal risk factors included socioeconomic status, difficult delivery (caesarean, forceps, vacuum), premature rupture of membranes, prolonged rupture of membranes, maternal fever, recurrent abortions, prenatal care received, urinary tract infection, history of stillbirth, amniocentesis and chorioamnionitis.

A total of 450 suspected patients of neonatal sepsis were included in the study. Neonatal septicemia was suspected if one or more of the following signs and symptoms were present: Convulsions, respiratory rate >60/min, severe chest in drawing, nasal flaring, grunting, bulging fontanel, pus draining from the ear, redness around umbilicus extending to the skin, temperature 37.5°C (99.5°F) or >36.4°C (97.52°F), lethargy, unconsciousness, reduced movements, not able to feed, not attaching to the breast, not suckling at all, crepts in lungs, cyanosis, and reduced digital capillary refill time.

Two milliliters of blood was collected from all neonates aseptically preferably before administration of the antibiotics and inoculated into 20ml of brain heart infusion broth (Hi-Media, India) on the bedside.

Blood culture bottles were transported immediately to the Microbiology Laboratory and were processed as per standard microbiological techniques and the isolates were identified.

Antibiotic sensitivity testing was performed on Mueller-Hinton agar plates. Screening for MRSA was done using a cefoxitin (30g) disc. Resistance to ceritazidimet (30g) disk was used as a screening method for detection of ESBL confirmed double test.

#### RESULT

Of a total of 450 neonates investigated with blood culture, 188(42%) were found to be positive for neonatal septicemia. Males (117) were more than females (71). Mean age at admission was  $3.77 \pm 5.02$  days. Sepsis in their-born neonates 111 (59%) were more common than out born 77(41%). Of 188 neonates, 106(56%) and 82(41%) were normal birth weight and LBW, respectively, and 73 (39%) were preterm. Very LBW neonates, that is, weight below 1.5kg were 19(11%). EOS and LOS were 92 (49%) and 96 (51%) neonates, respectively. EOS was seen more common in born neonates (56%) compared to the out born (39%).

The common clinical presentations were respiratory distress secondary to birth asphyxia (48%), fever (20%), neonatal jaundice (8.5%), pneumonia (8%), decreased acceptance of feeds and lethargy (7%), and seizures or meningitis (5%). The neonatal risk factors such as birth asphyxia, use of a nasal cannula, and prematurity showed association with culture-proven neonatal sepsis ( $P<0.05$ ).

Of the 188 positive blood cultures, the Gram-positive bacteria (GPB) and Gram-negative bacteria (GNB) accounted for (60%) and (40%) respectively. Among Grams positive organisms, 66% isolates were *S. aureus* and among Gram-negative organisms, NFGO was the most common organism isolated (40%).

The resistance to penicillin, amoxicillin and clavulanic acid and azithromycin was 87%, 66% respectively among GPB and GNB. Methicillin-resistance was detected in 29 (41%) of *S. aureus*. There were 30 (40%) MDR isolates among the total of 75 isolates.

Gram-negative organisms showed high resistance to the third generation cephalosporin. They also showed high resistance to amoxicillin and clavulanic acid combination (81%), netilmicin (67%) and gentamycin (63%). Resistance to ciprofloxacin and amikacin was observed in (52%) and (50%). ESBL production was detected in 24 (48%) of GNB that included *Klebsiella pneumonia* 12 (50%), *E. coli* 6 (25%), NFGO 4 (16%) and *Enterobacter* spp. 2 (8%).

High resistance against penicillin and amoxicillin and clavulanic was found for both GPB and GNB. The third generation cephalosporin showed weak activity against all tested bacteria. The considerable preponderance of amikacin activity over gentamicin and netilmicin was observed in GNB. Imipenem resistance was observed among 04% GNB. Out of the 45 *Enterobacteriaceae* isolates in our study 33 (73%) were MDR. All the *Acinetobacter* spp. were also MDR.

There were 22 (12%) mortality which was 17% among female neonates compared to 8.5% among male neonates. Highest mortality of neonates was seen with *Klebsiella pneumonia* (27.7%) followed by NFGO (20%) and *Enterobacter* spp. (20%). The neonatal factors significantly associated with mortality were female sex, LBW, birth asphyxia, and nasal cannula ( $P<0.05$ ).

#### DISCUSSION

Septicemia remains a significant cause of morbidity and mortality in the new-borns. The clinical diagnosis of neonatal sepsis is difficult as it presents with nonspecific signs as it present with non-specific signs and symptoms. An early diagnosis of neonatal septicemia is important to initiate appropriate and prompt treatment. The correct and timely identification of infectious agents and their antibiotic sensitivity patterns are essential to guide the clinicians regarding both the empirical and definitive treatment.

In the recent years, there has been a lot of improvement in medical

facilities and as a result, the survival rate of the preterm and LBW babies has improved. But at the same time, these neonates with immature immune defenses are exposed to NICU flora for a longer duration. Most of the neonatal septicemia cases now are either LBW or preterm. In the present study, 44% were LBW and 39% were preterm neonates which has led to more LOS (51%) as compared to EOS (49%). Mhada et al. reported 23% sepsis among preterm neonates in their study<sup>3</sup>. Among the maternal risk factors, the difficult delivery (32%) in the form of Caesarean, forceps or vacuum was found higher risk factor in our study as compared to (14.88%) by Tallure et al<sup>4</sup>.

The bacteriological profile has changed worldwide from predominant Gram-negative to a predominant Gram-positive bacteria isolation. Many recent studies have reported the emergence of some new emerging organisms such as CONS, NFGO, and *Candida* spp. as a cause of neonatal septicemia.

Our study showed a preponderance of Gram-positive isolates (60%) versus Gram-negative isolates (40%). Ballot et al., Kaufman and Fairchild and Hoogenet al.<sup>5,6,7</sup> reported the isolation of GPB in 54.9%, 68.2% and 75%, respectively, which is in concordance with the present study.

Our study showed *S. aureus* (66%) and CONS (31%) as the most common Gram-positive organisms which is quite high as compared to studies conducted by Agnihotri et al.<sup>8</sup> and Sundaram et al.<sup>9</sup> NFGO and *Klebsiella pneumoniae* were common Gram-negative isolates, which was comparable to the other studies in the region. NFGO tend to colonize and proliferate in nurseries and are transmitted by cross infection.

Both Gram-positive and Gram-negative isolates showed a high resistance to cephalosporin, penicillin, and amoxicillin and clavulanic acid. In the current study, it was observed that antibiotic resistance among the Gram-positive isolates was highest to penicillin (8%). Similar reports of high resistance to Ampicillin (71%) were reported by Bhat et al. Most of the Gram-positive isolates were sensitive to vancomycin. This results was similar to a study by Hoogenet al. In the present study, 41% *S. aureus* isolates were found to be methicillin-resistant, compared to 11.1% reported by Kaistha et al. Gram-negative isolates showed a high resistance to all cephalosporin which is similar to the resistance pattern reported by Agnihotri et al. *Klebsiella pneumoniae* showed resistance to all antibiotics tested except imipenem. In our study, the 48% were ESBL producers as compared to 72% as reported by Bhat et al<sup>10</sup>. This high resistance pattern could be attributed to the injudicious use of antibiotics in our region.

In the present study, overall mortality was observed in 11.7%, whereas a mortality of 45.5% in their study, which is quite high as compared to our study. This could be attributed to advancement in medical technology and better neonatal care in NICU.

## CONCLUSION

Our study highlighted the fact that Gram-positive organisms particularly *S. aureus* and CONS are now predominant organisms causing neonatal septicemia in our institution, as well as whole of North India as suggested by studies in past decade. There has been a shift from the predominance of Gram-negative organisms to Gram-positive organisms *S. aureus* in the past decade throughout the world. Among Gram-negative bacteria (GNB), NFGO are one of the newly emerging groups of organisms with high mortality next only to *Klebsiella* spp. High resistance to cephalosporin is a cause of concern, as they are one of the most common prescribed antibiotic groups in the region.

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