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PATTERN OF BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY AMONG BLOOD CULTURE POSITIVE NEONATAL SEPSIS IN A TERTIARY CARE HOSPITAL

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ABSTRACT: Background: Neonatal sepsis (NS) is among the most prevalent and potentially fatal conditions. Given the current surge in antimicrobial resistance, a thorough understanding of prevalent bacterial illnesses and their pattern of drug susceptibility is crucial. **Objectives:** To study the pattern of bacteriological profile and antibiotic susceptibility among blood culture-positive neonatal sepsis cases in a Tertiary care hospital. **Methods:** A Retrospective study was planned from Jan-Dec, 2023. All neonatal sepsis cases with positive blood culture from NICU admission were included, and neonates with multiple congenital malformations were excluded. A predetermined questionnaire was used to collect neonatal delivery details and the culture report. **Results:** Out of 1014 suspected cases, 194 were positive blood culture with 7.2% early onset sepsis and 92.7% late onset. NS was common in term deliveries with male predominance (72.2%) and in very low birth weight (53.6%). The most frequent causative organisms were gram positive among (65%), CoNS, 96(75.5%) was the predominant organism, followed by MRSA, 16(12.5%). Gram-negative isolates were seen in 67(34%), *Klebsiella species*-23(34%) is the most common cause, followed by Citrobacter-8(11.9%). Multi-drug-resistant organisms were seen in 21(10.8%) cases, was due to MRSA. The Gram-Positive organisms were mostly sensitive to Linezolid, Tigecycline and resistant to Benzylpenicillin and Oxacillin. The Gram-Negative organisms were mostly sensitive to Tigecycline and Cotrimoxazole and resistant to Ceftriaxone and Cefepime. **Conclusion:** CoNS, *Klebsiella species*, and MRSA are the major causative organism of neonatal sepsis. Understanding the antibiotic susceptibility will help in strengthening antibiotic stewardship and save neonates.

INTRODUCTION: Sepsis is a fatal medical disorder, usually occurs when microbes enter into the circulation. Neonatal sepsis (NS) is a common condition encountered in paediatric NICU (Neonatal Intensive Care Unit) and is divided into early-onset sepsis (EOS) and late-onset sepsis (LOS) based on number of days since birth.

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EOS refers to sepsis that occurs within the first 3 days of birth, while LOS occurs after 3 days of birth [1]. EOS is usually caused by organisms acquired from the mother during delivery or shortly after birth, while LOS is typically caused by organisms acquired from the environment, hospitals, or the community [2].

NS remains a major cause of neonatal morbidity and mortality, resulting in 2,25,000 deaths globally every year despite the advances in newborn care [3]. The high morbidity and mortality in NS is due to lack of host defence mechanisms in newborns, mainly in preterm and also lack of specific and sensitive tests to diagnose sepsis early, and less application of host defence modulating therapies [4]. The clinical indicators for neonatal sepsis includes respiratory distress starting after few hours of birth, need for mechanical ventilation, signs of shock, seizures, altered behaviour and muscle tone, difficulty in feeding, intolerance to feed, abnormal heart rate, apnoea, hypoxia, jaundice within 24 hours of birth, signs of neonatal encephalopathy, need for cardio–pulmonary resuscitation, temperature instability not explained by environment, unexplained bleeding disorder, oliguria beyond 24 hours after birth, altered glucose homeostasis, metabolic acidosis, and local signs of infection [5]. Though many investigations like complete blood count, ESR, C Reactive protein, Highly sensitive C-reactive protein, procalcitonin, Serum Amyloid A, Lipopolysaccharide-Binding Protein, tumour necrosis factor alpha, Interleukin 6, Interleukin 8 *etc* are available to diagnose neonatal sepsis, no single laboratory test is specific and sensitive for predicting neonatal infection [6, 7]. Blood culture is a gold standard method to identify bacterial infection and is done by isolating the etiological agent from a blood sample [8]. Hence, the results of laboratory tests must be assessed along with the presence of maternal or neonatal risk factors to correlate with the clinical signs of the sepsis.

The antibiotic regimens are given according to unit-based protocol concerning the antibiotic culture and sensitivity report. The probability of choosing a suitable antibiotic treatment is influenced by several aspects like, the types of bacterial pathogens common in that area, the patterns of resistance of these pathogens, and the unique clinical circumstances of the patient, including any existing comorbidities.

The emergence of antimicrobial resistance is a global concern [9]. It is important to have an adequate understanding of the prevalent bacterial pathogens and their antibiotic susceptibility when choosing empirical therapy [10]. As we have a limited reserve of antibiotics and the existing antimicrobials have developed resistance, managing NS is a challenging task. Reports around the world suggest that we will soon be approaching a post-antibiotic era [11]. Hence, the current research aimed to gain a complete understanding of the dominant microorganism and their patterns of antibiotic susceptibility. This in turn will aid in the establishment of departmental and institutional antibiotic stewardship policy in the NICU. Hence the present study was planned to study the pattern of bacteriological profile and antibiotic susceptibility among blood culture-positive neonatal sepsis cases in a tertiary care hospital.

MATERIALS AND METHODS: A retrospective observational study was performed at a tertiary care centre following approval from the ethical committee of the institute (BLDE(DU)/IEC/1086/2023-24). It included all cases of neonatal sepsis diagnosed with blood culture positive reports admitted to the NICU amongst Jan-Dec 2023. Cases involving neonates with multiple congenital malformations or complicated congenital heart disease were not included in the study. Demographic data for each neonate, such as type of delivery, gestational age, birth weight, gender, timing of infection onset, and birth asphyxia, were collected through a case record form. The VITEK method was used to characterise and assess the blood culture isolates' susceptibility to antibiotics.

TABLE 1:

Organism	Number
Pseudomonas species	5
Acinetobacter species	7
Enterobacteriaceae spp. *(-Citrobacter spp.* *-Enterobacter spp.* *-Klebsiella spp.* *-Escherichia spp.* *-Serratia spp.)*	44 (8+5+23+6+2)
Aeromonas species	1
Burkholderia species	7
Sphingomonas paucimobilis	1
Providencia rettgeri	1
Alloiococcus otitis	1

Statistical Analysis: The gathered data was input into a Microsoft Excel spreadsheet, and descriptive summary statistics were applied to outline the demographic characteristics, the organisms detected from the cultures, sensitivity patterns, and clinical results.

RESULTS: Throughout our study period 1014 were suspected for neonatal sepsis, out of which 194 were blood culture-positive. In positive cultures, 14 (7.2%) cases was EOS and 180 (92.7%) was LOS. About the type of delivery, 104

(53%) babies were term, and the remaining 90 (46.4%) were preterm. NS was common in males, accounting for 140 (72.2%), and only 54 (27.8%) were female babies. Neonatal sepsis was more predominant among very low birth weight babies, 104 (53.6%) and 90 (46.4%) were of normal weight.

Most of the culture-positive cases were gram-positive, accounting for 127(65%) and only 67(34%) were gram-negative. Out of 127 gram-positive organisms, 94 cases were Coagulase-negative Staphylococcus (CoNS), trailed by 7 cases of streptococcal species and 2 cases of *Kocuria rosea* **Table 1.** Among 67, gram-negative bacteria, entero-bacteriaceae species was frequently seen in 56 cases, *Klebsiella pneumoniae* in 23 cases, followed by *Burkholderia cepacia* in 7 cases **Table 2.**

TABLE 2: DISTRIBUTION OF GRAM-POSITIVE ORGANISMS

Organism	Number
Staphylococus spp.	119
-CoNS	
-*Staphylococcus aureus*	(96+7+16=119)
-MRSA	
Streptococcus species	6
Kocuria rosea	2
Total	127

Out of gram-positive isolates majority remained sensitive to Linezolid, Tigecycline, Nitrofurantoin, Vancomycin, Daptomycin, Tetracycline, Teicoplanin, Rifampicin, and Cotrimoxazole. But they were resistant to Oxacillin, Erythromycin, Clindamycin, Levofloxacin, and Ciprofloxacin **Table 3.**

TABLE 3: SENSITIVITY OF GRAM-POSITIVE ORGANISMS

Antibiotic	Sensitive	Resistant
Linezolid	115(90.5%)	3(2.3%)
Tigecycline	114(89.7%)	1(0.7%)
Nitrofurantoin	107(84.2%)	9(7%)
Vancomycin	97(76.3%)	5(3.9%)
Daptomycin	96(75.5%)	1(0.7%)
Tetracycline	95(74.8%)	19(14.9%)
Teicoplanin	94(74%)	12(9.4%)
Rifampicin	90(70.8%)	15(11.8%)
Cotrimoxazole	87(68.5%)	28(22%)
Gentamicin	67(52.7%)	47(37%)
Clindamycin	37(29.1%)	91(71%)
Ciprofloxacin	34(26.7%)	68(53.4%)
Levofloxacin	30(23.6%)	85(66.9%)
Erythromycin	22(17.3%)	92(72.4%)
Oxacillin	10(7.8%)	94(74%)
Chloramphenicol	4(3.1%)	NIL
Benzyl Penicillin	3(2.3%)	NIL
Cefoperazone/Sulbactam	1(0.78%)	NIL
Moxifloxacin	1(0.78%)	NIL
Minocycline	1(0.78%)	NIL
Ampicillin	1(0.78%)	NIL

Most of the gram-negative organisms remained susceptible to Tigecycline, Cotrimoxazole, Cefoperazone /Sulbactam, Amikacin, Gentamicin, and Colistin. But they showed resistance to Ceftriaxone, Cefipime, Ciprofloxacin, Cefuroxime, Cefuroxime axetil, and Imipenem **Table 4.**

TABLE 4: SENSITIVITY OF GRAM-NEGATIVE ORGANISMS

Antibiotic	Sensitive	Resistant
Tigecycline	48 (71.6 %)	5(7.4%)
Cotrimoxazole	40 (59.7%)	12(17.9)_
Cefoperazone / Sulbactam	33(49.2%)	19(28.3%)
Amikacin	30 (44.8%)	22(32.8)
Gentamicin	28 (41.8%)	21(31.3%)
Colistin	28 (41.8%)	20(29.8%)

Meropenem	25 (37.3%)	26(38.8%)
Fosfomycin	25 (37.3%)	16(23.8%)
Ciprofloxacin	23 (34.3%)	31(46.2%)
Imipenem	21(31.3%)	30(44.7%)
Piperacillin/Tazobactam	20(29.9%)	27(40.2%)
Cefipime	19(28.4%)	33(49.2%)
Ertapenem	13(19.4%)	21(31.3%)
Ceftriaxone	13(19.4%)	35(52.2%)
Amoxicillin/Clavulanic Acid	10(14.9%)	29(43.2%)
Cefuroxime	8(11.9%)	31(46.2%)
Daptomycin	8(11.9%)	NIL
Vancomycin	8(11.9%)	NIL
Tetracycline	8(11.9%)	2(2.9%)
Teicoplanin	7(10.4%)	NIL
Cefuroxime Axetil	6(8.9%)	30(44.7%)
Levofloxacin	5(7.4%)	10(14.9%)
Nitrofurantoin	4(5.9%)	NIL
Linezolid	3(4.4%)	NIL
Minocycline	3(4.4%)	1(1.4%)
Rifampicin	2(2.9%)	NIL
Benzyl Penicillin	2(2.9%)	NIL
Erythromycin	1(1.4%)	NIL
Doxycycline	1(1.4%)	NIL
Polymyxin B	1(1.4%)	NIL
Netilmycin	1(1.4%)	NIL
Tobramycin	1(1.4%)	NIL
Esbl	1(1.4%)	NIL
Aztreonam	1(1.4%)	NIL
Oxacillin	1(1.4%)	NIL
Ampicillin	1(1.4%)	NIL
Chloramphenicol	1(1.4%)	NIL
Ceftizoxime	1(1.4%)	NIL
Ceftolozane	1(1.4%)	NIL
Ceftazidime	1(1.4%)	NIL

In our study, 16 gram-positive organisms and 5 cases of gram-negative organisms were multidrug resistant. It includes mainly MRSA, *E. coli*, specifically carbapenem resistant entero-bacterales (CRE), *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* **Table 5**.

TABLE 5: DISTRIBUTION OF MDR ORGANISMS

Antibiotic	Frequency of MDR Organisms
MRSA	16
Escherichia coli (CRE)	3
Klebsiella pneumoniae (MDRO)	1
Pseudomonas aeruginosa (MDR)	1

DISCUSSION: Blood culture is highly sensitive and specific diagnostic method for neonatal sepsis. Guidelines for empirical antibiotic treatment are developed through continuous monitoring of the microbial spectrum accountable for neonatal sepsis and their altering antibiotic resistance patterns. Clinicians and microbiologists review sensitivity profiles and modify empiric antibiotic therapy accordingly [12]. Our study showed that gram-positive organisms were identified in 65% of all positive culture neonatal sepsis cases, while gram-negative organisms accounted for 34%. Coagulase-negative staphylococci (CoNS) were the frequently isolated organism in both early and late-onset sepsis, followed by *Klebsiella pneumoniae* and MRSA. A study by Mohammadi *et al.* also found CoNS to be the greatest recurrent causative agent [13]. CoNS are naturally present on human skin [14] and their presence in neonatal sepsis is common in the NICU, due to specific molecular strains among infants and healthcare staff [15].

Few strains of CoNS can continue in the NICU for years, which might be the reason for the high prevalence in our study (48%). Although CoNS are low virulent, they are responsible for serious infections in the bloodstream and other body areas [16]. Despite advanced intensive care, the mortality is high in neonatal sepsis cases because of the emergence of multidrug-resistant microbes. Initial detection of the bacteria and antibiogram directed therapy can aid manage neonatal sepsis. Our study showed high rates of multidrug resistance in gram-positive organisms, about 14% of MRSA, similar to the study by Ballot *et al.*[12] In an Egypt study conducted, the tested positive culture was only 9.2% for MDR. An increase in multidrug-resistant organisms (MDROs) is usually due to a lack of antimicrobial stewardship programs and inadequate implementation of infection control policies [17]. Cultures with MDROs remained mainly positive for gram-negative bacteria, and did not line up with antibiotic treatments, resulting in lengthy hospital stay. Most of the sepsis-positive instances were LOS (92.7%), while EOS accounted for just 7.2%. This indicates a greater occurrence of community acquired infections in newborns. The result of our study was in contrast to that of another study, where EOS was predominant, 78.3% [18].

The emergence of multidrug-resistant pathogens in neonatal healthcare makes it difficult to choose empirical antibiotic treatment for newborn sepsis. The implementation of rigorous antibiotic stewardship could protect neonates from acquiring multidrug-resistant organisms in the future. In our research, cases of late-onset sepsis outnumbered persons of early-onset sepsis. The majority of sepsis cases with positive cultures were gram-positive. Ongoing monitoring of neonatal sepsis is essential for analysing the infection patterns and revising appropriate antibiotic treatment at the institutional level. Transitioning from empirical to targeted therapy should occur following the identification of specific organisms and sensitivity assessments. Further long-term studies on neonatal sepsis will help in compiling similar data that can be used to develop the national guidelines.

CONCLUSION: Comprehending and tracking elements such as excessive antibiotic use, inadequate infection control measures, and irrational prescriptions among healthcare professionals may aid in effectively realizing antibiotic stewardship.

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CONFLICTS OF INTEREST: NIL

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