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Original Research Article

A Change in the Pattern of Antibiotic Susceptibility of Isolates: A Prospective Evaluation

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Abstract

Aim: To evaluates the changing Trend of Neonatal Septicemia and Antibiotic Susceptibility Pattern of Isolates. **Methods:** The present Prospective study was conducted in the Department of Paediatrics Vardhman Institute of Medical Science, Pawapuri Nalanda, Bihar, India for 15 months after taking the approval of the protocol review committee and institutional ethics committee. The blood cultures and the sensitivity reports of 100 newborns who were admitted with symptoms of sepsis to the NICU were studied. One to two ml of blood was collected from each neonate with aseptic precautions and inoculated into brain-heart infusion broth and incubated at 37^{O}C for 24 hrs. **Results:** Among the 100 significant culture-positive cases, there were 62 (62%) male and 38 (38%) female neonates with the male to female ratio of 1.63:1. Out of 180 cases, those of early-onset septicemia (EOS) were 120 and late-onset septicemia (LOS) was 60. Blood culture positivity was seen in 65 cases of EOS and 35 cases of LOS. Early-onset sepsis was more common than late-onset. 50 (50%) of the 100 bacterial growths were gram-negative bacilli (GNB) while 32 (32%) were gram-positive cocci (GPC) and 8 (8%) were candida isolates. 30% of the GNB were Klebsiella pneumoniae, thus making it the predominant GNB. Acinetobacter species constituted 21%, while Escherichia coli and Pseudomonas aeruginosa made up 4% each of the GNB. **Conclusion:** Multi-drug-resistant organisms were isolated from septicemia in neonates. Therefore, great caution is required in selection of antibiotic therapy.

Keywords: Jaundice, Sepsis, Neonates

Introduction

Neonatal sepsis refers to systemic infection of the newborn, characterized by nonspecific symptoms, and documented by positive blood culture[1]. An estimated 1.6 million deaths occur due to neonatal infections worldwide, 40% of them being limited to developing countries[2]. A multicentric study from India found sepsis as one of the most common causes of mortality, contributing to 19% of all neonatal deaths. The incidence of neonatal sepsis in the country is 30/1000 live births[3]. Considering the fact that these children are more likely to have neurodevelopmental side effects, this topic deserves paramount significance[4].

The spectrum of microbial etiology of neonatal sepsis varies from region to region and even varies in different hospitals of the same region. In addition, one organism or

group of organisms may be replaced by others over a period of time[5]. For example, in developed countries, E.coli and other Gram-negative organisms were the most common cause of neonatal sepsis in mid-1960s[6]. Thereafter, Group B Streptococcus and coagulase-negative Staphylococcus (CONS) species have been implicated frequently from 1970s[7,8]. Some scientists even documented the change in pattern of newborn sepsis over decades in a single study area[9]. In India, most of the studies so far concentrated on the prevalence of different organisms in neonatal sepsis. For example, Gram-negative bacteria till recently were reported to be the major cause of neonatal sepsis with predominance of Klebsiella pneumoniae although the proportion of cases due to Gram-positive bacteria, especially Staphylococcus aureus, has gradually increased over the last two decades[2,10]. A recent study from Mangalore suggested dominance of Gram-positive cocci in neonatal sepsis[11]. The shortcoming with the available research is their cross-sectional nature. To our knowledge, no study from India has tried to document the secular trend of bacterial etiology in neonatal sepsis. Widespread emergence of resistance to multiple and commonly used antibiotics in isolates is another challenge for determining appropriate empirical therapy[3]. In the absence of any national antibiotic policy, the practice at the present hospital for neonatal sepsis is cloxacillin and aminoglycoside. Ciprofloxacin was used for the treatment of extended-spectrum beta-lactamase (ESBL) producing isolates till carbapenem was introduced in 2004.

Material and methods

The present Prospective study was conducted in the Department of Paediatrics Vardhman Institute of Medical Science, Pawapuri Nalanda, Bihar, India for 15 months, after taking the approval from the protocol review committee and institutional ethics committee.

The blood cultures and the sensitivity reports of 100 newborns who were admitted with symptoms of sepsis to the NICU were studied. One to two ml of blood was collected from each neonate with aseptic precautions and inoculated into brain-heart infusion broth and incubated at $37^{O}C$ for 24 hrs.

Subcultures were made at 24 hr, 48 hr, 72 hr, and on the 7^{th} day on Blood agar and MacConkey agar. Any growth observed was identified as per standard guidelines. Antibiotic sensitivity testing was performed by Kirby-Bauer disc diffusion method and interpreted as per CLSI guidelines. Escherichia coli ATTC 25922, Staphylococcus aureus ATTC 25923, Pseudomonas aeruginosa ATTC 27853, Enterococcus faecalis ATTC 2921 were used as controls.

Results

During the study period, there were 340 neonates admitted in the NICU. Among them, blood cultures were done in 180 suspected cases of neonatal sepsis. The total numbers of culture-positive cases were found to be 100 with the culture positivity rate of 55.56%, and 80 (44.44%) remained sterile after 7 days of incubation.

Among the 100 significant culture-positive cases, there were 62 (62%) male and 38 (38%) female neonates with the male to female ratio of 1.63:1. Out of 180 cases, those of early-onset septicemia (EOS) were 120 and late-onset septicemia (LOS) was 60. Blood culture positivity was seen in 65 cases of EOS and 35 cases of LOS. Early-onset sepsis was more common than late-onset.

It is shown in Tables 1 and 2 that 50 (50%) of the 100 bacterial growths were gram-negative bacilli (GNB) while 32 (32%) were gram-positive cocci (GPC) and 8 (8%) were candida isolates. 30% of the GNB were Klebsiella pneumoniae, thus making it the predominant GNB. Acinetobacter species constituted 21%, while Escherichia coli and Pseudomonas aeruginosa made up 4% each of the GNB. Acinetobacter

speciation could not be done in our laboratory set up. Staphylococcus aureus made up 19 (19%) of the GPC while coagulase-negative staphylococcus (CONS) and Enterococcus faecalis constituted 10%, and 2%, respectively.

Discussion

Sepsis is one of the main causes of neonatal morbidity and mortality. Nosocomial sepsis frequency and microorganism profiles vary widely from center to center and from country to country. The frequency of infections in NICUs varies from 6% to 25% in the United States and from 8% to 10% in Europe[12]. There has been a wide variation in the growth positivity in India; a higher isolation rate of 52.63% was reported by Murty et al., probably due to a low sample size[13]. In this study, blood culture positivity rate in neonatal septicemia cases is 55.56%, which is much higher, and similar results were found by Kumhar GD et al., I roy et al., and Kairavi. J. Desai et al.[14,15] For the effective management of neonatal septicemia cases, study of the bacteriological profile with their antibiotic pattern plays a significant role.

There was a male preponderance in this study. This is similar to the previous studies carried out by various authors who hypothesized that incidence of septicemia was higher in males ranging from 59%-82% due to the presence of factors regulating the synthesis of gamma globulin on X chromosome[16].

We found in our study that early-onset sepsis (EOS) was more common than late-onset sepsis (LOS), which is compatible with the reports from the other developing countries. In our study, early-onset septicemia (EOS) was seen in 54.17% cases of neonatal septicemia, which was also seen by Movahedian AH et al. and A.K Mane, N.V. Nagdeo et al.[17] We obtained *Klebsiella spp* and S. *aureus* as most common cause of EOS as seen in other studies[18].

In our study, gram-negative bacteria (50%) were the principle pathogens, which caused septicemia. Similar results were reported by Roy I, Jain A et al.[14,19] Similar preponderance of the gram-negative rods has been reported in other studies conducted in Pakistan[20,21]. This is in contrast to the studies from abroad where gram-positive cocci including *Staphylococcus aureus*, coagulase-negative staphylococci, and group B streptococci are the predominant agents[22,23].

Klebsiella pneumonia and *Staphylococcus aureus* were the predominant isolates. *Klebsiella* and *Staphylococcus aureus* can survive in the environment for a relatively long time and fairly widely distributed in the hospital environment, and, therefore, have the potential for being transmitted from the environment to the patients through practices that breach infection control measures. This emphasizes the need for the establishment of effective and functional infection control programs in hospitals.

The most significant finding of this study was almost 83.33% of the *Klebsiella* isolates were resistant to commonly used antibiotics, especially gentamicin and the second and third generation cephalosporins. Screening for ESBL showed most of the *Klebsiella* isolates to be extended spectrum beta- lactamase (ESBL) producers. Antibiotic sensitivity testing of gram-negative bacteria showed high resistance to multiple drugs while imipenem is still the best for infections with multidrug-resistant gram-negative organism[17].

We isolated 20% isolates of *Staphylococcus aureus* in the present study. Our results also matched the reports of Narang A et al.[19] Gram-positive bacteria responded very well to vancomycin.

This situation is serious as these are the last line antibiotics available with us. If we continue using these, resistance will obviously emerge against these as well. To prevent, we should stress more upon preventive measures, so that minimum of

our neonates develop sepsis. These preventive measures should focus on recognition of high-risk infant, strict asepsis during labor[24].

Conclusion

Multi-drug-resistant organisms were isolated from septicemia in neonates. Therefore, great caution is required in selection of antibiotic therapy. Strict infection control in neonatal units, hand washing along with regular surveillance of neonatal sepsis is required in order to bring about changes in risk factors and antibiotic susceptibility patterns.

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