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BACTERIOLOGICAL PROFILE OF NEONATAL SEPTICEMIA IN A TERTIARY CARE HOSPITAL FROM CENTRAL INDIA

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ABSTRACT Neonatal sepsis is one among the major causes of morbidity and mortality of newborns accounting for about 30-50% of total neonatal deaths in developing countries. Surveillance of causative organisms and their antibiotic sensitivity pattern promotes appropriate empirical therapy and rational use of antibiotics. The present study was undertaken to determine the bacteriological profile and antimicrobial susceptibility pattern of prevalent pathogens isolated from the blood of septicemic neonates from Neonatal Intensive Care Unit (NICU) at Government Medical College Gondia, Maharashtra. Out of 210 neonates with clinical suspicion of sepsis admitted from January 2021 to January 2022, 110 neonates had blood culture positive sepsis. Sepsis was predominant in male babies accounting to 64.5%. Early onset sepsis (EOS) occurred in 58.1% of the cases and late onset sepsis (LOS) in 41.9% of the neonates. Gram-positive cocci constituted 67.52% of all isolates and gram negative 30.76%. The most frequently isolated organism in blood was methicillin resistant Staphylococci aureus (MRSA) (32.47%). Gram positive organisms included Methicillin resistant coagulase negative Staphylococcus (MRCoNS), Group B Streptococci (GBS) and Enterococci. Among Gram-negative organisms, Acinetobacter was most frequently isolated followed by Klebsiella, Escherichia coli, Pseudomonas, Citrobacter. Gram negative organisms were most resistant to ampicillin and cephalosporins. Gram positive isolates were least resistant to vancomycin and linezolid. This concludes broad range of bacteria are associated with neonatal sepsis and revealed variation in antibiotic susceptibility pattern among bacterial isolates. This study highlights the predominance of Gram positive organisms in causing neonatal sepsis and emergence of multi-drug-resistant strains in our set up.

KEYWORDS : Neonatal sepsis, Antibiotics, Blood culture, Mortality

INTRODUCTION:

Septicemia is the significant cause of morbidity and mortality in neonates and is responsible for 30-50% of total neonatal deaths each year in developing countries. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes.[1] In India, according to National Perinatal Database (NNPD) 2020-21, the incidence of neonatal septicemia has been reported to be 30/1000 live births.[2]

Early diagnosis and appropriate therapy of septicemia is of utmost importance to prevent morbidity and mortality.[3] Neonates are immune compromised and defend weakly to bacterial infections. The bacterial agents associated with neonatal sepsis are Group B Streptococci, *Escherichia coli*, *Listeria monocytogenes*, coagulase-negative Staphylococci (CoNS), Staphylococcus aureus, Enterococci, Klebsiella spp., Enterobacter spp., Pseudomonas spp., Salmonella spp., H. infuenzae, *Neisseria meningitidis*, and *Streptococcus pneumoniae*.[4-6]

AIM AND OBJECTIVES:

The present study was carried out to determine the bacteriological profile and antimicrobial susceptibility pattern of prevalent pathogens isolated from the blood of septicemic neonates from Neonatal Intensive Care Unit (NICU) at Government Medical College Gondia.

MATERIAL AND METHODS:

The present Hospital based Cross sectional Prospective study was carried out in the department of Microbiology for period of 12 months from January 2021 to January 2022. 210 neonates with clinical suspicion of septicemia admitted in NICU were studied bacteriologically. Blood samples of these neonates were collected with strict aseptic precautions.

Blood culture was done by BD BACTEC method and Antimicrobial susceptibility testing was performed by Kirby-Bauer disc diffusion susceptibility method in accordance to Clinical Laboratory Standards Institute (CLSI) guidelines 2021.[7] Culture positive sepsis was defined as isolation of bacterial pathogen from blood in neonates with clinical suspicion of sepsis. Cases of sepsis were divided into early onset sepsis (EOS) and late onset sepsis (LOS). Early onset sepsis was defined as onset of sepsis within 72 hours of life and late onset as after 72 hours of life.

RESULTS:

A total of 117 organisms were isolated from 110 blood cultures, of which 78 were gram positive organisms which constituted 66.66%, 37 were gram negative organisms which constituted 31.63% and 10 fungal isolates constituted 8.54%. Gram positive organisms included methicillin resistant coagulase negative Staphylococcus (MRCoNS), methicillin resistant Staphylococci aureus (MRSA), Group B Streptococci (GBS), *Staphylococcus aureus* and *Enterococcus feacalis*. Among the gram-negative organisms, Acinetobacter was the commonest organism isolated, followed by Klebsiella, *Escherichia coli*, Pseudomonas, Citrobacter species. Six blood cultures had polymicrobial growth. Distribution of isolated organisms from blood samples of septicemic neonates is detailed in Table No.1. The most frequently isolated organism in the blood was MRSA (32.47%) followed by MRCoNS (13.70%), Group B Streptococci (7.7%) and Acinetobacter (7.7%). Methicillin resistant staphylococcus aureus was the most common pathogen isolated in early onset sepsis (EOS) as well as late onset sepsis (LOS).

Table No.1: Distribution of Isolated Organisms Among Septicemic Neonates

ORGANISMS	NUMBER OF ISOLATES (n = 117)	PERCENTAGE (%)
MRSA	38	32.47%
MRCoNS	16	13.70%
Group B Streptococcus (GBS)	9	7.7%
Acinetobacter species	9	7.7%
Staphylococcus aureus	8	6.83%
Klebsiella pneumoniae	8	6.83%
E. coli	5	4.30%

Pseudomonas species	4	3.42%
Citrobacter species	3	2.56%
Enterococcus fecalis	3	2.56%
Candida species	10	8.54%
Staphylococcus sciuri	1	0.85%
Enterobacter cloacae	1	0.85%
Moraxella species	1	0.85%
Acromobacter species	1	0.85%

MRCoNS- Methicillin resistant coagulase negative Staphylococci; MRSA- Methicillin resistant Staphylococcus aureus; GBS- Group B Streptococci; E. coli - *Escherichia coli*

Among the Gram-positive organisms, only Group B Streptococci showed good sensitivity to amoxicillin (55.55%), ampicillin (88.88%) and ceftriaxone (55.55%). It also showed good sensitivity to fluoroquinolones. *Enterococcus feacalis* was 100% sensitive to ampicillin. *Enterococcus fecalis*, Group B Streptococci, *Stahpylococcus aureus* and MRSA showed 100% sensitivity to vancomycin, linezolid and tiecoplanin. High sensitivity pattern was observed for amikacin in isolates of MRCoNS (81.57%), Staphylococcus aureus (75%) and MRSA (75%). Methicillin resistant coagulase negative staphylococci and MRSA were resistant to most of the antibiotics tested and were highly resistant to amoxiciilin, ampicillin and cephalosporins. All isolates of *Stalylococcus aureus* were resistant to amoxiciilin and ampicillin but showed good sensistivity to ceftriaxone and levofloxacin (62.2% each), 100% to vancomycin, linezolid and teicoplanin as shown in TABLE No.2

Gram negative organisms were highly resistant to ceftriaxone, amoxicillin, ampicillin. Among them, Citrobacter showed 100% sensitivity to most of the antibiotics tested. Klebsiella and Pseudomonas showed good sensitivity to aminoglycosides and fluoroquinolones. Most of the gram-negative isolates showed 100% sensitivity to colistin except Pseudomonas. Although Acinetobacter was highly resistant to most of the antibiotics, all isolates were sensitive to colistin as explained in Table No.3.

Table No.2: Antibiotic Sensitivity of Gram Positive Organisms

ORGANISMS	MRSA n = 38 (%)	MRCONS n = 16 (%)	GBS n = 9 (%)	Staphylococcus aureus n = 8 (%)	Enterococcus faecalis n = 3 (%)
ANTIBIOTICS					
Amoxicillin	3 (18.75%)	1 (2.6%)	5 (55.55 %)	0	2 (66.66%)
Ampicillin	1 (6.25%)	2 (5.2%)	8 (88.88 %)	0	3 (100)
Ceftriaxone	3 (18.75%)	2 (5.2%)	5 (55.55 %)	5 (62.5%)	0
Amikacin	12 (75)	31 (81.57%)	0	6 (75%)	0
Gentamicin	4 (25%)	19 (50 %)	0	3 (37.5 %)	0
Ciprofloxacin	3 (18.75%)	5 (13.15%)	6 (66.66 %)	4 (50%)	1 (33.33%)
Levofloxacin	6 (37.5%)	11 (28.94%)	8 (88.88 %)	5 (62.5%)	1 (33.33%)
Clindamycin	9 (56.25%)	12 (31.57%)	6 (66.66 %)	5 (62.5%)	2 (66.66%)
Linezolid	16 (100%)	38 (100%)	9 (100%)	8 (100%)	3 (100%)
Vancomycin	16 (100%)	38 (100%)	9 (100%)	8 (100%)	3 (100%)
Teicoplanin	16 (100%)	32 (84.21%)	9 (100%)	8 (100%)	3 (100%)

MRCoNS- Methicillin resistant coagulase negative Staphylococcus ; MRSA- Methicillin resistant Staphylococci aureus; GBS- Group B Streptococci

Table No.3: Antibiotic Sensitivity of Gram Negative Organisms

ORGANISMS	E. coli n = 5 (%)	Klebsiella n = 8 (%)	Acinetobacter n = 9 (%)	Citrobacter n = 3 (%)	Pseudomonas n = 4 (%)
ANTIBIOTICS					
Amoxicillin	0	0	0	0	1 (33.33%)
Ampicillin	0	1 (12.5%)	0	0	0
Ceftriaxone	0	2 (5.2%)	5 (55.55%)	5 (62.5%)	0
Amikacin	4 (80%)	5 (62.5%)	2 (22.22%)	3 (100%)	3 (75%)
Gentamicin	2 (40%)	6 (75%)	2 (22.22%)	2 (66.66 %)	1 (33.33%)
Ciprofloxacin	1 (20%)	6 (75%)	2 (22.22%)	3 (100%)	3 (75%)
Levofloxacin	3 (60%)	7 (87.5%)	2 (22.22%)	3 (100%)	3 (75%)
Colistin	5 (100%)	8 (100%)	9 (100%)	3 (100%)	3 (76%)
Piperacillin - azobactam	5 (100%)	7 (87.5%)	1 (11.11%)	3 (100%)	1 (25%)
Meropenam	5 (100%)	7 (87.5%)	1 (11.11%)	3 (100%)	0
Ceftazidime	0	0	0	0	1 (25%)

DISCUSSION:

The selection of empirical antibiotics for neonatal sepsis should cover most of the common organisms and should be started immediately after obtaining cultures as neonatal sepsis is an important cause for mortality[8] Although blood culture is gold standard for diagnosis of neonatal sepsis, the use of intra-partum antibiotics and empirical antibiotics prior to collecting blood for culture decreases yield of culture.[9-11] The blood culture positivity in neonates with clinical suspicion of sepsis was 26.57% during the given study period which was similar to study done by Roy et al.[11] It was 18% in Bhat et al study and was higher (42.8%) in a study done in Egypt by Moshen et al. [12]

Similar results were observed in studies done by Jain et al and Galhotra et al. [13,14] Contrary to this, 72% presented with poor activity / poor cry in Reddy K V et al, study.[15] The most common type of sepsis in present study was early onset sepsis which is in parallel to studies by Galhotra et al, and Madavi et al. [14,16] whereas studies done in India by Goyal and Ozkal et al showed late onset sepsis as common sepsis type[17,18] The major organism causing early onset sepsis and late onset sepsis was MRSA in the current study which was in line with Ozkal's et al, study whereas in a study carried out by Sethi et al, Klebsiella was relatively more common in late onset sepsis while Enterococcus was more frequent in early onset sepsis.[18,19] All nine Group B Streptococcus organisms isolated in this study caused early onset sepsis which suggests possible association of maternal genital tract infection with early onset sepsis in neonates.

Worldwide, gram negative organisms are more common causes for neonatal sepsis and main organisms are Klebsiella spp, E. coli, Pseudomonas and Salmonella. *Staphylococcus aureus,* CONS, *Streptococcus pneumoniae* and *Streptococcus pyogenes* are most commonly isolated gram-positive organisms. In developing countries, E. coli, Group B Streptococcus, Enterobacter, Enterococcus, and Listeria are mostly associated with early onset sepsis. Klebsiella, Acinetobacter, CoNS and Staphylococcus aureus are associated with both early onset and Late Onset Sepsis. Pseudomonas, Salmonella, and Serratia are more often associated with late onset sepsis (LOS).[20] Present results indicate that, gram positive organisms are predominant over the gram-negative organisms corresponding to other studies done in Ghana and China.[21,22] Many studies have documented high antimicrobial resistance of the organisms causing neonatal sepsis[23]. In present study, methicillin resistance was seen in 97.36% of Staphylococcus aureus and 66.66% of CoNS. Staphylococcus aureus showed 100% resistance to amoxicillin-clavulanate and ampicillin, 62.5% to azithromycin, levofloxacin and gentamycin and 50% to ciprofloxacin. A study done by Iregbu K. C, showed decreases in susceptibility of Staphylococcus aureus to various antibiotics observed in two time periods 2002- 2004 and 2013-2015.[24] A decrease

in sensitivity of amoxicillin-clavulanate (85% to 76%), cefuroxime (45% to 0%), ciprofloxacin (71% to 67%), erythromycin (64% to 30%), gentamicin (40% to 29%) and ceftriaxone (36% to 27%) between the 2 study periods was observed. Non fermenting gram-negative bacilli (NFGNB) are emerging organisms causing neonatal sepsis. They exhibit multidrug resistance. Commonly isolated NFGNBs include Pseudomonas, Acinetobacter, and Burkholderia. In the current study, gram negative organisms, mainly Acinetobacter were highly resistant to many antimicrobials. Six out of nine Acinetobacter isolates were sensitive only to colistin and resistant to all other antimicrobials tested. Even though sepsis rate was more among gram positive organisms, the mortality was high in gram negative sepsis, in comparison to results of study done by Upadhay et al.[25]

CONCLUSION:

Gram positive sepsis was found to be common in present study. Careful measures have to be taken to overcome the change in trend of organisms causing sepsis, and selection of antibiotics should be prudent. Proper antibiotic guidelines and its effective implementation could be milestone for revolution in the field of antibiotic resistance control. The epidemiology of neonatal sepsis, causative risk factors and antibiotic resistance pattern of pathogens may be used to develop guidelines for management of neonatal sepsis. An effective infection control programme, regular antibiotic susceptibility surveillance and evaluation, and the enforcement and periodic review of the antibiotic policy of the hospital as well as the encouragement of rational antibiotic use will reduce the rates of acquiring nosocomial infections and development of bacterial resistance. Every NICU should develop their antibiogram in order to have appropriate antibiotic stewardship and decrease incidence of Multi Drug Resistance.

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