INTRODUCTION

Incidence of neonatal sepsis varies from 7.1 to 38 per 1000 live births in Asia.\(^1\) In India, neonatal sepsicaemia occurs in 10.97 to 27 per 1000 live births.\(^2\)

The bacteriological profile of neonatal sepsis is constantly under change with advances in the early diagnosis and treatment of sepsis and the increased survival of preterm babies. \textit{Acinetobacter} species are gaining importance as a potential pathogen in neonatal sepsicaemia because of frequent isolation in the recent years and is also responsible for increased mortality in the neonates.\(^3\,^4\)

Therefore, a retrospective study was conducted to find out the mortality-associated risk factors in neonatal sepsis due to \textit{Acinetobacter} infection.

MATERIALS AND METHODS

It was a retrospective study conducted for one and a half years in a tertiary care hospital, after approval from the Institutional Ethics Committee. Inclusion criteria were neonatal sepsis cases, where \textit{Acinetobacter} species were isolated from blood cultures and exclusion criteria were immunocompromised status. The case records of neonates admitted in this hospital over one and a half year period were analyzed retrospectively in a predesigned proforma, by accessing the case papers from the medical record office (MRO) of the hospital. Analysis of various parameters was done, e.g. predominant signs and symptoms, maternal, and foetal risk factors, treatment given and outcome in all cases of neonatal \textit{Acinetobacter} sepsis.

One to two millilitre blood was collected from each neonate by venepuncture and was inoculated in 10-15 mL of Hartley’s digest broth (HiMedia Laboratories Pvt. Ltd., Mumbai) in McCartney bottles. Bottles were incubated at 37°C and checked for turbidity every day. First subculture was done after 24 h (day 2) onto Blood agar (BA) and Mac Conkey agar (MA) plates (HiMedia Laboratories Pvt.)
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Acinetobacters are Gram negative cocccobacilli, non motile, non fermentative, oxygenase negative, utilises glucose oxidatively, utilises citrate as the sole source of carbon and is resistant to penicillin. They were further speciated by standard biochemical tests, which included catalase test, urea hydrolysis, gelatin hydrolysis, fermentation of 10% lactose, and growth at 37 and 44°C.[7,8]

The retrieved data were analyzed on SPSS version 15.0.

RESULTS

Blood culture positivity during the study period was 21.8% (871/3995), of which 9.18% (80/871) was Acinetobacter species. Pure growth of Acinetobacter was obtained in all 80 neonates. All of them had early onset sepsis (<7 days), of which 65 (81.25%) were 1 day old and 15 (18.75%) were 2–30 days of age. Out of 80 neonates, 78 (97.5%) were born in this hospital and 2 (2.5%) were outborn babies. Out of 80, males were 47 (58.75%) and females were 33 (41.25%), with male to female ratio being 1.42:1. Twenty three neonates (28.75%) weighed ≤1 kg and 57 (71.25%) weighed >1 kg. Sixteen neonates (20%) were preterm and 64 (80%) were term. Acinetobacter baumanii was the predominant species – 67.5% (54/80), followed by A. junii – 20% (16/80), A. calcoacticans – 11.25% (9/80), and A. lwoffii – 1.25% (1/80).

Table 1 shows the major symptoms and signs, major maternal and fetal risk factors, interventions and duration of hospital stay in 80 cases of neonatal Acinetobacter sepsis. Forty (50%) neonates showed symptoms. Fifty five (68.75%) neonates had signs of tachypnoea, rib retraction, respiratory distress, tachycardia, and jaundice [Table 1]. Maternal risk factors were seen in 40% (32/80) cases. The remaining 60% (48/80) mothers had normal delivery. One mother had premature rupture of membrane (PROM) and one had intrapartum pyrexia. In the neonates born to these mothers, A. baumanii was isolated and both mothers had lower segment caesarean section (LSCS) delivery. Ninety percent (72/80) neonates had fetal risk factors [Table 1], of which 1 had intrauterine growth retardation (IUGR) and 1 was small for gestational age and in both of them A. baumanii were isolated. By Chi square analysis, none of the risk factors were significantly associated with A. baumanii in comparison to non baumanii isolates.

Twenty percent (16/80) Acinetobacter strains were sensitive to all antibiotics tested, but 53.75% (43/80) were multidrug resistant (MDR), i.e., resistant to more than three antibiotics. The major antibiotic combinations given to the neonates were Ampicillin and Gentamycin in 32.5%
(26/80) cases, Amikacin and Amoxycillin-Clavulanic acid in 16.25% (13/80) cases, and Amikacin and Cefotaxime in 12.5% (10/80) cases. Thirty percent (24/80) neonates did not receive any antibiotics.

Mortality due to neonatal *Acinetobacter* sepsis was 20% (16/80) in this study. Of total deaths, *A. baumannii* was encountered in 68.75% (11/16) cases, *A. junii* in 25% (4/16) cases, and *A. lwoffi* in 6.25% (1/16) case. Rest of the neonates (80%) were treated successfully and discharged from the hospital. Duration of hospital stay for the discharged babies was ≥8 days for 46.25% (37/80) neonates and <8 days for 33.75% (27/80) neonates.

Table 2 shows the significant prognostic factors identified in 16 neonates of *Acinetobacter* sepsis. Other fetal risk factors were perinatal asphyxia in 2 and IUGR in 1. All the 16 neonates (100%) who expired were on IV catheters.

**DISCUSSION**

Since the last three decades, *Acinetobacter* species has emerged as an important nosocomial pathogen and have been implicated in wide spectrum of infections, of which lower respiratory tract, blood stream, and urinary tract are common sites causing significant morbidity and mortality in the patients. The present study was an attempt to correlate the various risk factors and outcome in cases of *Acinetobacter* neonatal sepsis.

In India, the incidence of *Acinetobacter* sepsis reported varies from 6.5 to 31.5%.[5,6,9,10] In the present study, the incidence was 9.18%, which is almost similar to other reports from India.[3,13] A recent study from Pune have reported 10.8% *Acinetobacter* species from cases of neonatal sepsis.[11]

*A. baumannii* was the predominant species in this study (67.5%). The main species responsible for neonatal sepsis in other studies was also *A. baumannii*. However, unlike this study, other Indian studies have not reported *A. junii* and *A. calcoaceticus*.

The symptoms seen in bacterial sepsis are irritability, lethargy, convulsions, reduced movements, fever, poor feeding, etc.[6,13-18] In this study, lethargy, poor feeding, and fever were the major symptoms [Table 1]. An Indian study has reported slightly less lethargy and fever in neonates diagnosed as *Acinetobacter* sepsis.[5] A characteristic finding in this study was hypothermia [Table 1]. Others have reported hypothermia slightly higher than that of our study.[6]

Signs were seen in 68.75% (55/80) neonates, major signs being tachypnoea, rib retraction, and respiratory distress. A study from South India is exactly similar to this study[5] [Table 1]. Because bacterial sepsis can be readily progressive, the clinician must be alert to the signs and symptoms of possible infection and initiate diagnostic evaluation and empirical therapy in timely manner.[13] Moreover, clinical presentation is indistinguishable from Gram-negative sepsis, but life threatening complications can occur due to *Acinetobacters*.[6]

LSCS delivery in neonatal sepsis cases reported in one study was slightly less than ours.[13] We reported PROM in one case. Others have reported PROM in 13-21% cases.[6,10,15] The most important neonatal factor predisposing to infection is prematurity and/or LBW.[13] In this study, 90% of neonates had fetal risk factors, major ones being LBW and prematurity [Table 1]. In a study from Brazil, LBW was significantly associated with *A. baumannii* infection in neonates.[13] Others have reported LBW in 73-79% cases.[3,6,10] A recent study from Pakistan has also reported that prematurity and LBW were associated with increasing risk of *Acinetobacter* infection in neonates.[16]

Preterm infants have a 3-10 fold higher incidence of infection than full term infants. Therefore, they often require prolonged intravenous access, endotracheal intubation or other invasive procedures that provide a portal of entry for infection.[13] Fetal distress and multiple births in this study were more in *A. baumannii* as compared to non *baumannii* isolates [Table 1].

In the Brazilian study, duration of hospitalization for >7 days was a significant risk factor for *A. baumannii*
infection. In this study, A. baumanii with duration of hospital stay of ≥8 days was not significant as compared to non baumanii isolates. A relationship between A. baumanii and each risk factor separately as compared with non baumanii is shown in Table 1. Resistance to more than two drugs (MDR) was statistically significant in A. baumanii as compared with non baumanii [Table 1].

Acinetobacter septicemia is common in babies with IV catheterization and artificial ventilation. In one study, 50% received mechanical ventilation, whereas in this study, 22.5% had received the same. Use of both central venous catheter and mechanical ventilation were significant risk factors for neonatal A. baumanii septicemia in the Brazilian study. In this study however, these interventions were not significant with A. baumanii as compared to non baumanii isolates [Table 1].

The usual treatment for A. baumanii bacteraemia is an active β-lactam alone or in association with an aminoglycoside. Protocol followed in NICU of this hospital is giving a combination of two antibiotics – first line being Ampicillin with Gentamycin and second line is Amikacin with Amoxyceillin-Clavulanic acid or Amikacin with Cefotaxime. Based on the antibiotic susceptibility report from the laboratory, or if the neonates do not respond within 3 days, the antibiotics are changed accordingly.

A progressive decrease in effectiveness in third generation cephalosporins against Acinetobacter have been coupled with increased use of these antibiotics. Therefore cefotaxime and ceftazidime use should be discontinued where resistant strains for these antibiotics are being reported increasingly.

Generally, imipenem is most active against A. baumanii. However, in a study by Cisneros and Rodriguez-Bano, imipenem susceptibility of A. baumanii isolates was 100% in 1991, which reduced to 50% in 2000. The present study also encountered almost 41% imipenem resistance in A. baumanii. Though ciprofloxacin can be given as an alternative to those who do not respond to first line antibiotics, it is not considered safe for neonates. Therefore, we are left with only colistin for the resistant cases.

Mortality due to neonatal Acinetobacter sepsis was 20% in this study. Various Indian studies have reported the same in 11–42% cases. In all documented studies from western countries, the mortality due to neonatal Acinetobacter sepsis ranges from 13.9 to 83%. In a recent study from Pakistan, mortality due to neonatal Acinetobacter sepsis was 47%. In the present study, mortality due to A. baumanii was higher than due to non baumanii isolates. Bivariate analysis and their association with mortality were done to assess the prognostic factors. The factors significantly associated with worst prognosis were symptom like lethargy, signs like tachypnoea, rib retraction, tachycardia, respiratory distress, and intervention like mechanical ventilation [Table 2]. In a Pondicherry study, mechanical ventilation was significantly associated with mortality in Acinetobacter infection.

CONCLUSION

Mulidrug-resistant Acinetobacter septicaemia may cause severe clinical disease in neonates, that is associated with a high mortality. This study highlights the need for an effective infection control policy and rational antibiotic use in neonatal intensive care areas of each hospital in order to control neonatal sepsis due to Acinetobacter species. As MDR Acinetobacter strains are being increasingly isolated, antibiotics should be used judiciously, including the cephalosporins, fluoroquinolones and imipenem. Appropriate corrective measures should be taken at the earliest sign of Acinetobacter infection in NICU. A. baumanii should be differentiated from non baumanii species, as A. baumanii has a direct bearing on mortality.

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