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Bacteriological Profile of Neonatal Septicemia in a Tertiary Care Hospital, Western U.P., India

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A B S T R A C T

Neonatal septicemia remains one of the most important causes of mortality despite considerable progress in hygiene, introduction of new antimicrobial agents and advanced measures for early diagnosis and treatment. Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture in the first four weeks of life. To isolate and identify the bacterial etiologic agents responsible for neonatal sepsis and determine the antibiotic susceptibility pattern of isolates in a tertiary care hospital in Greater Noida, Western U.P. Blood samples from the suspected infants were collected and processed in the bacteriology laboratory. The growth was identified by standard microbiological protocol and the antibiotic sensitivity testing was carried out on MHA by Kirby-Bauer disk diffusion method as recommended in CLSI guidelines. Out of the 147 suspected blood culture samples, 52 (35.4%) shows blood culture positive. 46 (88.5%) had Gram positive and 6 (11.5%) neonates had Gram negative septicemia. 31 (59.6%) cases were due to early onset septicemia. CoNS (55.8%) was the predominant Gram positive organism and *Klebsiella* species (7.7%) was the predominant Gram negative organism Best overall sensitivity among Gram positive isolates was to vancomycin (100%) and linezolid (100%) followed by amikacin (93.3%) and ciprofloxacin (63%). Gram negative isolates demonstrated highest sensitivity against imipenem (100%) and ciprofloxacin (100%) followed by meropenem (83.3%) and amikacin (83.3%). The result of our study reveals that the CoNS, *Staphylococcus aureus* and *Klebsiella pneumoniae* are the most common etiological agents of neonatal septicemia. In particular, since rate of CoNS causing sepsis is alarming, prompting concern to curb the excess burden of CoNS infection is necessary.

Introduction

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. When pathogenic bacteria gain access into the bloodstream, they may cause overwhelming infection without much localization (septicemia) or may be predominantly localized to the lung (pneumonia) or the meninges (meningitis). Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture in the

first four weeks of life (Agnihotri *et al.*, 2004). Neonatal septicemia remains one of the most important causes of mortality despite considerable progress in hygiene, introduction of new antimicrobial agents and advanced measures for early diagnosis and treatment (Gotoff, 1996; Haque, 1988). Prior to the antibiotic era, the mortality from septicemia was 90% but it declined to 24-58% after antibiotics came into use (Kaushik *et al.*, 1998). According to World Health Organization (WHO) estimate, there are about 5 million neonatal deaths a year, with 98% occurring in developing countries (World Health Organization, 1996). The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. The NNPD network comprising of 18 tertiary care neonatal units across India found sepsis to be one of the commonest causes of neonatal mortality contributing to 19% of all neonatal deaths (National Neonatal Perinatal Database, 2002-03).

Neonatal sepsis is classified as early onset when it occurs within the first 72 hours of life and late onset when it occurs after 72 hours of life (Al-Zwani, 2002; Bukhari and Alrabiaah, 2011; Chacko and Sohi, 2005). Early onset sepsis is caused by organisms prevalent in the maternal genital tract, labour room or operating theatre (Bellig and Ohning, 2013; Zaidi *et al.*, 2008) while late onset sepsisusually results from nosocomial or community-acquired infection (Zaidi *et al.*, 2008; Sankar *et al.*, 2008). Among intramural births, *Klebsiella pneumoniae* is the most frequently isolated pathogen (32.5%), followed by *Staphylococcus aureus* (13.6%). Among extramural neonates (referred from community/other hospitals), *Klebsiella pneumoniae* is again the commonest organism (27%), followed by *Staphylococcus aureus* (15%) and *Pseudomonas* (13%) (National Neonatal Perinatal Database, 2002-03).

Sepsis is one of the most common causes of neonatal hospital admissions (Sankar *et al.*, 2008; Darmstadt *et al.*, 2009; Sundaram *et al.*, 2009). Newborns are particularly susceptible to sepsis as a result of their immature immune system, the decreased phagocytic activity of their white blood cells and their incompletely developed skin barriers (Levy, 2007; Shah *et al.*, 2006; Trotman *et al.*, 2006). Common risk factors for neonatal sepsis in Northern India have been identified as low birth weight, perinatal asphyxia, preterm labour and premature rupture of membranes (Roy *et al.*, 2002).

Neonatal sepsis is a medical emergency which presents with subtle, diverse and nonspecific symptoms and signs (Ahmed *et al.*, 2005). Delay in diagnosis and commencement of appropriate treatment may result in high morbidity and mortality rates (Ahmed *et al.*, 2005). Blood culture, which is the gold standard for the diagnosis of sepsis, takes at least 48 hours to obtain preliminary results (Buttery, 2002). It is therefore necessary to initiate an empirical choice of antibiotics based on the epidemiology of causative agents and antibiotic sensitivity patterns in a locality (Asuquo, 1996). Periodic bacterial surveillance is a necessity in every unit because the organisms responsible for neonatal sepsis have been shown to vary across geographical boundaries and with time of onset of illness (Al-Zwani, 2002). So, the present study has been undertaken to determine the bacteriological profile and antimicrobial sensitivity patterns from blood cultures of neonates in a Tertiary Care Hospital in Greater Noida, India.

Materials and Methods

This was a cross sectional study conducted in the Department of Microbiology, School of Medical Science and Research, Greater Noida. The study was conducted over a period of 12

months from January 2015 February 2016. During the study, a total of 147 non repeat blood samples obtained from septicemia suspected neonates who were admitted in NICU. Ethical considerations: Ethical approval for the study was obtained from the Institutional Ethics and Research Committee.

Blood culture sample included a single sample collected from a peripheral vein under aseptic conditions. The local site was cleaned with 70% alcohol and povidone iodine (1%), followed by 70% alcohol again. Approximately, 1-3 ml of blood was inoculated into "BacT/ALERT PF Plus" aerobic pediatric culture bottle aspetically. The culture bottle was kept in BacT/ALERT Microbial Detection System. The positive culture bottle was taken out of the BacT/ALERT instrument after signal. The sample was sub cultured on Blood agar and Mac Conkey agar. Isolates were identified by their characteristic appearance on their respective media, Gram staining and confirmed by the pattern of biochemical reactions using the standard method (Mackie and McCartney, 2006).

Antimicrobial susceptibility testing were performed for all blood culture isolates on Muller-Hinton agar by Kirby–Bauer disc diffusion method as recommended in the CLSI (Clinical And Laboratory Standards Institute) guidelines (Clinical and Laboratory Standards Institute, 2014). The inhibition zone standards for antimicrobial susceptibility were considered from tables for interpretative zone diameters of CLSI.

Results and Discussion

A total of 147 blood samples collected and processed using standard procedures, 95 (64.6%) were culture negative and 52 (35.4%) showed culture positive result. Among the culture positive cases, 30 (57.69%) were male and 22 (42.31%) were female neonates with the male to female ratio 1.3:1. The culture positive samples were further processed and analysed. Of which, 46 (88.5%) were found to be Gram positive cocci (GPC) while 6 (11.5%) were Gram negative bacilli (GNB).

Among Gram positive cocci, Coagulase negative *Staphylococcus* (55.8%) was predominant organism isolated followed by *Staphylococcus aureus* (30.8%). While among Gram negative bacilli, *Klebsiella* species (7.7%) was predominant (Table 1).

Early onset sepsis (sepsis which occurs in first 72 hours of life) cases were found to be higher than late onset sepsis (sepsis which occurs after 72 hours of life). Out of 52 culture positive cases, 31 (59.6%) had early-onset sepsis and 21 (40.4%) had late-onset sepsis (Table 1).

Various risk factors in mother and neonates were studied which showed preterm labour 30.8% as the most common maternal risk factor. While the most frequently associated neonatal risk factor was low birth weight affecting 59.6% of the neonates (Table 2).

The antimicrobial sensitivity pattern of various organisms was also studied. All Gram positive cocci demonstrated highest sensitivity against vancomycin (100%) and linezolid (100%) followed by amikacin (93.3%) and ciprofloxacin (63%). High resistance was shown against penicillin (84.8%) (Table 3).

All Gram negative bacilli which includes *Klebsiella* species and *E. coli* demonstrated highest sensitivity against imipenem (100%) and ciprofloxacin (100%) followed by meropenem (83.3%) and amikacin (83.3%). Resistance was shown against cefixime (83.3%), cefotaxime (83.3%), cefuroxime (66.3%) and amoxicillin/clavulanic acid (66.3%) (Table 4).

Table.1 Distribution of isolated microorganisms

Organisms	Number (%)	Early onset (%)	Late onset (%)
Gram Positive Cocci	**46 (88.5%)**		
CoNS	29 (55.8%)	19 (61.3 %)	10 (47.6%)
S. aureus	16 (30.8%)	9 (29%)	7 (33.3%)
Enterococcus	1 (1.9%)	-	1 (4.8%)
Gram Negative Bacilli	**6 (11.5%)**		
***Klebsiella* species**	4 (7.7%)	2 (6.5%)	2 (9.5%)
E. coli	2 (3.8%)	1 (3.2%)	1 (4.8%)
Total	**52 (100%)**	**31 (59.6%)**	**21 (40.4%)**

Table.2 Risk factors associated with neonatal septicemia

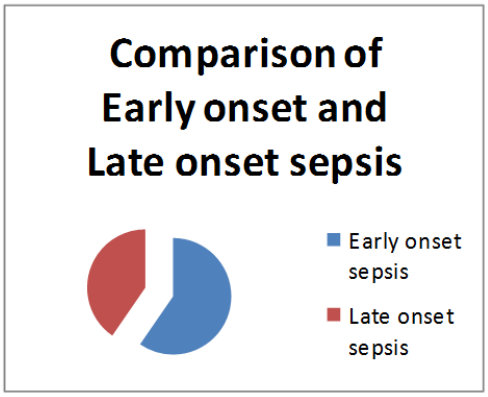
Risk factors	Number	Percentage
Neonatal risk factors		
Low birth weight	31	59.6%
Perinatal asphyxia	18	34.6%
Prematurity	15	28.9%
Maternal risk factors		
Preterm labour	16	30.8%
PROM	9	17.3%
Intrapartum fever	5	9.6%

Table.3 Antibiotic sensitivity of Gram positive cocci (GPC)

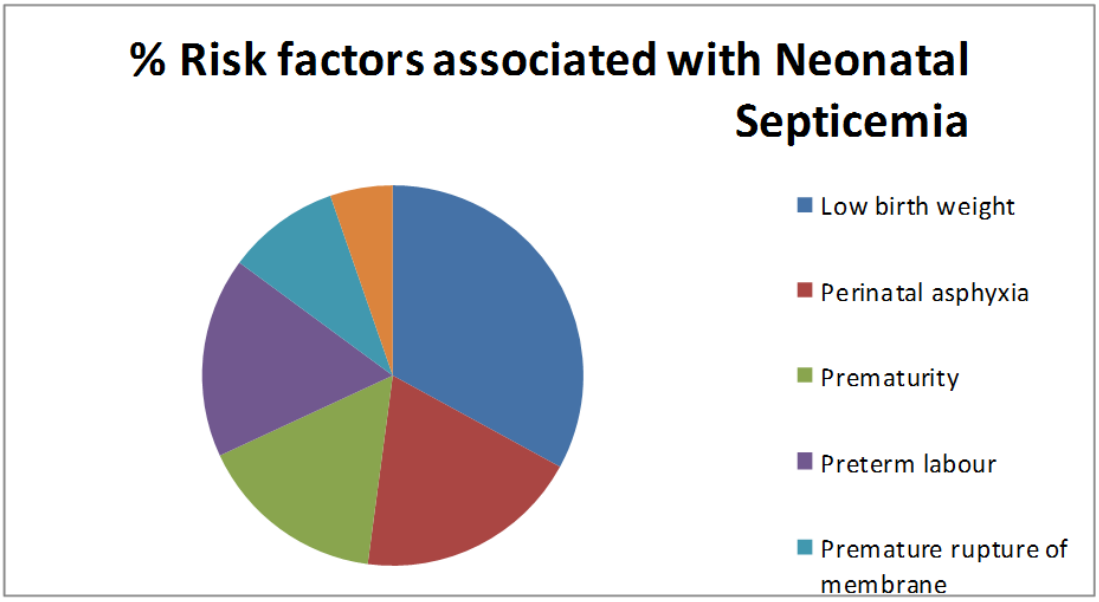
Antibiotics	Sensitivity			Total Sensitivity of GPC
	CoNS (%) (n=29)	S. aureus (%) (n=16)	Enterococcus (%) (n=1)	
Penicillin	5 (17.2%)	2 (12.5%)	0 (0%)	15.2%
Cefoxitin	13 (44.8%)	10 (62.5%)	-	51.1%
Vancomycin	29 (100%)	16 (100%)	1 (100%)	100%
Amikacin	27 (93.1%)	15 (93.8%)	-	93.3%
Erythromycin	13 (44.8%)	7 (46.7%)	-	44.4%
Ciprofloxacin	18 (62%)	10 (62.5%)	1 (100%)	63%
Clindamycin	20 (69%)	7 (43.8%)	-	60%
Linezolid	29 (100%)	16 (100%)	1 (100%)	100%

Table.4 Antibiotic sensitivity of Gram negative bacilli (GNB)

Antibiotics	Sensitivity		Total Sensitivity of GNB
	Klebsiella (%) (n=4)	E. coli (%) (n=2)	
Amoxycillin/Clavulanic acid	1 (25%)	1 (50%)	33.7%
Cefixime	0 (0%)	1 (50%)	16.7%
Cefotaxime	1 (25%)	0 (0%)	16.7%
Cefuroxime	1 (25%)	1 (50%)	33.7%
Imipenem	4 (100%)	2 (100%)	100%
Meropenem	4 (100%)	1 (50%)	83.3%
Amikacin	4 (100%)	1 (50%)	83.3%
Gentamicin	2 (50%)	1 (50%)	50%
Ciprofloxacin	4 (100%)	2 (100%)	100%
Levofloxacin	3 (75%)	1 (50%)	66.7%



Comparison of early onset and late onset sepsis in confirmed cases



Percentage of risk factors associated with neonatal septicemia

The clinical signs and symptoms of neonatal sepsis are subtle and nonspecific, making its early diagnosis difficult and it can interfere with other life-threatening diseases, such as necrotizing enterocolitis and perinatal asphyxia (English, 2004; The Young Infant Clinical Study Group, 2008). So for effectual management of septicemia cases, study of bacteriological profile along with the antimicrobial sensitivity pattern plays a noteworthy role.

During the study period, out of 147 neonates who were admitted in NICU with signs and symptoms of neonatal sepsis, 52 neonates (35.4 %) were confirmed to have bloodstream infection. This result was comparable to results reported by Ahmed *et al.,* (2002) (34.9%), Mondal *et al.,* (1991) (36%) and Mugalu *et al.,* (2006) (37%). However, negative blood culture does not exclude sepsis as about 26% of all neonatal sepsis could be due to anaerobes (Shrestha *et al.,* 2008).

In this study, a male preponderance with male to female ratio of 1.3:1 was found which was in accordance with the report of (Shah *et al.,* 2012) (1.2:1) and (Shehab El-Din *et al.,* 2015) (1.3:1). This might be because of more number of male infants born compared to female infants born.

In the present study, Gram negative and Gram positive organisms accounted for 88.5% and 11.5% of the cases respectively. Among Gram positive cocci, Coagulase negative *Staphylococcus* (55.8%) was predominant organism isolated. While among Gram negative bacilli, *Klebsiella* species (7.7%) was predominant. Similar results were also reported by (Kohli-Kochar *et al.,* 2011) from Nairobi, Kenya.

Group B streptococcal (GBS) sepsis is the most important cause of neonatal sepsis in Europe and North America (Fisher *et al.,* 1983). But GBS was not isolated in our study. The insignificance of GBS as a pathogen in many developing countries is supported by a number of other studies (Walsh and Hutchins, 1989; Duruvilla *et al.,* 1999). This might be attributable to low prevalence of GBS colonization of pregnant mothers in this area or possibly, to the presence of strains with low virulence.

In the present study, early onset septicemia was observed in 59.6% cases, while it was 55.3% in studies by (Vinod Kumar *et al.,* 2008), 61.8% by Kohli-Kochar *et al.,* (2011) and 64.7% by Aletayeb *et al.,* (2011).

In our study, maternal risk factors commonly associated were preterm labour (30.8%) and premature rupture of membrane (17.3%) while the common neonatal risk factor was low birth weight (59.6%) followed by perinatal asphyxia (34.6%). These findings were similar to the study conducted by Roy *et al.,* (2002) which showed preterm labour (32%) and premature rupture of membrane (PROM) (28.9%) as commonly associated maternal risk factors while low birth weight (63.8%) and perinatal asphyxia (37.5%) as neonatal risk factors.

Antibiotic resistance is today a global problem. Reports of multi‐ resistant bacteria causing neonatal sepsis in developing countries are increasing. The wide availability of over the counter antibiotics and the inappropriate use of broad‐ spectrum antibiotics in the community may explain this situation. It is difficult to compare antibiotic resistance between countries because the epidemiology of neonatal sepsis is extremely variable (Vergnano *et al.,* 2005).

In our study, all Gram positive isolates were frequently found to be penicillin resistant (84.8%). Most sensitivity was shown against vancomycin (100%) and linezolid (100%)

followed by amikacin (93.3%) and ciprofloxacin (63%). Similar findings were reported in the study done by Sudarshan *et al.,* (2013), Shah *et al.,* (2012) and Roy *et al.,* (2002). In the present study, all Gram negative isolates demonstrated highest sensitivity to antibiotics like imipenem (100%), ciprofloxacin (100%), meropenem (83.3%) and amikacin (83.3%). These results were results were similar to the previous study (Sudarshan *et al.,* 2013).

The epidemiology of neonatal septicemia is a changing landscape. Early and late onset sepsis continues to be associated with significant morbidity and mortality, including long term morbidity. Therefore, there is need of regular periodic surveillance of the causative organisms of neonatal sepsis as well as their antibiotic susceptibility patterns to inform the choice of empirical antibiotic prescription while awaiting blood culture results. Furthermore, health education should be provided to the public on the dangers of indiscriminate use of antibiotics, which is currently considered to be a menace in our society and which has been responsible for the ineffectiveness of most commonly used antibiotics such as penicillin, as observed in our study.

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