Int.J.Curr.Microbiol.App.Sci (2018) *7*(8): 3999-4005

International Journal of Current Microbiology and Applied Sciences
***ISSN: 2319-7706* Volume 7 Number 08 (2018)**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2018.708.414

Bacteriological Profile and Antibiogram of Neonatal Septicemia in a Tertiary Care Hospital

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Keywords

Neonatal sepsis, Blood culture, Antibiogram, CoNS, *Klebsiella*

Article Info

Accepted:
22 July 2018
Available Online:
10 August 2018

A B S T R A C T

Septicemia in neonates refers to generalized bacterial infection documented by positive blood culture in the first four weeks of life. Neonatal septicaemia 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. In this cross-sectional study, 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 neonates (M: F = 1.3: 1) admitted to the NICU, 52 (35.4%) shows blood culture positive. Gram positive was the major organism isolated 46 (88.5%), followed by Gram negative organism 6 (11.5%). CoNS (63%) was the predominant Gram positive organism and *Klebsiella* species (66.6%) was the predominant Gram negative organism. Best overall sensitivity among Gram positive isolates was to vancomycin (100%) and linezolid (100%). High level resistance was seen against penicillin and fluoroquinolones. Gram negative isolates demonstrated highest sensitivity against imipenem (100%) and ciprofloxacin (100%). High level resistance was seen against cephalosporins. Neonatal septicaemia is associated with the significant mortality and morbidity. Due to changing micrbiological and antibiotic pattern, a regular surveillance is necessary and blood culture is the gold standard method for diagnosis and should be done in all the suspected cases of neonatal sepsis.

Introduction

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteraemia 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 septicaemia 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) 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. (http://www.newbornwhocc.org/pdf/nnpd_report_2002-03.pdf)

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; 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 sepsis usually 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%) (http://www.newbornwhocc.org/pdf/nnpd_report_2002-03.pdf).

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. 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 our hospital.

Materials and Methods

The present study was conducted in Microbiology department at tertiary care centre sharda hospital, Greater Noida over a period of one year on 147 neonates admitted in neonatal intensive care unit with clinically suspected septicemia.

Blood sample was collected from a peripheral vein under aseptic conditions. Approximately, 1-3 ml of blood was inoculated into "BacT/ALERT PF Plus" aerobic pediatric culture bottle aseptically. Blood culture was performed using a Bectec Dickson ped plus aerobic bottles and incubation was performed in Bactec 9240 system. All the bottles were subjected to gram stain and subculture on

Blood agar and MacConkey Agar. The plates were incubated at 37oC for 24hrs. Growth was identified by colony morphology, gram stain and standard biochemical tests. (Mackie and McCartney, 2006)

Antimicrobial susceptibility testing was performed on Muller-Hinton agar by Kirby–Bauer disc diffusion method as recommended in the CLSI guidelines 2014 (CLSI, 2014). Antibiotic disks were procured from Himedia and were penicillin (10 units), cefoxitin (30 µg), vancomycin (30 µg), amikacin (30 µg),erythromycin (15 µg), ciprofloxacin (5 µg), clindamycin (2 µg), linezolid (30 µg), amoxicillin/clavulanic acid (20/10 µg), cefixime (5 µg), cefotaxime (30 µg), imipenem (10 µg), meropenem (10 µg), amikacin (30 µg), gentamicin (10 µg), ciprofloxacin (5 µg) and levofloxacin (5 µg).

Results and Discussion

During the study period, 147 non repeat blood samples were collected from suspected neonatal septicemia patients. Blood culture positive were seen in 52(35.4%) neonates. Of which 30(57.6%) cases were male and 22(42.3%) were female with male to female ratio 1.3:1. Gram positive isolates constituted major group 46(88.5%) followed by Gram negative isolates 6(11.5%). Among gram positive isolates, *Coagulase Negative Staphylococcus* species (CoNS) was found to be the predominant pathogen 29(63%) followed by *Staphylococcus aureus* 16(34.7%). While, among gram negative isolates, *Klebsiella* species 4(66.6%) was predominant organism (Table 1).

Antibiogram of gram positive organisms is shown in Table 2. 100% sensitivity was seen against vancomycin and linezolid. Antibiogram of gram negative isolates is shown in Table 3. 100% sensitivity was seen against carbapenems and ciprofloxacin. The changing microbiological patterns of neonatal septicemia warrant the need of monitoring of causative organism and their antibiotic sensitivity pattern. Also the clinical signs and symptoms of neonatal sepsis are subtle and nonspecific, making its early diagnosis difficult. So for effectual management of septicemia cases, study of bacteriological profile along with the antimicrobial sensitivity pattern plays an important role (English *et al.,* 2014; The Young Infant Clinical Study Group, 2008).

In our study, out of 147 clinically suspected cases of sepsis, 52 were culture positive with blood culture positivity rate of 35.4%. There has been a wide variation in growth positivity obtained by blood culture over the years. A high isolation rate was reported by Murty *et al.,* (52.6%), Roy *et al.,* (47.5%) and *Thakur et al.,* (47%). (Murty and Gyaneshwari, 2007; Roy *et al.,* 2002; Thakur *et al.,* 2016) A lower positivity rate 26.6%, was observed by Vrishali muley *et al.,* which was comparable with the present study (Muley *et al.,* 2015). Relative low isolation rate seen in our study may be due to several reasons like administration of antibiotic before blood collection. Even negative blood culture does not exclude sepsis as about 26% of all neonatal sepsis could be due to anaerobes (Jyothi *et al.,* 2013).

The pathogens most often implicated in neonatal sepsis in developing countries from those seen in developed countries. In our study, the isolation rate of Gram positive and Gram negative organism was 88.5% and 11.5% respectively. Similarly, the higher isolation of Gram positive organism has been reported by previous studies (Ballot *et al.,* 2012; Kaufman and Fairchild, 2004; Van den Hoogen *et al.,* 2010; Galhotra *et al.,* 2015). While other authors reported gram negative organism as a predominant organism (Muley *et al.,* 2015; Jyothi *et al.,* 2013). The

predominance of gram positive organism in our study may be due to many reasons like overcrowding in NICU, lack of knowledge about infection control measure among Healthcare providers (Thakur *et al.*, 2016).

Table.1 Species distribution

Organisms	Number (%)
Gram Positive Cocci	**46 (88.5)**
CoNS	29 (63)
S. aureus	16 (34.7)
Enterococcus	1(2.1)
Gram Negative Bacilli	**6 (11.5)**
***Klebsiella* species**	4 (66.6)
E. coli	2 (33.3)
Total	**52 (100%)**

Table.2 Antibiotic resistant profile of Gram positive organisms

Antibiotics	Organism		
	***CoNS* (%) (n=29)**	***S. aureus* (%) (n=16)**	***Enterococcus* (%) (n=1)**
Penicillin	82.7	87.5	100
Cefoxitin	55.1	37.5	-
Vancomycin	-	-	-
Amikacin	6.8	6.2	100
Erythromycin	55.1	56.2	100
Ciprofloxacin	37.9	37.5	-
Clindamycin	31	56.2	100
Linezolid	-	-	-

Table.3 Antibiotic resistance pattern of Gram negative bacilli (GNB)

Antibiotics	Organism	
	Klebsiella (%) (n=4)	**E. coli (%) (n=2)**
Amoxycillin/Clavulanic acid	75	50%
Cefixime	100	50
Cefotaxime	75	100
Imipenem	-	-
Meropenem	-	-
Amikacin	-	50
Gentamicin	50	50
Ciprofloxacin	-	-
Levofloxacin	25	50

CoNS (63%) was the predominant gram positive organism isolated in this study. Similarly, Gheibi *et al.,* reported *CoNS* (54.6%) as predominant gram positive organism (Gheibi *et al.,* 2008). Some of the previous studies also observed *CoNS* as their predominant pathogen (Muley *et al.,* 2015; Sneha Ann Oommen *et al.,* 2015) In present study, *S.aureus* was isolated from 34.7% cases and was the next common pathogen following *CoNS*. While *S. aureus* was reported as predominant pathogen by (Thakur *et al.,* 2016) most common gram negative organism isolated in our study was *Klebseilla species* (66.6%), which was comparable with the previous studies findings (Roy *et al.,* 2002; Muley *et al.,* 2015).

This change of bacteriological profile from predominant gram negative to predominant gram positive isolation has been observed worldwide. Many recent studies have reported the emergence of new emerging organism such as *CoNS, Candida species* as a cause of neonatal sepsis (Thakur *et al.,* 2016). The colonization of skin and nasopharynx by *CoNS* and *S.aureus* in healthcare workers and improper hand washing technique leading to horizontal transmission to neonates further leads to increase in isolation rate of gram positive organism in them (Thakur *et al.,* 2016)

In our study, a male preponderance was seen with male to female ratio of 1.3:1 which was in concordance with previous studies (Jyothi *et al.,* 2013; Galhotra *et al.,* 2015). This might be because of more number of male infants born compared to female infants born.

The antibiotic sensitivity pattern differs in different studies at different times in the same hospital worldwide. This is mainly due to indiscriminate use of antibiotics (Tsering *et al.,* 2011). In present study, maximum number of organism was resistant to commonly used antibiotics. Antibiogram of our study revealed that majority of Gram positive isolates (*CoNS and S. aureus)* were resistant to penicillin (82.7% and 87.5%). Similar findings were reported by (Roy *et al.,* 2002; Jyothi *et al.,* 2013; Tsering *et al.,* 2011) All gram positive isolates showed 100% sensitivity against Vancomycin and Linezolid, which was in concordance with the previous studies findings (Roy *et al.,* 2002; Jyothi *et al.,* 2013). Hence, these drugs can be effectively be used in multi-drug resistance cases.

Among gram negative isolates, *Klebsiella spps* and *E.coli* resistant pattern were as follows respectively; Amoxycillin/clavulinic acid (75% and 50%), Cefotaxime (75% and 100%), Cefixime (100 % and 50%), Gentamicin (50% and 50%), Levofloxacin (25% and 50%). All gram negative isolates were 100% sensitive to carbapenems. Gram negative isolates showed resistance to β-lactam combination antibiotics and extended spectrum cephalosporins at high level. Similarly, high level resistance was reported by Roy *et al.,* (2002), Jyothi *et al.,* (2013), Galhotra *et al.,* (2015). Therefore, these drugs can't be used as empiric treatment for neonatal sepsis. However, low resistance was seen against flouroquinolones and carbapenems. These drugs can be used as empirical therapy in order to prevent multidrug resistance, but it should be used cautiously.

The microbiological pattern of neonatal septicemia is a changing landscape and is 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 treatment while awaiting blood culture results. *CoNS* and *Klebsiella*

was observed to be the leading cause of neonatal sepsis in our study and were resistance to commonly used antibiotics. Therefore, regular monitoring of antibiotic resistance is necessary and depending on the antibiotic sensitivity pattern of the isolates, antibiotic should be used. Blood culture is a Gold Standard for diagnosis of neonatal sepsis and should be done in all the suspected cases of neonatal sepsis.

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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How to cite this article:

Bipin Gupta, Sneha Mohan, Anjali Agarwal and Renu Dutta. 2018. Bacteriological Profile and Antibiogram of Neonatal Septicemia in a Tertiary Care Hospital. *Int.J.Curr.Microbiol.App.Sci.* 7(08): 3999-4005. doi: https://doi.org/10.20546/ijcmas.2018.708.414