



Original Article

A Study on Antimicrobial Resistance Profile of Bacterial Pathogens Isolated from Neonatal Sepsis Cases

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ABSTRACT

Background: Neonatal sepsis remains one of the leading causes of neonatal morbidity and mortality worldwide, particularly in developing countries. Despite significant advances in neonatal intensive care, infections continue to contribute substantially to adverse neonatal outcomes. The increasing emergence of antimicrobial resistance among bacterial pathogens causing neonatal sepsis has complicated treatment strategies and has become a major public health concern. Continuous surveillance of etiological agents and their antimicrobial susceptibility patterns is therefore essential for effective management and prevention of neonatal infections.

Aim: To determine the bacteriological profile and antimicrobial resistance patterns of bacterial pathogens causing neonatal sepsis in a tertiary care hospital.

Materials and Methods: A hospital-based observational cross-sectional study was conducted among 102 neonates clinically suspected of sepsis and admitted to the Neonatal Intensive Care Unit (NICU). Blood samples were collected aseptically and processed according to standard microbiological protocols. Bacterial isolates were identified by conventional culture methods, and antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion method according to CLSI guidelines.

Results: Out of 102 clinically suspected neonatal sepsis cases, only 8 (7.8%) blood cultures were positive. Gram-negative bacteria accounted for 75.0% of isolates, whereas Gram-positive organisms constituted 25.0%. *Klebsiella pneumoniae* was the most common pathogen (37.5%), followed by *Escherichia coli* (25.0%). High resistance was observed against ampicillin (83.3%) and third-generation cephalosporins (66.7%). Meropenem, vancomycin, and linezolid showed excellent susceptibility. Multidrug resistance was detected in 25.0% of isolates, while ESBL production was observed in 16.7% of Gram-negative organisms.

Conclusion: Gram-negative organisms predominated among neonatal sepsis isolates and demonstrated considerable resistance to commonly used antibiotics. Regular antimicrobial surveillance and antibiotic stewardship programs are necessary to optimize empirical therapy and reduce antimicrobial resistance.

Keywords: Neonatal sepsis, antimicrobial resistance, *Klebsiella pneumoniae*, multidrug resistance, ESBL, NICU.

INTRODUCTION

Neonatal sepsis is a life-threatening clinical syndrome characterized by systemic signs and symptoms of infection occurring during the first 28 days of life. It continues to be one of the major causes of neonatal morbidity and mortality globally, particularly in low- and middle-income countries where healthcare resources remain limited and infectious diseases

contribute substantially to neonatal deaths. Neonates represent a highly vulnerable population because of their immature immune system, reduced neutrophil storage pool, impaired complement activity, and inadequate humoral and cellular immune responses. These factors make newborns particularly susceptible to invasive bacterial infections.[1]

The burden of neonatal sepsis remains enormous despite improvements in maternal healthcare services, neonatal intensive care facilities, and antimicrobial therapy. According to estimates by the World Health Organization, neonatal infections contribute significantly to neonatal mortality worldwide, especially in South Asia and Sub-Saharan Africa.[2] India bears a substantial proportion of the global burden of neonatal deaths, with sepsis being one of the leading causes. The high incidence of neonatal infections in developing countries is associated with poor socioeconomic conditions, inadequate infection control practices, overcrowding in healthcare facilities, and limited access to quality antenatal and perinatal care.[3]

Neonatal sepsis is broadly categorized into early-onset sepsis (EOS) and late-onset sepsis (LOS). Early-onset sepsis occurs within the first 72 hours of life and is usually acquired vertically from the maternal genital tract before or during delivery. Common risk factors include prolonged rupture of membranes, maternal fever, chorioamnionitis, urinary tract infections during pregnancy, preterm labor, and unhygienic delivery practices.[4] In contrast, late-onset sepsis develops after 72 hours of life and is primarily associated with environmental and hospital-acquired pathogens. Factors such as prolonged hospitalization, invasive procedures, mechanical ventilation, central venous catheterization, and poor hand hygiene significantly contribute to the occurrence of LOS.[5]

The clinical presentation of neonatal sepsis is often nonspecific and variable, making early diagnosis challenging. Symptoms may include lethargy, poor feeding, temperature instability, respiratory distress, apnea, irritability, abdominal distension, jaundice, and circulatory instability.[6] Because these manifestations overlap with several noninfectious neonatal conditions, prompt laboratory diagnosis becomes crucial for initiating appropriate antimicrobial therapy. Blood culture remains the gold standard for diagnosis; however, its sensitivity may be reduced due to prior antibiotic exposure, inadequate blood volume, or low-level bacteremia.[7]

The bacteriological spectrum of neonatal sepsis varies considerably across geographical regions, healthcare settings, and periods. In developed countries, Group B *Streptococcus* and *Escherichia coli* are commonly reported pathogens, whereas Gram-negative organisms such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species predominate in many developing countries.[8] Gram-positive organisms including *Staphylococcus aureus* and coagulase-negative staphylococci have also emerged as important causes of neonatal bloodstream infections, particularly among hospitalized neonates receiving intensive care.[9]

One of the most alarming challenges in neonatal healthcare is the increasing prevalence of antimicrobial resistance among bacterial pathogens. The widespread use and misuse of antibiotics have accelerated the emergence of resistant strains, resulting in reduced effectiveness of commonly used antimicrobial agents.[10] Resistance mechanisms such as beta-lactamase production, extended-spectrum beta-lactamase (ESBL) production, carbapenemase production, methicillin resistance, and multidrug resistance have become increasingly prevalent among neonatal pathogens.[11]

Antimicrobial resistance significantly complicates the management of neonatal sepsis. Delayed initiation of effective antimicrobial therapy has been associated with increased mortality, prolonged hospitalization, higher treatment costs, and adverse neurodevelopmental outcomes.[12] Consequently, continuous monitoring of local bacterial profiles and antimicrobial susceptibility patterns is essential for guiding empirical antibiotic therapy and formulating antibiotic policies.

Klebsiella pneumoniae has emerged as one of the most important pathogens responsible for neonatal bloodstream infections in tertiary care hospitals. This organism possesses numerous virulence factors, including capsular polysaccharides, siderophores, adhesins, and endotoxins that enhance its pathogenic potential.[13] Furthermore, increasing reports of ESBL-producing and carbapenem-resistant *Klebsiella* strains have raised serious concerns regarding treatment options.[14]

Similarly, *Escherichia coli* remains an important pathogen causing both early-onset and late-onset neonatal sepsis. Neonates infected with resistant *E. coli* strains often experience severe clinical outcomes because of delayed therapeutic response and limited antibiotic choices.[15] *Acinetobacter baumannii* and *Pseudomonas aeruginosa* have also gained prominence as opportunistic pathogens capable of surviving in hospital environments and developing resistance to multiple antibiotic classes.[16]

The emergence of multidrug-resistant organisms (MDROs) in NICUs represents a serious threat to neonatal survival. Multidrug resistance is generally defined as resistance to at least one agent in three or more antimicrobial classes.[17] The increasing prevalence of MDR pathogens has been attributed to prolonged hospital stays, excessive antibiotic exposure, invasive medical interventions, and inadequate infection control measures.[18]

Extended-spectrum beta-lactamase-producing organisms constitute another growing concern in neonatal intensive care units. ESBL enzymes confer resistance to penicillins, cephalosporins, and aztreonam, thereby limiting therapeutic options and increasing dependence on carbapenems.[19] The spread of ESBL-producing organisms within healthcare settings has been associated with outbreaks of neonatal sepsis and increased mortality rates.[20]

In India, several studies have documented changing trends in neonatal sepsis pathogens and increasing resistance to first-line antibiotics such as ampicillin, gentamicin, and third-generation cephalosporins.[21] These observations emphasize the necessity of region-specific antimicrobial surveillance programs to monitor evolving resistance patterns and guide rational antibiotic use.

The present study was therefore undertaken to evaluate the bacteriological profile of neonatal sepsis and determine the antimicrobial resistance patterns of bacterial pathogens isolated from neonates admitted to a tertiary care hospital. Understanding local epidemiological trends and resistance profiles will help clinicians optimize empirical antibiotic therapy, improve treatment outcomes, and strengthen antimicrobial stewardship initiatives.

MATERIALS AND METHODS

Study Design

This was a Hospital-based observational cross-sectional study carried out for a period of 12 months at a tertiary care centre in the Department of Pediatrics.

Study Setting

Neonatal Intensive Care Unit (NICU) and Department of Microbiology of a tertiary care teaching hospital.

Study Population

Neonates aged 0–28 days admitted with clinical suspicion of sepsis.

Sample Size

102 clinically suspected neonatal sepsis cases.

Inclusion Criteria

1. Neonates aged less than 28 days.
2. Neonates with clinical signs suggestive of sepsis.
3. Neonates admitted to NICU during the study period.
4. Parents/guardians providing informed consent.

Exclusion Criteria

1. Neonates already receiving prolonged antibiotic therapy before admission.
2. Neonates with major congenital anomalies.
3. Neonates whose blood samples were inadequate for culture.
4. Cases with incomplete clinical records.

Sample Collection

Approximately 1–2 mL venous blood was collected aseptically before initiation of antibiotic therapy and inoculated into blood culture bottles.

Laboratory Procedures

Blood cultures were incubated and monitored for bacterial growth. Positive cultures were subcultured on Blood agar and MacConkey agar. Identification was performed using standard microbiological methods. Antimicrobial susceptibility testing was carried out by Kirby-Bauer disc diffusion method according to CLSI guidelines.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software. Results were expressed as frequency and percentage.

RESULTS

A total of **102 neonates** with clinical suspicion of sepsis were included in the study. Blood culture positivity was observed in **8 (7.8%)** cases, while **94 (92.2%)** samples showed no bacterial growth.

Table 1. Blood Culture Positivity among Suspected Neonatal Sepsis Cases (n=102)

Culture Result	Number	Percentage (%)
Positive	8	7.8

Negative	94	92.2
Total	102	100

Table 1. Blood Culture Positivity among Suspected Neonatal Sepsis Cases (n=102)

In the present study, a total of 102 neonates admitted with clinical suspicion of sepsis were investigated microbiologically through blood culture examination. Among these, only 8 cases (7.8%) demonstrated positive bacterial growth, whereas 94 cases (92.2%) were culture-negative. The low culture positivity rate observed in the present study may be attributed to several factors, including prior administration of empirical antibiotics before sample collection, low bacterial load in neonatal bloodstream infections, inadequate blood volume obtained for culture, or infections caused by fastidious organisms that are difficult to isolate by conventional culture methods. Although the majority of clinically suspected cases were culture-negative, the findings do not exclude the possibility of infection because neonatal sepsis often presents with non-specific symptoms and laboratory evidence may be limited. Therefore, clinical judgment remains essential in the management of neonatal sepsis. The low isolation rate highlights the importance of improving microbiological diagnostic techniques and ensuring timely specimen collection before antibiotic administration.

Table 2. Demographic Characteristics of Study Population (n=102)

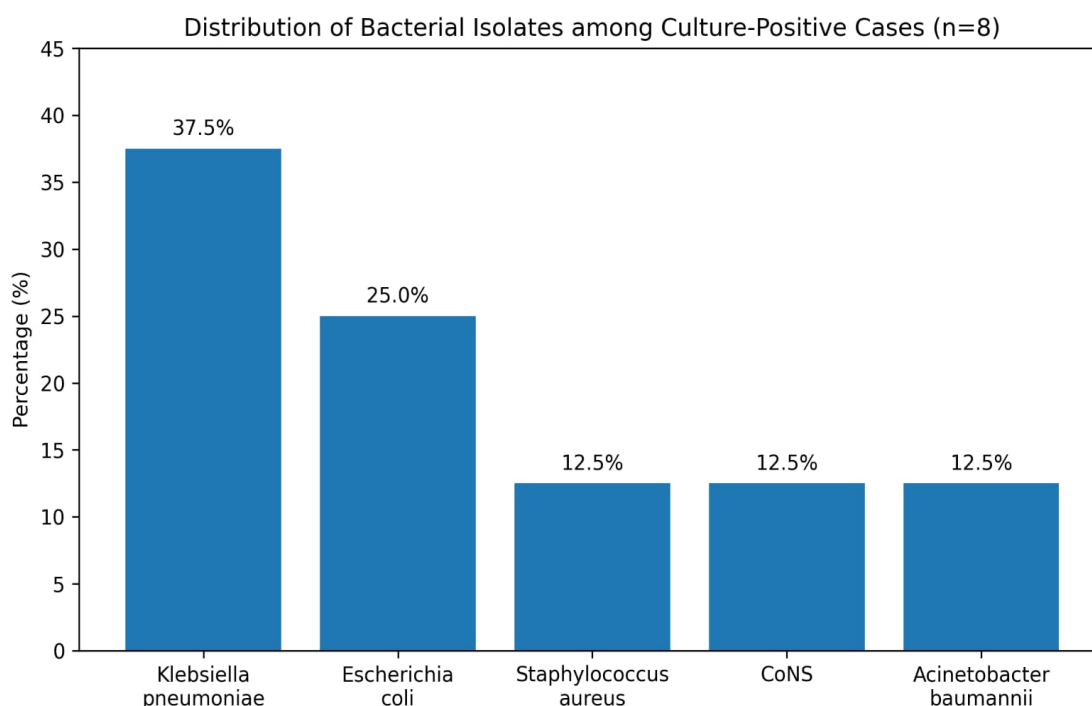
Variable	Number	Percentage (%)
Male	58	56.9
Female	44	43.1
Early-onset Sepsis (<72 hrs)	69	67.6
Late-onset Sepsis (>72 hrs)	33	32.4

Table 2. Demographic Characteristics of Study Population (n=102)

Analysis of demographic characteristics revealed that male neonates constituted 58 (56.9%) of the study population, while female neonates accounted for 44 (43.1%). This male predominance has been reported in several studies and may be related to increased susceptibility of male infants to neonatal infections due to genetic, hormonal, and immunological factors. With regard to the timing of infection, early-onset sepsis (EOS), occurring within the first 72 hours of life, was observed in 69 neonates (67.6%), whereas late-onset sepsis (LOS), occurring after 72 hours of life, was identified in 33 neonates (32.4%). The higher incidence of EOS suggests that maternal and perinatal factors such as premature rupture of membranes, maternal fever, prolonged labor, chorioamnionitis, and unhygienic delivery practices may play a major role in the occurrence of neonatal sepsis in the study setting. The predominance of EOS underscores the importance of antenatal care, infection screening during pregnancy, and strict aseptic practices during delivery.

Table 3. Distribution of Bacterial Isolates among Culture-Positive Cases (n=8)

Organism	Number	Percentage (%)
<i>Klebsiella pneumoniae</i>	3	37.5
<i>Escherichia coli</i>	2	25.0
<i>Staphylococcus aureus</i>	1	12.5
Coagulase-negative Staphylococci (CoNS)	1	12.5
<i>Acinetobacter baumannii</i>	1	12.5
Total	8	100



Graph 1: Distribution of Bacterial Isolates among Culture-Positive Cases

Table 3. Distribution of Bacterial Isolates among Culture-Positive Cases (n=8)

Among the eight culture-positive neonatal sepsis cases, *Klebsiella pneumoniae* emerged as the most common bacterial pathogen, accounting for three isolates (37.5%). This was followed by *Escherichia coli*, which was isolated from two cases (25.0%). One isolate each of *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), and *Acinetobacter baumannii* was recovered, representing 12.5% each of the total isolates. The predominance of *Klebsiella pneumoniae* is a matter of concern because it is a well-recognized nosocomial pathogen associated with severe neonatal infections and multidrug resistance. Similarly, *E. coli* remains one of the leading causes of neonatal sepsis worldwide, particularly in early-onset infections acquired from the maternal genital tract. The isolation of CoNS and *Staphylococcus aureus* reflects the role of skin flora and invasive medical procedures in neonatal intensive care units. The presence of *Acinetobacter baumannii*, although limited to one isolate, is clinically significant because of its well-known ability to survive in hospital environments and develop resistance to multiple antibiotics. These findings suggest that both community-acquired and hospital-acquired pathogens contribute to the burden of neonatal sepsis.

Table 4. Distribution of Gram-Positive and Gram-Negative Isolates (n=8)

Organism Type	Number	Percentage (%)
Gram-negative bacteria	6	75.0
Gram-positive bacteria	2	25.0
Total	8	100

Table 4. Distribution of Gram-Positive and Gram-Negative Isolates (n=8)

Categorization of the isolated pathogens according to Gram staining characteristics demonstrated a clear predominance of Gram-negative bacteria. Out of eight isolates, six (75.0%) were Gram-negative organisms, whereas only two (25.0%) were Gram-positive bacteria. The predominance of Gram-negative pathogens in neonatal sepsis has been consistently reported in developing countries and is often associated with increased morbidity and mortality due to their virulent nature and resistance mechanisms. Gram-negative organisms such as *Klebsiella pneumoniae*, *Escherichia coli*, and *Acinetobacter baumannii* possess endotoxins and various virulence factors that can trigger severe systemic inflammatory responses, leading to septic shock and multiple organ dysfunction. In contrast, Gram-positive organisms represented a smaller proportion of isolates. The findings indicate that empirical antibiotic regimens in the neonatal intensive care unit should provide adequate coverage against Gram-negative pathogens while considering local antimicrobial susceptibility patterns.

Table 5. Antibiotic Resistance Pattern among Gram-Negative Isolates (n=6)

Antibiotic	Resistant n (%)
Ampicillin	5 (83.3)
Cefotaxime	4 (66.7)
Ceftriaxone	4 (66.7)
Gentamicin	2 (33.3)
Amikacin	1 (16.7)
Piperacillin-Tazobactam	1 (16.7)
Meropenem	0 (0.0)

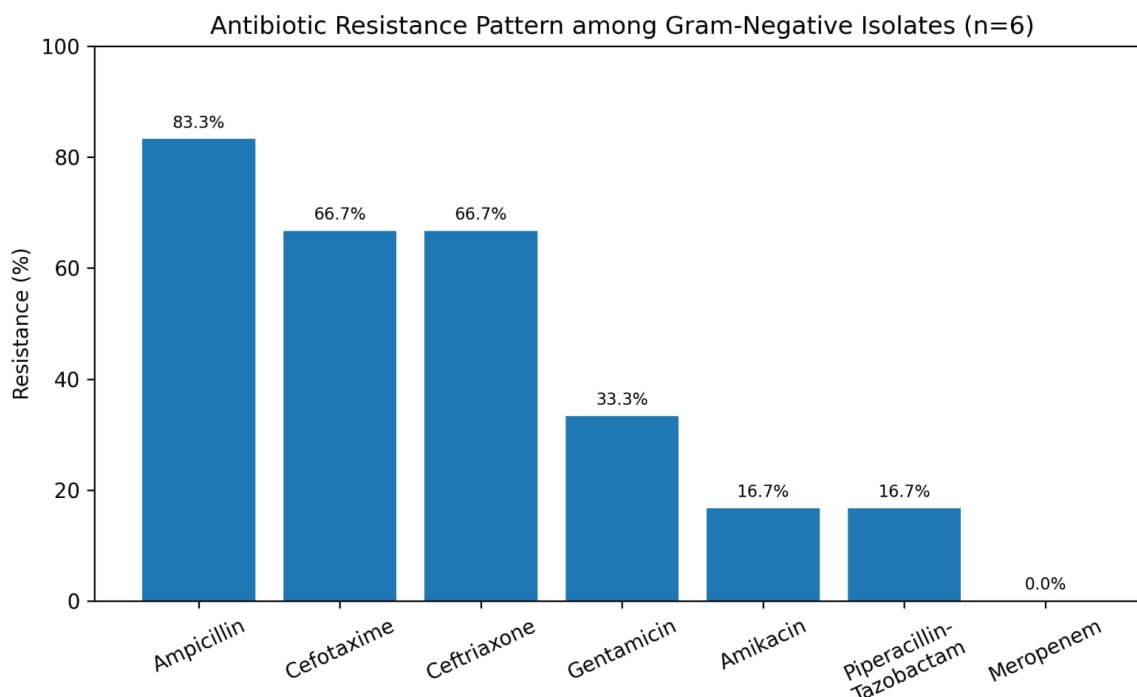
**Graph 2: Antibiotic Resistance Pattern among Gram-Negative Isolates (n=6)**

Table 5. Antibiotic Resistance Pattern among Gram-Negative Isolates (n=6)

Evaluation of the antimicrobial susceptibility pattern of Gram-negative isolates revealed substantial resistance to commonly prescribed antibiotics. Ampicillin exhibited the highest resistance rate, with five of the six isolates (83.3%) being resistant. Resistance to cefotaxime and ceftriaxone was observed in four isolates each (66.7%), indicating reduced effectiveness of third-generation cephalosporins. Gentamicin resistance was identified in two isolates (33.3%), whereas only one isolate (16.7%) showed resistance to amikacin and piperacillin-tazobactam. Importantly, none of the Gram-negative isolates demonstrated resistance to meropenem, indicating complete susceptibility to this carbapenem antibiotic. The high resistance observed against ampicillin and cephalosporins may be explained by their widespread and often empirical use in neonatal care settings, leading to selective pressure and emergence of resistant strains. The preservation of susceptibility to meropenem suggests that carbapenems remain valuable therapeutic options for severe infections caused by resistant Gram-negative bacteria. However, judicious use of these agents is necessary to prevent the development of carbapenem resistance in the future.

Table 6. Antibiotic Resistance Pattern among Gram-Positive Isolates (n=2)

Antibiotic	Resistant n (%)
Penicillin	2 (100)
Erythromycin	1 (50.0)
Clindamycin	0 (0.0)
Ciprofloxacin	0 (0.0)
Vancomycin	0 (0.0)
Linezolid	0 (0.0)

Table 6. Antibiotic Resistance Pattern among Gram-Positive Isolates (n=2)

The antibiotic susceptibility profile of Gram-positive isolates demonstrated complete resistance to penicillin, as both isolates (100%) were resistant. Resistance to erythromycin was observed in one isolate (50.0%), whereas no resistance was

detected against clindamycin, ciprofloxacin, vancomycin, or linezolid. The universal resistance to penicillin observed in this study reflects the widespread dissemination of beta-lactamase-producing Gram-positive organisms and the long-standing use of penicillin-class antibiotics. The preservation of susceptibility to vancomycin and linezolid is encouraging because these agents are considered important therapeutic options for severe infections caused by resistant Gram-positive pathogens, including methicillin-resistant staphylococci. Although the number of Gram-positive isolates in the present study was limited, the findings suggest that resistance among these organisms remains relatively lower compared to Gram-negative bacteria. Continuous monitoring of susceptibility patterns is nevertheless necessary to detect emerging resistance trends and ensure appropriate antimicrobial therapy.

Table 7. Multidrug Resistance among Isolates (n=8)

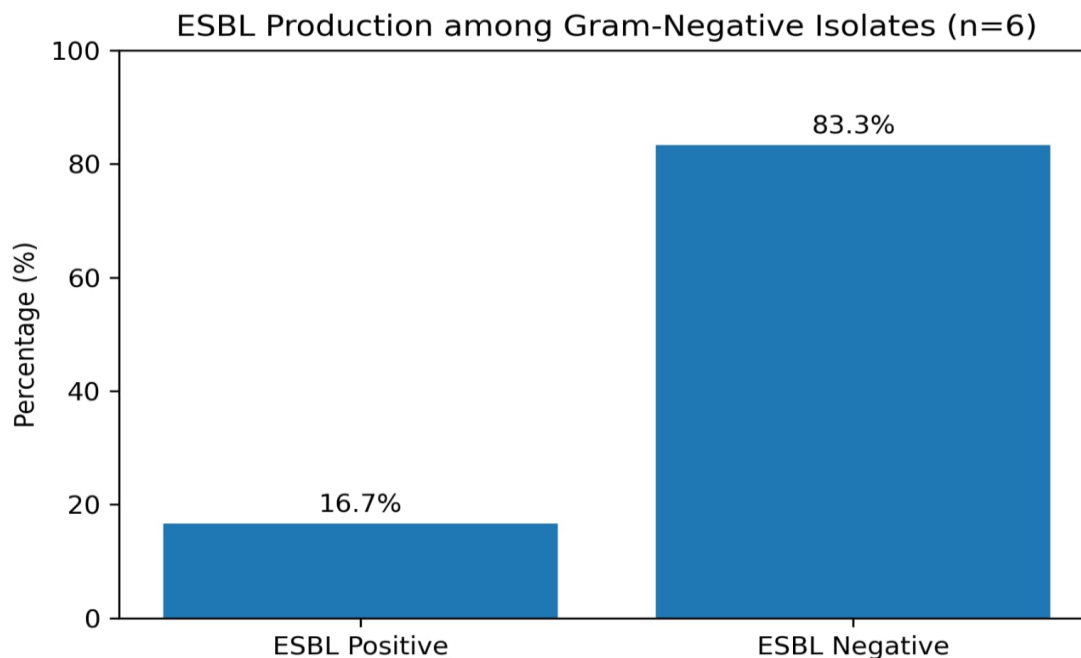
MDR Status	Number	Percentage (%)
MDR Positive	2	25.0
MDR Negative	6	75.0
Total	8	100

Table 7. Multidrug Resistance among Isolates (n=8)

Assessment of multidrug resistance (MDR) revealed that two of the eight bacterial isolates (25.0%) were resistant to at least three classes of antimicrobial agents and were therefore classified as MDR organisms. The remaining six isolates (75.0%) did not meet the criteria for multidrug resistance. The presence of MDR pathogens in neonatal intensive care units is a major public health concern because such organisms limit treatment options, increase healthcare costs, prolong hospital stay, and contribute to adverse clinical outcomes. Neonates are particularly vulnerable to MDR infections due to their immature immune systems and frequent exposure to invasive procedures, broad-spectrum antibiotics, and prolonged hospitalization. Although the proportion of MDR isolates in the present study was relatively low, the detection of these organisms highlights the need for effective infection control measures, rational antibiotic prescribing practices, and ongoing surveillance programs to prevent further dissemination of resistant strains.

Table 8. ESBL Production among Gram-Negative Isolates (n=6)

ESBL Status	Number	Percentage (%)
ESBL Positive	1	16.7
ESBL Negative	5	83.3
Total	6	100



Graph 3: ESBL Production among Gram-Negative Isolates (n=6)

Table 8. ESBL Production among Gram-Negative Isolates (n=6)

Among the six Gram-negative bacterial isolates recovered in the study, one isolate (16.7%) was identified as an extended-spectrum beta-lactamase (ESBL) producer, while the remaining five isolates (83.3%) were ESBL-negative. ESBL-producing bacteria possess enzymes capable of hydrolyzing third-generation cephalosporins and other beta-lactam

antibiotics, thereby rendering these drugs ineffective. The detection of ESBL-producing organisms in neonatal sepsis is clinically important because such pathogens are associated with limited treatment options, delayed recovery, and increased risk of complications. Although the prevalence of ESBL production in the present study was relatively low, its presence indicates the emergence of resistant bacterial strains within the neonatal care environment. Continuous microbiological surveillance and strict antimicrobial stewardship practices are therefore essential to prevent the spread of ESBL-producing organisms and preserve the effectiveness of currently available antibiotics.

Out of 102 neonates with suspected sepsis, only **8 (7.8%)** blood cultures yielded bacterial growth. Gram-negative bacteria accounted for **75.0%** of all isolates, with *Klebsiella pneumoniae* being the most common pathogen. Resistance was highest against ampicillin and cephalosporins, whereas meropenem, vancomycin, and linezolid demonstrated excellent activity. Multidrug resistance was observed in **25.0%** of isolates, and **16.7%** of Gram-negative bacteria were ESBL producers. These findings indicate a low culture positivity rate but highlight the continued presence of antimicrobial resistance among neonatal sepsis pathogens.

DISCUSSION

The present study was conducted to evaluate the bacteriological profile and antimicrobial resistance patterns of bacterial pathogens causing neonatal sepsis in a tertiary care teaching hospital. Neonatal sepsis continues to remain one of the leading causes of neonatal morbidity and mortality worldwide despite major advancements in neonatal intensive care, antimicrobial therapy, and infection prevention strategies. The emergence of antimicrobial resistance among neonatal pathogens has further complicated treatment and poses a major challenge for clinicians managing critically ill neonates.

In the present study, the blood culture positivity rate was found to be 7.8%. This positivity rate was comparatively lower than several previously reported studies from India and other developing countries. Shah et al. reported a culture positivity rate of approximately 22%, while Muley et al. observed positivity rates ranging between 20% and 35% among clinically suspected neonatal sepsis cases.[22,23] Similarly, Jyothi et al. documented culture positivity in nearly 28% of neonates admitted with suspected sepsis.[25] The lower positivity rate observed in the current study may be explained by multiple factors including prior administration of empirical antibiotics before blood collection, low bacterial load in neonatal bloodstream infections, inadequate sample volume, and limitations of conventional culture techniques. In many tertiary care settings, antibiotics are initiated immediately after clinical suspicion of sepsis due to the life-threatening nature of the disease, which significantly reduces culture yield. Furthermore, some infections may be caused by fastidious organisms or anaerobic bacteria that are difficult to isolate using routine laboratory methods.

The present study demonstrated a male predominance, with male neonates accounting for 56.9% of the total study population. Similar observations have been reported in several national and international studies. Tewari et al. reported male predominance in neonatal sepsis cases, while Peterside et al. also observed a higher incidence among male neonates.[24,28] The increased susceptibility of male neonates to infections has been attributed to genetic and immunological factors. The presence of immune regulatory genes on the X chromosome may provide females with a relative immunological advantage. Additionally, hormonal influences and differences in innate immune responses have been proposed as contributing factors.

Early-onset sepsis constituted 67.6% of cases in the present study and was more common than late-onset sepsis. This finding is comparable with observations reported by the National Neonatal Perinatal Database and several Indian neonatal surveillance studies.[26] Early-onset sepsis is generally associated with maternal and perinatal risk factors such as prolonged rupture of membranes, maternal fever, urinary tract infections during pregnancy, preterm labor, meconium-stained liquor, and unhygienic delivery practices. The predominance of EOS in the current study suggests that maternal and intrapartum infections continue to contribute substantially to neonatal morbidity. Strengthening antenatal screening programs and ensuring safe delivery practices are therefore essential preventive measures.

Among the bacterial isolates recovered in this study, *Klebsiella pneumoniae* emerged as the predominant pathogen, accounting for 37.5% of all isolates. Similar findings have been documented in numerous studies conducted across India, Asia, and Africa. The Delhi Neonatal Infection Study (DeNIS) identified *Klebsiella* species as one of the leading causes of neonatal bloodstream infections.[21,27] Investigators from tertiary care hospitals in North India, South India, and Bangladesh have also reported *Klebsiella pneumoniae* as the most common pathogen responsible for neonatal sepsis.[29,31] The predominance of *Klebsiella* may be related to its remarkable ability to survive in hospital environments, colonize medical equipment, and acquire antimicrobial resistance determinants through plasmid-mediated mechanisms. *Klebsiella* possesses multiple virulence factors including polysaccharide capsules, fimbriae, endotoxins, and siderophores, which enhance its pathogenicity and facilitate invasive infections in neonates.

Escherichia coli was identified as the second most common pathogen in the present study, accounting for 25.0% of isolates. *E. coli* remains a major pathogen associated with neonatal sepsis worldwide, particularly in early-onset infections transmitted vertically from the maternal genital tract.[15] Similar findings have been reported by Stoll et al., who identified *E. coli* as one of the leading causes of neonatal bloodstream infections in both developed and developing countries.[15]

The increasing prevalence of resistant *E. coli* strains is particularly concerning because these organisms frequently harbor ESBL genes, thereby limiting therapeutic options.

The present study also isolated *Acinetobacter baumannii*, *Staphylococcus aureus*, and coagulase-negative staphylococci (CoNS). Although their frequency was relatively low, these organisms remain clinically significant. *Acinetobacter baumannii* has emerged as an important nosocomial pathogen due to its remarkable ability to survive on hospital surfaces and rapidly acquire multidrug resistance.[16] Numerous outbreaks of neonatal sepsis caused by *Acinetobacter* species have been reported from intensive care units worldwide. CoNS and *Staphylococcus aureus* are commonly associated with invasive procedures, indwelling catheters, prolonged hospitalization, and breaches in aseptic techniques.[9]

The predominance of Gram-negative organisms observed in the current study is consistent with findings from many developing countries. Gram-negative bacteria accounted for 75.0% of isolates, whereas Gram-positive organisms constituted only 25.0%. Similar results were reported by Peterside et al., Fitchett et al., and investigators participating in the DeNIS collaboration.[21,28,29] Gram-negative organisms are particularly problematic in neonatal intensive care units because they possess endotoxins and multiple virulence mechanisms capable of inducing severe inflammatory responses, septic shock, disseminated intravascular coagulation, and multiorgan failure. Furthermore, these pathogens frequently exhibit multidrug resistance, making treatment increasingly difficult.

Antimicrobial susceptibility testing in the present study revealed alarmingly high resistance rates against commonly used antibiotics. Ampicillin resistance was observed in 83.3% of Gram-negative isolates, while resistance to cefotaxime and ceftriaxone was documented in 66.7% of isolates. Similar resistance patterns have been reported in several recent studies. Li et al. demonstrated high levels of resistance to beta-lactam antibiotics among neonatal pathogens, particularly *Klebsiella* and *E. coli* isolates.[30] Likewise, Folgori et al. reported increasing resistance to first-line antibiotics across neonatal intensive care units globally.[18] The widespread use and misuse of broad-spectrum antibiotics have contributed significantly to the emergence of resistant organisms through selective evolutionary pressure.

The reduced effectiveness of third-generation cephalosporins observed in the current study is clinically important because these agents are commonly used as empirical therapy for neonatal sepsis. Several studies have reported increasing cephalosporin resistance among Enterobacterales due to ESBL production.[19,20] The emergence of cephalosporin-resistant pathogens necessitates careful antibiotic selection and highlights the importance of local antimicrobial surveillance programs.

Meropenem demonstrated complete activity against Gram-negative isolates in the present study. Similar findings have been reported in surveillance studies from India and Southeast Asia.[30,32] Carbapenems remain among the most effective therapeutic options for severe infections caused by ESBL-producing organisms. However, increasing reports of carbapenem-resistant Enterobacterales worldwide have raised serious concerns regarding the future effectiveness of these reserve antibiotics.[14] Therefore, carbapenems should be used judiciously and reserved for confirmed or strongly suspected resistant infections.

Among Gram-positive organisms, complete resistance to penicillin was observed, whereas vancomycin and linezolid retained excellent activity. Similar findings have been reported by Dong et al. and other investigators studying neonatal bloodstream infections.[9] The preservation of susceptibility to vancomycin and linezolid is encouraging because these agents continue to serve as reliable treatment options for resistant Gram-positive infections. Nevertheless, increasing reports of vancomycin-intermediate and linezolid-resistant strains emphasize the need for continuous monitoring.

Multidrug resistance was detected in 25.0% of bacterial isolates in the current study. This finding is comparable to reports from various tertiary care hospitals where MDR prevalence among neonatal pathogens ranges between 20% and 50%.[17,18] The emergence of MDR organisms represents a major healthcare challenge because such infections are associated with prolonged hospitalization, increased treatment costs, therapeutic failure, and higher mortality rates. Neonates are particularly vulnerable due to their immature immune systems and frequent exposure to invasive interventions. The increasing burden of MDR pathogens emphasizes the urgent need for robust antimicrobial stewardship programs and infection control measures.

The present study also detected ESBL production in 16.7% of Gram-negative isolates. Although the prevalence was relatively low, the presence of ESBL-producing organisms remains clinically significant. Paterson and Bonomo described ESBL-producing Enterobacterales as one of the most important global antimicrobial resistance threats.[19] ESBL enzymes hydrolyze penicillins, cephalosporins, and monobactams, resulting in limited therapeutic options and increased dependence on carbapenems. Logan and Weinstein similarly emphasized the role of ESBL-producing organisms in healthcare-associated infections and outbreaks.[20]

The findings of the present study highlight the dynamic and evolving nature of neonatal sepsis pathogens and their resistance patterns. Continuous surveillance is essential because antimicrobial susceptibility profiles vary significantly across institutions and geographical regions. Periodic review of antibiotic policies based on local microbiological data can help improve treatment outcomes and reduce unnecessary exposure to broad-spectrum agents.

A 2025 study by Sau et al. evaluated the bacteriological profile and antimicrobial resistance patterns among neonates with suspected sepsis in a tertiary care hospital. The investigators reported that Gram-negative bacteria were the predominant pathogens, with *Klebsiella pneumoniae* and *Escherichia coli* accounting for the majority of bloodstream infections. High resistance rates were observed against ampicillin, cefotaxime, and ceftriaxone, while carbapenems retained comparatively better sensitivity. The study emphasized the increasing burden of multidrug-resistant (MDR) organisms in neonatal intensive care units and highlighted the need for continuous antimicrobial surveillance and evidence-based antibiotic stewardship programs to optimize empirical therapy and improve neonatal outcomes [34].

In a multicenter study conducted by Zhang et al. in 2025, pathogen distribution and antimicrobial resistance patterns in neonatal sepsis were analyzed across neonatal intensive care units. The study demonstrated that neonatal sepsis remained a major healthcare challenge due to the increasing prevalence of antimicrobial-resistant organisms. Gram-negative bacteria, particularly *Klebsiella pneumoniae* and *Escherichia coli*, were the predominant isolates. The authors reported substantial resistance to third-generation cephalosporins and aminoglycosides, whereas carbapenem antibiotics maintained relatively high effectiveness. The study also found that resistant infections were associated with prolonged hospitalization and increased healthcare expenditure. The authors recommended strengthening infection control measures and implementing local antibiogram-guided treatment protocols [35].

A 2026 study by Gurmu et al. investigated culture-confirmed neonatal sepsis and antimicrobial resistance patterns among neonates admitted to tertiary healthcare facilities. The researchers reported a high prevalence of multidrug-resistant bacterial pathogens, with Gram-negative organisms accounting for the majority of infections. *Klebsiella pneumoniae*, coagulase-negative staphylococci, and *Escherichia coli* were among the most commonly isolated organisms. Significant resistance was observed against ampicillin, cephalosporins, and gentamicin, while meropenem and linezolid retained higher susceptibility. The study concluded that antimicrobial resistance among neonatal pathogens continues to rise and represents a serious threat to effective neonatal care, emphasizing the urgent need for antimicrobial stewardship and regular resistance monitoring programs [36].

Infection prevention and control measures remain fundamental components of neonatal healthcare. Strict hand hygiene, environmental disinfection, aseptic handling of invasive devices, rational antibiotic prescribing, and staff education can significantly reduce the incidence of healthcare-associated infections. Furthermore, strengthening microbiological diagnostic facilities and implementing rapid molecular diagnostic techniques may facilitate earlier pathogen detection and targeted therapy.

Overall, the present study reinforces global concerns regarding increasing antimicrobial resistance among neonatal pathogens. The predominance of Gram-negative organisms, high resistance to first-line antibiotics, emergence of multidrug-resistant strains, and detection of ESBL-producing bacteria emphasize the urgent need for coordinated antimicrobial stewardship programs, continuous surveillance systems, and evidence-based infection control practices in neonatal intensive care units.

CONCLUSION

Neonatal sepsis continues to be an important cause of neonatal morbidity. Gram-negative bacteria, particularly *Klebsiella pneumoniae*, were the predominant pathogens isolated. High resistance was observed against ampicillin and cephalosporins, whereas meropenem, vancomycin, and linezolid remained highly effective. Continuous antimicrobial surveillance and implementation of antibiotic stewardship programs are essential for improving neonatal outcomes.

Limitation

The study with a relatively small number of culture-positive isolates.

DECLARATIONS:

Conflicts of interest: There is no any conflict of interest associated with this study

Consent to participate: There is consent to participate.

Consent for publication: There is consent for the publication of this paper.

Authors' contributions: Author equally contributed the work.

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