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Neonatal Sepsis and Associated Pathogens in Raipur Institute of Medical Sciences and Hospital

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Introduction

Neonatal sepsis is defined as a clinical syndrome in an infant 28 days of life or younger, manifested by systemic signs of infection and isolation of a bacterial pathogen from the bloodstream.[1] Neonatal sepsis is one of the leading causes of morbidityand mortality both among term and preterm infants in spite of recent advances in health care units.[2] The majority of these deaths occur in low-income countries i.e. developing and under developed countries and almost 1 million of these deaths are attributed to infectious causes including neonatal sepsis, meningitis, and pneumonia.[3] There is significant contribution of sepsis to mortality and morbidity among very-low-birth-weight (VLBW, <1500 g) infants in Neonatal Intensive Care Units (NICUs).[4] Neonatal sepsis present in nonspecific form hence diagnosis and management of sepsis are a great challenge facing neonatologists in NICUs. These sign and symptoms include fever or hypothermia, respiratory distress including cyanosis and apnea, feeding difficulties, lethargy or irritability, seizures, hypotonia bulging fontanel, bleeding problems, poor perfusion abdominal distention, gauiac-positive stools, hepatomegaly unexplained jaundice etc.[5,6] Clinical diagnosis of neonatal sepsis is difficult due to nonspecific signs and symptoms and laboratory diagnosis is lengthy and time consuming. Due to this clinician starts the empirical antibiotic therapy till the suspected sepsis is ruled out and increased multidrug resistant organisms make the treatment less effective and treatment is delayed.[7] Neonatal sepsis is generally caused by Gram-positive and Gram-negative bacteria and Candida. As sepsis is a systemic inflammatory response to infection, isolation of bacteria from blood is considered as gold standard for the diagnosis of sepsis.[8] but it takes 24–48 hours for results. Also less blood is available for Inoculation (0.5–1.0 ml) which decreases its sensitivity, as approximately 60–70% of infants have a low level of bacteraemia.[9]

Various studies have been performed to evaluate the complete blood count (CBC), differential count, and immature to total leukocyte ratio (I: T) for the diagnosis of neonatal sepsis. Although predictive value is less, normal values can be used to increase the prediction of neonatal sepsis. The aim of the study was to find and evaluate the incidence of neonatal sepsis and characterize the pathogens associated of neonatal sepsis and resistance pattern of the isolates to evaluate the empirical antibiotic used in neonatal units of referral hospital in RIMS.

Materials and Methods

Study Design

This prospective study was conducted over a period of Nov 2017 and April 2018 at the NICU (Neonatal intensive care unit) of RIMS Raipur. All admitted neonates with signs and symptoms of sepsis at the time of admission in the hospital or who developed sepsis during their hospital stay were included in the study.

Patient data

All neonates were examined giving special emphasis on birth weight, mode of delivery, normal or LSCS, Home or hospital delivery, gestational age, premature rupture of membranes (PROM), maternal infections and vaccinations. Neonatal sepsis was classified into two groups according to the infant age, at the onset of symptoms, EONS- Early onset neonatal sepsis (≤72 hours of life) and LONS- Late onset neonatal sepsis (>72 hours of life)[11]

Sample collection

Neonates with suspected sepsis blood samples were collected from the for blood cultures CRP and CBC. About 2 ml of blood was inoculated directly into blood culture medium bottles and sent to clinical microbiology laboratory for culture and sensitivity and subsequent processing.

Processing of Specimens

The blood cultures were incubated aerobically at 37°C and cultured on Blood agar, McConkey agar and chocolate agar after 24 hours, 48 hours and 7 days of incubation and examined for growth after 24–48 hours of incubation. Growth obtained were isolated and identified by standard microbiological techniques, namely, Gram staining, colony characteristics, and biochemical properties. Candida and fungal isolates were confirmed by growth on Sabouraud media and germ tube test.

Antimicrobial Susceptibility Testing

Antibacterial susceptibility testing of all bacterial isolates was performed by the Kirby-Bauer disc diffusion method on Mueller-Hinton agar according to the CLSI guidelines. Multidrug Resistant (MDR) Bacteria were defined by resistance to three or more antimicrobial classes and pan drug resistant to those resistant to 1st and 2nd line drugs.[12]

Results

A total of 157 neonates with suspected cases of sepsis were enrolled in the study. 18 cases were excluded: 8 blood cultures were contaminated, 10 patients were discharged against medical advice or absconded. Final figure for study purpose was 139.

Total number of neonates admitted in the NICU during study period was 356. The incidence of suspected neonatal sepsis among the admitted neonates at the neonatal intensive care unit was 44.10% (157/356). Among the 139 neonates EONS was 67 (48.20%) and LONS was 72 (51.79%) according to age of the infants.

Of the 139 suspected neonatal sepsis cases 35 (25.17) were low birth weight (<2500 g) and 94 (67.62) were very low birth weight (<1500 g).

Table 1: Neonates with EONS and LONS, their sex distribution and culture positivity

	Neonates with EONS (≤72 hr) number (%)	Neonates with LONS (>72 hr) number (%)	Total number (%)
Total	67 (48.20)	72 (51.80)	139
Sex			
Male	33 (49.25)	32 (44.44)	65 (46.76)
Female	34 (50.75)	40 (55.56)	74 (53.24)
Blood culture results			
Proven sepsis	28 (41.79)	36 (50.00)	64 (46.04)
Possible sepsis	39 (58.21)	36 (50.00)	75 (53.95)

By positive blood culture, sepsis was proved in 64 (46.04%) out of which 28(43.75%) were EONS and 36 (56.25) were LONS. Among the neonates 65 (46.76%) were male and 74 (53.24%) were females. Of the 139 suspected neonatal sepsis cases 35 (25.17) were low birth weight (<2500 g) and 94 (67.62) were very low birth weight (<1500 g)

CRP (C reactive protein) Out of 139 suspected neonatal sepsis cases CRP level was significantly increased (>6 mg/L) in 121 (87.05%) cases.

White Blood Cell count CBC was determined in 139 cases, in 11 (7.91%) infants leucopenia (WBC < 5,000/mm3), 24 (17.26%) leukocytosis (WBC > 20,000/mm3), 26 (18.70%) neutropenia was observed.

Isolation of organisms Out of 139 blood culture 54 (38.84) were culture positive of which 53 (38.12%) showed growth of bacteria and one isolate of candida albicans (0.71%). Out of 53 bacterial isolates Coagulase negative staphylococci (CoNS) were the most frequent isolated organism 24 (44.44%) followed by Klebsiealla pneumonia 12(22.22%) and Staphylococcus aureus 5(9.25%)

Antibiotic sensitivity pattern Gram-Negative Bacteria. They were highly resistant to the first- and second-line antibiotics: ampicillin (>90%), amoxicillin-clavulanic acid (>90%), gentamicin (>60%) and amikacin (>65%), and 3rd generation cephalosporins (>85%). Best sensitivity was observed to imipenem and ciprofloxacin.

Gram-Positive Bacteria. All isolates were sensitive to vancomycin. They showed high resistance to ampicillin and penicillin (>90%), but were sensitive to imipenam and ciprofloxacin.

Multidrug resistant isolates- out of 54 isolates 45 (83.33%) were multidrug resistant.

Discussion

Early diagnosis is difficult in neonatal sepsis due to nonspecific sign and symptoms and can lead to necrotizing enterocolitis, multi organ failure and perinatal asphyxia.[13,14] In the United States, widespread intrapartum antibiotic prophylaxis (IAP) to reduce vertical transmission of Group B Streptococcal infections in high-risk women has resulted in a significant reduction in rates of EOS GBS infection.[15] Rates of LONS are most common in preterm low birthweight infants. Very low birth weight preterm infants shows more risk for LONS because of prolonged hospitalization, prolonged use of indwelling cathetersand

other invasive procedures.[16,17] Coagulase negative staphylococci (CoNS) have emerged as the most commonly isolated pathogens among VLBW infants with LONS. Neonates, especially preterm infants, are immunocompromised because of immaturity of the immune system as well as decreased placental passage of maternal antibodiesand contribute to increased susceptibility to serious bacterial, fungal, and viral infections.[18] CoNS have emerged as the single most commonly isolated pathogen among VLBW infants with LONS and capable of adhering to plastic surfaces with the subsequent formation of biofilms.[19]

Gram-negative bacteria are associated with about one-third of cases of LONS, but 40–69% of deaths due to sepsis in this age group. Transmission generally occurs from the hands of health-care workers, colonization of the GI tract, contamination of total parenteral nutrition or formulas, and bladder catheterization devices.[20,21] Pseudomonas Infections have been associated with the highest mortality.[22]

Candida Infections are the third leading cause of neonatal sepsis in premature infants. Risk factors of infection are low birth weight, use of broad-spectrum antibiotics, male gender and lack of enteral feedings.[23] In our study, the incidence of suspected neonatal sepsis during the study period was 44.10% (157/356), Similar high rates were previously reported in other developing countries such as Tanzania 39% and Cameroon 34.7%.[24,25]

Out of 157 clinically suspected neonatal sepsis during study period only 54 (34.39%) were blood culture positive. This rate was similar with other studies from Bangladesh, Ethiopia and Nigeria.[26,27,28]

The incidence of neonatal sepsis in both EONS and LONS was mostly associated with Gram-positive cocci, specifically CoNS compared to Gram-negative andCandida albicans. High rate of CoNS infection were reported from other countries like China, Mexico, and Kenya.[29,30,31] Inspite of the role of CoNS as etiological agents of neonatal sepsis, determination of the identity of CoNS isolates as a true pathogens or contaminants is still problematic. Candida spp. was isolated only in 1 case 1.85% (1/54), this neonate wea preterm ans VLBW which is a known risk factor for candidemia.[32]

Gram-negative bacteria were the 2nd cause of neonatal sepsis especially LONS, in our study Klebsiealla pneumonia 12(22.22%) was isolated. Ampicillin and Gentamicin are the first-line antibiotics used in our NICUs. Quinolones are not recommended for neonates. For culture-proven sepsis with bacteria resistant to other antibiotics sensitivities are tested. In our study the best sensitivity was observed with imipenem.

In our study all Staphylococcal isolates were sensitive to Vancomycin, but its overprescription may result in the development of vancomycin-resistant strains. In our study best sensitivity amongst Gram negative was found in imipenem and quinolones and in Gram positive vancomycin followed by imipenem and amikacin. But empirical antibiotic priscription with higher antibiotics is again a question mark as in culture positivity and clinically suspected cases there is a vast difference.

Conclusion

Aggressive managementis necessary to prevent adverse events following neonatal sepsis.also antibiotic sensitivity patterns are to be studied widely to start the empirical treatment in neonatal sepsis. Also identification of sepsis source and proper training should be given to the health care workers and parents to decrease the rate of neonatal sepsis.

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