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Original Research Article

EMERGING ANTIMICROBIAL RESISTANCE PATTERN IN NEONATAL SEPSIS PATIENTS ADMITTED IN NEONATAL INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL IN UTTAR PRADESH, INDIA: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: The neonatal period, comprising the first 28 days of life, is a critical phase marked by increased vulnerability to infections due to immature immune defences. In India, early-onset sepsis (EOS), occurring within 72 hours of birth, is more prevalent than late-onset sepsis (LOS). A growing concern in Neonatal intensive care units (NICU) is the rise of antimicrobial resistance (AMR), driven by the widespread use of broad-spectrum antibiotics.

Materials and Methods: This descriptive cross-sectional study was conducted in the Postgraduate Department of Microbiology at M.L.N. Medical College, Prayagraj, following approval from the Institutional Ethics Committee. Blood samples from 427 patients was cultured on Blood, MacConkey agar. Antimicrobial susceptibility testing of all isolates was conducted using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar, interpreted per CLSI M100 guidelines 33rd edition.

Results: Of the 427 neonates studied, 23.6% (n=101) had culture-confirmed sepsis. Gram-negative organisms were the most commonly isolated pathogens (14.3%), with Klebsiella pneumoniae (7.8%) and Escherichia coli (4.9%) being predominant. Gram-positive bacteria accounted for 6.3%, with Enterococcus spp. (3.3%) and
Staphylococcus aureus (1.6%) being the most common. Fungal isolates, including Candida albicans and non-albicans species, were found in 3% of cases.

Conclusion: In conclusion, this study highlights the growing challenge of antimicrobial resistance in neonatal sepsis. Strengthening infection control practices, optimizing antibiotic stewardship, and implementing targeted treatment based on local resistance patterns are imperative to combat the rising threat of AMR in neonatal care.

Keywords: Antimicrobial resistance, early onset sepsis, late onset sepsis, Neonates.

INTRODUCTION

The neonatal period is defined as the first 28 days of life. It is a critical window where infants are highly susceptible to infections due to their immature immune systems.[1] Neonatal sepsis is a significant global health concern, particularly in low- and middle-income countries (LMICs).[2] Neonatal sepsis is a life-threatening condition caused by a systemic infection in newborns less than 28 days old.[3] Globally, neonatal sepsis accounts for a substantial proportion of neonatal deaths. According to the Global Burden of Disease Study 2019, there were approximately 6.31 million incident cases of neonatal

sepsis and 0.23 million deaths due to neonatal sepsis worldwide.[4]

India bears a disproportionately high burden of neonatal sepsis. The country has one of the highest incidences of neonatal sepsis globally, with significant regional disparities in healthcare access and quality.[5] Several factors contribute to the high incidence of neonatal sepsis in India, including poor maternal health, inadequate antenatal care, and suboptimal infection control practices in healthcare settings.[6] Early-onset neonatal sepsis (EOS), which occurs within 72 hours of birth, is more common in India compared to LOS. EOS is often associated with intrauterine infections, maternal infections, and poor hygiene practices during delivery.[7]

The high incidence of neonatal sepsis in India underscores the urgent need for improved healthcare infrastructure, better infection control practices, and enhanced maternal and neonatal care.[7] The pathogens responsible for neonatal sepsis are diverse, including Gram-positive and Gram-negative bacteria, as well as fungi.[8] In NICUs, the frequent use of broad-spectrum antibiotics for empirical treatment of suspected infections can drive the selection of resistant strains.

The World Health Organization (WHO) has identified AMR as one of the top ten global public health threats, underscoring the urgency of addressing this issue through coordinated efforts at local, national, and global levels.[9] Understanding the local epidemiology of AMR in neonatal sepsis is crucial for several reasons.

In this study, we aim to elucidate the emerging patterns of AMR among neonatal sepsis patients in the NICU of the tertiary care hospital in Uttar Pradesh.

Aims and Objective

Aim

To determine the emerging antimicrobial resistance pattern in Neonatal sepsis patients admitted in Neonatal Intensive Care Unit of a Tertiary Care Hospital of Uttar Pradesh, India.

Objective

1. To study bacterial pathogens causing neonatal sepsis.
2. To Determine antimicrobial sensitivity pattern of aerobic bacteria causing neonatal sepsis.
3. To provide antibiogram to pediatrician for better patient management.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in the Postgraduate Department of Microbiology at M.L.N. Medical College, Prayagraj, following approval from the Institutional Ethics Committee. Prior to enrollment, written informed consent was obtained from the parents or legal guardians of all neonates. The study population comprised neonates aged up to 28 days who were admitted to the NICU of Sarojini Naidu Children Hospital, Prayagraj, with clinical suspicion of sepsis or a positive sepsis screen. Blood samples from these neonates were collected and processed in the Department of Microbiology.

The required sample size was calculated to be 237, based on the assumption that 19% of neonates would have the outcome of interest, with a five% absolute precision and a 95% confidence level.

Clinical information was obtained through detailed history-taking and examination, using a structured proforma. Data included demographic variables, maternal and perinatal history, birth details, feeding practices, NICU stay duration, and hygiene practices of caregivers. Blood samples were collected aseptically. Blood samples were transported in paired culture bottles containing Brain Heart Infusion (BHI) broth within two hour. Cultures were performed using conventional techniques, with subcultures on Blood, MacConkey agar.

Antimicrobial susceptibility testing of all isolates was conducted using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar, interpreted per CLSI M100 guidelines 33rd edition. Data were entered in MS Excel and analyzed using IBM SPSS version 22. Descriptive statistics, chi-square test, t-test, ANOVA, and Cochran's Q test were used where appropriate, with p-values <0.05 considered significant. All data were anonymized and securely stored in a password-protected spreadsheet.

RESULTS

Of the 427 neonates studied, 23.6% (n=101) had culture-confirmed sepsis. The majority (58.1%) were under seven days old, indicating early-onset sepsis. Males comprised 55.3% of the cohort. Most neonates had normal birth weight (>2.5 kg, 59.5%), and the predominant delivery mode was institutional vaginal delivery (60.9%). Sepsis (42.7%) and respiratory distress (40.3%) were the leading causes of NICU admission.

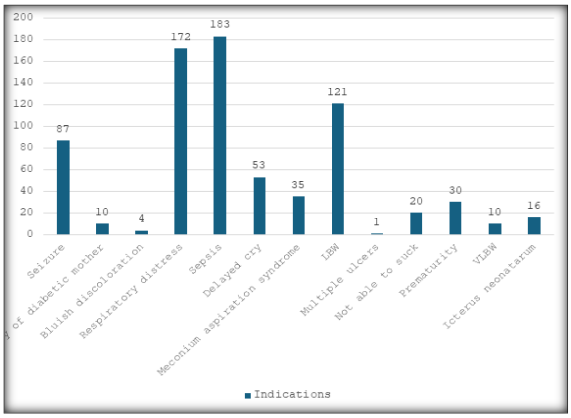

Figure 1: Distribution of neonates according to indication for NICU admission (n=427)

Table 1: Distribution of neonates according to birth weight (n=427)

Birth weight	Frequency	Percentage
LBW	121	28.3
VLBW	10	2.3
Normal	296	69.4
Total	427	100

The first blood culture results revealed that 361 neonates (84.5%) had sterile cultures. Among the positive cultures, Escherichia coli (4%), Klebsiella pneumoniae (5.2%) and Staphylococcus aureus (2.3%) were the most commonly isolated pathogens, followed by coagulase-negative Staphylococcus aureus (1.2%), Enterococcus spp. (1.2%), and Pseudomonas aeruginosa (1.2%). Fungal isolates included Candida albicans (0.9%) and non-albicans Candida (0.4%).

On repeat cultures, 391 neonates (91.6%) continued to show sterile results. Among the 36 positive cases, Klebsiella pneumoniae (3.5%), Candida albicans (0.9%), Escherichia coli (0.9%), and Staphylococcus aureus (0.9%) were the most frequent isolates, with smaller frequencies of non-albicans Candida (0.7%), coagulase-negative Staphylococcus aureus (0.5%), and Pseudomonas aeruginosa (0.5%).

Table 2: Culture positivity rate (n=427)

Culture findings	Frequency	Percentage
Positive	101	23.6
Negative	326	76.4
Total	427	100

Overall Gram-negative organisms were the most commonly isolated pathogens (14.3%), with Klebsiella pneumoniae (7.8%) and E. coli (4.9%) being predominant. Gram-positive bacteria accounted for 6.3%, with Enterococcus spp. (3.3%) and Staphylococcus aureus (1.6%) being the most common. Fungal isolates, including Candida albicans and non-albicans species, were found in 3% of cases. Antimicrobial resistance was highest against ceftriaxone (90.2%), cefepime (78.7%), ampicillin (72.1%), and ciprofloxacin (68.9%) among Gram-negative organisms. Resistance to imipenem (68.9%) and meropenem (63.9%) was also substantial. Among Gram-positive isolates, erythromycin and penicillin resistance reached 85.2%. No statistically significant association was found between resistance patterns and demographic variables. Amphotericin B retained effectiveness among fungal isolates. The overall findings highlighted the alarming resistance to first-line antibiotics, necessitating urgent antimicrobial stewardship.

DISCUSSION

This study sought to elucidate the emerging antimicrobial resistance (AMR) patterns in neonatal sepsis among patients admitted to the NICU of a tertiary care hospital in Uttar Pradesh. A total of 427 neonates were included, of whom 23.6% had culture-confirmed sepsis. The findings highlighted the predominance of Gram-negative organisms, substantial resistance to commonly used antibiotics, and the lack of statistically significant association between resistance and demographic or clinical variables. These results align with and further validate several trends observed in the literature on neonatal sepsis and antimicrobial resistance.

The majority of neonates (58.1%) were under 7 days of age at admission, indicating early-onset sepsis (EOS) as the predominant presentation. This was consistent with studies such as that by Bandyopadhyay et al. (2018), which reported early-onset sepsis in 59% of their cohort.[10] Similarly, Mehar et al. (2013) found EOS in 57% of cases, underscoring that vertical transmission during birth remains a significant contributor to neonatal infections in Indian settings.[11]

Most neonates in the present study weighed more than 2.5 kg (59.5%), while 37.7% were in the 1.5–2.5 kg range, and 2.8% weighed below 1.5 kg. Though lower birth weight is a known risk factor for neonatal sepsis, as highlighted by Eshetu et al. (2020) who found a higher prevalence of sepsis among preterm and low-birth-weight infants, the current findings suggest that neonatal sepsis is not confined to this subgroup.[12]

The most common indications for NICU admission were sepsis (42.7%) and respiratory distress (40.3%), followed by low birth weight (28.3%), seizures (20.6%), and delayed cry (12.9%). These results are consistent with Zakariya et al. (2011), who reported that neonatal sepsis commonly presented with respiratory symptoms and poor feeding, often prompting NICU referral.[13]

The culture positivity rate of 23.6% observed in this study is in line with global data. Bandyopadhyay et al. (2018) and Viswanathan et al. (2011) reported rates of 24.8% and 22.3% respectively.

Gram-negative bacteria predominated in this study, constituting 14.3% of total isolates. Klebsiella pneumoniae (6.6%) and E.coli (4.9%) were the most common Gram-negative organisms. Patel et al. (2014) also identified Klebsiella spp. (42.4%) as the leading isolate, followed by E. coli (9.1%). Sands et al. (2021) echoed this pattern, with Klebsiella pneumoniae and E. coli being the most prevalent

pathogens in a multicenter study of over 2,400 sepsis cases.[14,15]

Among Gram-positive organisms, Enterococcus spp. (3.3%), Staphylococcus aureus (1.6%), and CONS (1.4%) were isolated. This is in agreement with the findings of Bandyopadhyay et al. (2018), where Staphylococcus aureus (24.5%) and CONS (22.9%) were among the most frequently identified Gram-positive isolates.[10]

The study also detected fungal isolates in 3% of cases, including Candida albicans (1.9%) and non-albicans Candida (1.2%).

Antimicrobial sensitivity testing revealed alarming resistance among Gram-negative organisms. Ceftriaxone resistance was highest at 90.2%, followed by cefepime (78.7%), ampicillin (72.1%), and cefoperazone-sulbactam (70.5%). These findings are mirrored by Patel et al. (2014), who reported 94.87% resistance to cephalosporins among Klebsiella isolates and 92% among E. coli.[14]

Resistance to fluoroquinolones, such as ciprofloxacin (68.9%) and levofloxacin (65.6%), was also prominent in this study.

Interestingly, resistance to aminoglycosides such as amikacin (57.4%) and gentamicin (59%) was also substantial. This trend is consistent with the work of Mohsen et al. (2017), who found resistance to aminoglycosides ranging from 36% to 52% among Gram-negative isolates.[16]

Among Gram-positive organisms, resistance was highest to erythromycin (85.2%) and penicillin (85.2%), followed by clindamycin (77.8%). These rates echo those found by Bandyopadhyay et al. (2018), where methicillin resistance was detected in 24.4% of S. aureus and 62.5% of Enterococcus spp.[10] Though vancomycin and linezolid retained some efficacy in the present study, resistance levels of 59.3% and 37% respectively raise concern, particularly in light of similar resistance trends noted by Patel et al. (2014), who reported vancomycin resistance in 20% of Enterococci and methicillin resistance in 33% of Staphylococci.[14]

Fungal isolates in this study showed the least resistance to amphotericin B (7.7%) and the highest resistance to ketoconazole and clotrimazole (both 53.8%). While many studies in the review focused primarily on bacterial pathogens, Mehar et al. (2013) and Minotti et al. (2023) reported Candida species as emerging agents of neonatal sepsis, highlighting the importance of monitoring antifungal resistance as well.[11,17]

Repeat cultures in this study showed continued positivity in 8.4% of cases, with Klebsiella pneumoniae again emerging as the most common pathogen

Notably, this study found no statistically significant associations between antimicrobial resistance and variables such as age, sex, weight, or mode of delivery. Although certain trends—such as a slightly higher resistance among males and neonates under 1.5 kg—were observed, these did not reach statistical significance. This finding contrasts with Solomon et al. (2021), who found that low birth weight and late-onset sepsis were associated with higher resistance rates.[18]

It was also seen that there was no statistically significant association between culture positivity and demographic variables such as age, sex, weight, or mode of delivery. While culture positivity appeared slightly higher in neonates aged ≥7 days and in males, the findings did not achieve statistical significance ($p > 0.05$). These results mirrored the observations by Bandyopadhyay et al. (2018), who also reported no significant demographic predictors of positive cultures.[10] Conversely, Solomon et al. (2021) found that low birth weight and late-onset sepsis were significantly associated with higher culture positivity and multidrug resistance.[18] However, such associations were not evident in the present cohort. The absence of significant predictors suggests that clinical suspicion for sepsis should remain high across all neonatal groups, irrespective of demographic profile. These findings underscore the importance of universal vigilance and routine culture testing for early diagnosis, rather than relying solely on risk profiling based on age, birth weight, or delivery mode.

CONCLUSION

The study highlights the growing challenge of antimicrobial resistance in neonatal sepsis in a tertiary care setting. Gram-negative bacteria, particularly Klebsiella pneumoniae and E. coli, were the predominant pathogens, showing high resistance to commonly used antibiotics, including cephalosporins, aminoglycosides, and carbapenems. Similarly, Gram-positive organisms demonstrated significant resistance to penicillin and erythromycin, although agents like vancomycin and linezolid retained moderate efficacy. Fungal infections, though less frequent, showed notable resistance to several antifungal agents, with amphotericin B remaining relatively effective.

No statistically significant association was observed between antimicrobial resistance or culture positivity and demographic variables such as age, sex, weight, or delivery mode, indicating that all neonates are at risk, regardless of these factors. These findings underscore the need for early culture-based diagnosis, routine resistance monitoring, and judicious antibiotic use. The provision of an updated antibiogram can significantly aid clinicians in choosing effective empirical therapy. Strengthening infection control measures and promoting antimicrobial stewardship are imperative to combat rising resistance in NICUs.

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