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A Retrospective Study on Antibiotic Sensitivity Pattern of Pathogens Isolated from Blood Culture in Cases of Late-Onset Neonatal Sepsis at a Neonatal Intensive Care Unit

[1]Adesh Patidar, [2]Girish Ramesh Rane, [3]Shubhangam Sharma and [4]Sanjay Singh

[1]Department of Pharmacology, Shyam Shah Medical College, Rewa, Madhya Pradesh, India
[2]Department of Pediatrics, Government Medical College, Jalgaon, Maharashtra, India
[3]Department of Pediatrics, RKMC and RC ,Bhopal, Madhya Pradesh, India
[4]Department of Microbiology, Atal Bihari Vajpayee Government Medical College, Vidisha, Madhya Pradesh, India

Abstract
Despite significant advancements in neonatal intensive care, late-onset neonatal sepsis (LONS) remains a substantial contributor to neonatal morbidity and mortality. The etiological agents responsible for LONS and their susceptibilities to antibiotics vary regionally, influencing the selection of empiric antibiotic therapy in suspected cases of sepsis. This study aimed to ascertain the drug sensitivity profiles of commonly isolated pathogens in cases of LONS. A Retrospective analysis was performed on blood culture sensitivity data from neonates admitted and managed for LONS at the neonatal intensive care unit of an Indian Hospital over a one-year period. A total of 123 neonates were admitted with suspected LONS, comprising 79 males and 44 females. The microbial analysis revealed Gram-positive organisms, specifically coagulase-negative staphylococci (CoNS), as the primary cause of culture-positive cases. Klebsiella pneumoniae was the most prevalent Gram-negative pathogen, ranking second after CoNS. Other pathogens included Pseudomonas, Acinetobacter, enterococci, Citrobacter, collectively known as the ESKAPE group. Notably, all isolates exhibited resistance to penicillin, while ampicillin and gentamicin displayed the lowest efficacy against these bacteria. Moderate sensitivity was observed with third-generation cephalosporins (e.g., ceftriaxone, cefotaxime), whereas meropenem, imipenem and linezolid demonstrated the highest sensitivity. Our findings indicate an upward trend in resistance to commonly prescribed first-line empiric antibiotics like ampicillin and gentamicin. Therefore, regular surveillance of antibiotic susceptibility is crucial for guiding appropriate empiric antibiotic selection.

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Key Words
Neonatal sepsis, blood culture, antibiotics, antibiotic sensitivity

Corresponding Author
Sanjay Singh,
Department of Microbiology, Atal Bihari Vajpayee Government Medical College, Vidisha, Madhya Pradesh, India
kirarsanjay@gmail.com

Author Designation
[1]Professor
[2-4]Assistant Professor

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INTRODUCTION

Neonatal sepsis is a significant contributor to morbidity and mortality among newborns, accounting for a substantial portion of neonatal deaths, particularly in developing countries. India, in particular, bears a significant burden, with more than half of its neonatal deaths attributed to infections. The preventability of neonatal mortality due to sepsis lies in the implementation of appropriate antimicrobial therapy and robust supportive care[1,2].

Neonatal sepsis is categorized into early onset neonatal sepsis (EONS) and late onset neonatal sepsis (LONS) based on the age of onset. EONS typically manifests within the first 72 hours of life, primarily originating from the maternal genital tract. In contrast, LONS occurs after 72 hours and can stem from either nosocomial or community-acquired sources, often presenting with septicemia, pneumonia, or meningitis. The prevalence of LONS has risen alongside advances in premature infant survival, particularly in those with very low birth weight, implicating hospitalization and medical devices in the genesis of neonatal LONS[3-5].

The Infectious Diseases Society of America has identified a group of nosocomial pathogens referred to as "ESKAPE pathogens," including Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species. These bacteria pose a significant threat due to their potential for drug resistance mechanisms[6,7].

The prompt and accurate diagnosis of LONS is crucial, given its associated mortality rate and long-term adverse effects. However, diagnosing neonatal infections can be challenging due to subtle and nonspecific clinical manifestations. Therefore, in suspected cases of sepsis, empirical antibiotic therapy should commence immediately after obtaining cultures, without waiting for results. Ampicillin (or penicillin) plus gentamicin are recommended as first-line antimicrobials for both EONS and LONS by the World Health Organization (WHO)[8,9].

Understanding the regional pattern of causative pathogens and their susceptibility is essential for selecting appropriate antimicrobial agents. Hence, this study aimed to ascertain the microbiological characteristics, including causative organisms and their antimicrobial susceptibility, in suspected cases of LONS.

MATERIALS AND METHODS

This investigation was conducted retrospectively, analyzing blood culture sensitivity data from neonates admitted as suspected cases of late-onset neonatal sepsis (LONS) over a one-year period. Excluded from the study were neonates with surgical issues, major congenital malformations, those already on antibiotics, or those born to mothers who had received antibiotics before delivery. Standard microbiological techniques were employed for blood culture and subsequent reports were analyzed.

Results revealed that among the 123 neonates admitted as suspected LONS cases, 79 were male and 44 were female. Analysis of the culture sensitivity reports from these cases showed 64 to be culture positive. Of the bacterial isolates obtained, 78.13% (50) were Gram-positive, while 21.87% (14) were Gram-negative. The most commonly isolated organism was coagulase-negative Staphylococcus aureus, followed by Klebsiella pneumoniae, along with isolates of Pseudomonas, Acinetobacter and Enterococci.

In terms of sensitivity patterns, all isolates exhibited low sensitivity to ampicillin, amikacin and gentamicin, moderate sensitivity to cefotaxime, ceftriaxone and ciprofloxacin and the highest sensitivity to imipenem, meropenem and linezolid.

RESULTS AND DISCUSSION

A total of 123 neonates were admitted with suspected LONS, comprising 79 males and 44 females. The microbial analysis revealed Gram-positive organisms, specifically coagulase-negative staphylococci (CoNS), as the primary cause of culture-positive cases. Klebsiella pneumoniae was the most prevalent Gram-negative pathogen, ranking second after CoNS. Other pathogens included Pseudomonas, Acinetobacter, enterococci, Citrobacter, collectively known as the ESKAPE group. Notably, all isolates exhibited resistance to penicillin, while ampicillin and gentamicin displayed the lowest efficacy against these bacteria. Moderate sensitivity was observed with third-generation cephalosporins (e.g., ceftriaxone, cefotaxime), whereas meropenem, imipenem and linezolid demonstrated the highest sensitivity.

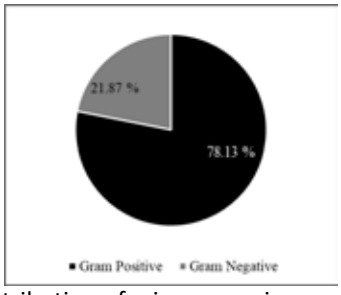

Fig. 1: Distribution of micro-organisms

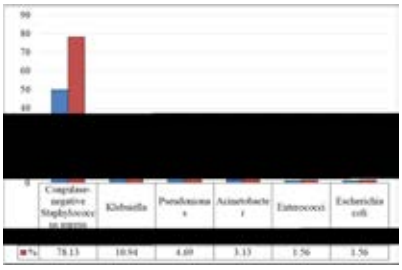

Fig. 2: Distribution of micro-organisms (ESKAPE group)

Table 1: Resistance pattern of ESKAPE organisms to various drugs

Drug	% Resistance
Imipenem	2.30
Meropenem	2.30
Linezolid	2.30
Ciprofloxacin	35.77
Ceftriaxone	37.58
Cefotaxime	37.58
Amikacin	52.76
Gentamicin	52.76
Ampicillin	75.15
Amoxycillin	75.15

Table 2: Resistance pattern of micro-organisms to ampicillin and gentamicin

Micro-organism	% resistance to Ampicillin	% resistance to Gentamicin
Staphylococcus aureus	81.06	53.15
Klebsiella pneumoniae	66	66
Acinetobacter	47.5	28.5
E. Coli	47.5	28.5
Citrobacter	47.5	28.5
Pseudomonas	47.5	28.5

Comparing our study's culture positivity rate of 52.03% with Shah *et al.*[11] (31.75%), Shaw *et al*.[12] (54.64%) and Bhattacharjee *et al*.[13] (32%), variability in positivity rates across studies underscores factors influencing blood culture outcomes. Interpretation challenges arise particularly with potential pathogen -contaminants, notably CoNS. Contextual interpretation within clinical scenarios is imperative[14]. CoNS predominated in our study, followed by Klebsiella, aligning with Gandhi *et al.'s* findings[15]. CoNS, increasingly implicated in Late-Onset Sepsis (LOS), vary significantly in prevalence across regions and time due to patient demographics, nosocomial microflora and antibiotic usage policies[3,10]. These pathogens are exhibiting resistance mechanisms against common antibiotics, with ampicillin and gentamicin showing consistent low efficacy. This echoes findings by Tallur *et al*.[17].

Meropenem, imipenem and linezolid consistently demonstrated high sensitivity, mirroring previous studies on ESKAPE organisms[18-20]. Our study focused on identifying LONS-causing pathogens despite aseptic measures in tertiary centers, highlighting increasing morbidity and prolonged hospital stays. Limitations include a small sample size and retrospective nature, impeding comprehensive clinical data retrieval for a deeper understanding of LONS development.

CONCLUSION

The progress in neonatal intensive care has heightened the risk of neonatal LONS. As LONS is primarily hospital-acquired, preventive measures should focus on rigorous hand hygiene and evaluating potential reservoirs as bacterial sources and transmission routes. Nonetheless, early suspicion and treatment of neonatal sepsis with empirical antibiotics remain crucial for mitigating neonatal morbidity and mortality. Presently, the World Health Organization (WHO) recommends ampicillin and gentamicin as first-line empirical antibiotics for managing LONS. The escalating resistance to these widely used antibiotics underscores the unintended consequences of antibiotic use. Therefore, it is imperative to periodically update the prevailing strain patterns and their drug susceptibilities in a given region to curtail and rationalize antibiotic usage.

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