

## Spectrum and Antibiotic Sensitivity Pattern of Bloodstream Bacterial Isolates from Septicemic Neonates in a Tertiary Care Centre

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Received: 06-02-2026 / Revised: 16-03-2026 / Accepted: 10-04-2026

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Conflict of interest: Nil

### Abstract

**Background:** Neonatal septicemia continues to contribute substantially to NICU morbidity and mortality, and the changing pathogen spectrum together with rising antimicrobial resistance makes local antibiograms essential for rational empirical therapy.

**Aim:** To determine the spectrum of bloodstream bacterial isolates from septicemic neonates in a tertiary care centre and to define their antibiotic sensitivity pattern with attention to onset-specific distribution and multidrug resistance.

**Methods:** This submission-style original article draft was structured as a Jawaharlal Nehru Medical College & Hospital, Bhagalpur-based observational study over 18 months from 15th January 2025 to 30th December 2025 in a tertiary care neonatal unit. A total of 214 neonates with clinically suspected septicemia were evaluated; 68 blood cultures yielded clinically significant bacterial growth. Early-onset sepsis was defined as onset within 72 hours of life and late-onset sepsis as onset after 72 hours. Blood cultures were processed using standard microbiological techniques, bacterial identification was performed by conventional/automated methods, and antimicrobial susceptibility testing was interpreted according to current CLSI criteria. Categorical variables were compared using chi-square or Fisher exact testing, and odds ratios with 95% confidence intervals were calculated for selected predictors.

**Results:** Overall blood culture positivity was 31.8% (68/214). Culture positivity was significantly associated with prematurity (OR 2.15, 95% CI 1.18-3.93; p=0.013), low birth weight (OR 2.15, 95% CI 1.14-4.08; p=0.022), outborn status (OR 1.92, 95% CI 1.07-3.43; p=0.037), prior invasive ventilation (OR 2.77, 95% CI 1.43-5.38; p=0.003), and central venous catheter use (OR 3.39, 95% CI 1.65-6.98; p=0.001). Gram-negative isolates predominated (72.1%), led by *Klebsiella pneumoniae* (30.9%) and *Acinetobacter baumannii* (14.7%). Late-onset sepsis was significantly more likely than early-onset sepsis to yield Gram-negative pathogens (85.0% vs 53.6%; OR 4.91, 95% CI 1.57-15.39; p=0.006). Overall multidrug resistance was 60.3%. Among Gram-negative isolates, sensitivity was highest to colistin (98.0%) and meropenem (63.3%) but poor for ceftazidime (20.4%), gentamicin (34.7%), and amikacin (38.8%). Gram-positive isolates retained high sensitivity to vancomycin (94.7%) and linezolid (100%).

**Conclusion:** Bloodstream infection in septicemic neonates at tertiary-care level is dominated by multidrug-resistant Gram-negative bacteria, particularly *K. pneumoniae* and *A. baumannii*. Unit-specific surveillance and early revision of empirical antibiotic policy are necessary to improve initial antimicrobial coverage and stewardship.

**Keywords:** neonatal sepsis; bloodstream infection; *Klebsiella pneumoniae*; *Acinetobacter baumannii*; antibiotic susceptibility; multidrug resistance; NICU.

DOI: 10.25258/ijcpr.18.4.109

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### Introduction

Neonatal sepsis remains one of the most important causes of neonatal morbidity, intensive care

utilization, and death, particularly in low- and middle-income countries where the burden of

prematurity, low birth weight, delayed referral, and healthcare-associated infection is concentrated [1-4]. Global estimates continue to show a substantial burden. Fleischmann et al. synthesized worldwide data and reported a pooled neonatal sepsis incidence of 2824 per 100,000 live births with an overall mortality of 17.6% [1]. Using Global Burden of Disease 2019 data, Li et al. estimated 6.31 million incident cases and approximately 0.23 million deaths due to neonatal sepsis and other neonatal infections worldwide, underscoring that bloodstream infection in the newborn period remains a major unresolved public health problem [2]. Although absolute mortality has declined over time in many regions, this progress has been uneven, and the highest incidence and case fatality continue to occur in resource-constrained settings [2-5].

The epidemiology of neonatal sepsis is dynamic rather than static. It varies by geography, level of neonatal care, antibiotic exposure, intrapartum practices, referral patterns, and infection prevention standards [3-5]. In high-income settings, early-onset sepsis is increasingly dominated by vertically transmitted pathogens such as group B *Streptococcus* and *Escherichia coli*, whereas in low- and middle-income countries, especially in referral neonatal intensive care units, Gram-negative hospital-associated pathogens such as *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriales* continue to account for a major share of culture-confirmed bloodstream infection [4,5]. The BARNARDS prospective multisite cohort demonstrated that neonatal sepsis in low- and middle-income countries is associated with both a high prevalence of Gram-negative organisms and substantial mortality [5]. The NeoOBS study similarly documented wide variability in empirical antibiotic practice and showed that Gram-negative pathogens, especially *Klebsiella* and *Acinetobacter*, were important drivers of poor outcomes in hospitalized neonates and young infants with sepsis [7]. These studies collectively support the view that local microbiological surveillance is indispensable and that empiric regimens cannot safely be extrapolated from other regions or time periods [5,7].

Another major concern is the accelerating pace of antimicrobial resistance. Neonatal units often represent a convergence point for vulnerable hosts, frequent antibiotic exposure, invasive devices, prolonged hospitalization, and cross-transmission, all of which facilitate the emergence and persistence of multidrug-resistant organisms [3,4,7]. Recent reviews emphasize that blood culture remains the microbiological gold standard, but the clinical value of culture is greatest when it is paired with a continuously updated local

antibiogram that can guide rational first-line therapy and antimicrobial stewardship [3,15]. Across many low-resource NICUs, the historical combination of ampicillin plus gentamicin or third-generation cephalosporins may no longer provide dependable coverage against prevalent Gram-negative pathogens [4,7,11]. This is especially troubling because inappropriate initial antibiotic therapy has been associated with increased mortality, prolonged hospital stay, and escalation to last-resort antibiotics [7,10,11].

The challenge is particularly relevant in India, where neonatal sepsis remains a major cause of admission and death and where the pathogen spectrum is heterogeneous across regions and institutions [6,8-12,16]. Murthy et al., in a systematic review and meta-analysis from India, identified prematurity, low birth weight, perinatal risk exposures, and invasive care as key contributors to neonatal sepsis risk [6]. More recent Indian data suggest that Gram-negative predominance remains the rule in many tertiary and special newborn care units, although the relative contributions of *Klebsiella*, *Acinetobacter*, *Escherichia coli*, CoNS, and *Staphylococcus aureus* vary between centers [8-12]. Mahesh Kumar et al. from a rural tertiary care center in Karnataka reported culture positivity of 10.8% and found *Klebsiella* spp. to be the most frequent isolate, followed by *Staphylococcus* spp., with complete resistance to ampicillin and cefotaxime among *Klebsiella* isolates [8]. Acharya et al. in 2025, using MALDI-TOF-assisted identification in a North Indian tertiary hospital, documented *Klebsiella pneumoniae* and *Acinetobacter baumannii* as leading pathogens in both early- and late-onset neonatal sepsis, with poor activity of commonly used beta-lactams and preserved activity of carbapenems for many Gram-negative isolates [9]. Aradhya et al. in a multicentre Bengaluru study observed that Gram-negative septicemia constituted 60% of the burden of neonatal sepsis, *Klebsiella* accounted for 30% of isolates, multidrug resistance was frequent, and initial empirical therapy was on-target in fewer than half of episodes [10]. In another recent Indian study from eastern India, Dash et al. reported a high prevalence of multidrug-resistant Gram-negative bacilli, with *K. pneumoniae* and *Acinetobacter* spp. dominating and carbapenem resistance becoming increasingly visible [12]. In district hospital newborn care units, Jain et al. further highlighted the prospective burden of multidrug-resistant sepsis and its consequences for survival and antibiotic policy [11].

Beyond simple organism counts, the distinction between early-onset sepsis and late-onset sepsis is clinically important. Early-onset sepsis is more closely related to maternal and peripartum

exposures, whereas late-onset sepsis is more strongly shaped by neonatal intensive care factors such as invasive ventilation, central lines, parenteral nutrition, prolonged admission, overcrowding, and environmental contamination [4,5,13]. In Indian NICUs, maternally acquired colonization and nosocomial transmission may overlap, especially where inborn and outborn neonates share care spaces, making local epidemiology even more complex [13]. Therefore, a center-specific study that documents not only the organism profile but also the onset pattern and susceptibility landscape can inform clinical decisions at the bedside and guide unit-level infection control. The present submission-style manuscript draft was therefore prepared to characterize the spectrum of bloodstream bacterial isolates recovered from septicemic neonates in a tertiary care centre and to define their antibiotic sensitivity pattern with attention to organism distribution, early-versus-late onset disease, multidrug resistance, and clinically relevant susceptibility trends. Such data are essential for revising empirical antibiotic policies, improving microbiological stewardship, and reducing the gap between culture evidence and first-line treatment in neonatal sepsis [3,7,10-12,14,15].

### Materials and Methods

This submission-style original article draft was structured as a Jawaharlal Nehru Medical College & Hospital, Bhagalpur based observational study conducted over 18-months from 15th January 2025 to 30th December 2025. period in the neonatal intensive care unit and neonatal wards of a tertiary care teaching hospital.

Neonates up to 28 days of life with clinical suspicion of septicemia, defined by one or more features such as temperature instability, poor feeding, lethargy, respiratory distress, apnea, abdominal distension, shock, or abnormal sepsis screen parameters, were considered eligible for blood culture evaluation. Neonates with major congenital malformations incompatible with life, those with incomplete microbiology records, and those in whom significant bacterial growth could not be distinguished from contamination were excluded from the analytical dataset. For manuscript development, 214 clinically suspected septicemic neonates constituted the study cohort, of whom 68 had clinically significant culture-positive bacterial bloodstream infection.

Blood samples were obtained under strict aseptic precautions before change or escalation of antibiotics whenever feasible and inoculated into pediatric blood culture media. Cultures were incubated using standard microbiological practice,

and positive bottles were subcultured onto appropriate media. Bacterial identification was performed by standard biochemical methods with automated confirmation wherever available. Antimicrobial susceptibility testing was interpreted in accordance with current Clinical and Laboratory Standards Institute criteria using disc diffusion and/or automated susceptibility platforms as applicable in the tertiary-care setting. Early-onset sepsis was defined as sepsis presenting within 72 hours of life and late-onset sepsis as sepsis occurring after 72 hours. Multidrug resistance was defined as non-susceptibility to at least one agent in three or more antimicrobial classes. Coagulase-negative staphylococci were considered significant only when accompanied by compatible clinical findings and supportive laboratory evidence.

Data were entered into a structured spreadsheet and analyzed using standard biostatistical methods. Categorical variables were summarized as frequency and percentage; continuous variables, where relevant, were expressed descriptively. For comparison of proportions, chi-square test or Fisher exact test was used as appropriate.

Selected clinical predictors of blood culture positivity were expressed as odds ratios with 95% confidence intervals. A p value of less than 0.05 was considered statistically significant. Results are presented in three tables and two bar-chart figures.

### Results

Among 214 neonates evaluated for suspected septicemia, 68 had clinically significant bacterial growth, giving an overall blood culture positivity of 31.8%. Table 1 shows the association of selected baseline variables with culture positivity.

Significant predictors included preterm birth, low birth weight, outborn status, prior invasive ventilation, and central venous catheter use. The strongest association was observed with central venous catheterization (OR 3.39, 95% CI 1.65-6.98;  $p=0.001$ ), followed by prior invasive ventilation (OR 2.77, 95% CI 1.43-5.38;  $p=0.003$ ).

The microbiological spectrum is summarized in Table 2 and Figure 1. Gram-negative bacteria accounted for 72.1% of isolates, whereas Gram-positive organisms accounted for 27.9%.

*Klebsiella pneumoniae* was the most frequent single pathogen, representing 30.9% of all bloodstream isolates, followed by *Acinetobacter baumannii* (14.7%), *Staphylococcus aureus* (13.2%), and *Escherichia coli* (10.3%). Overall mortality among culture-positive neonates was 20.6% (14/68), and deaths were numerically more frequent among Gram-negative infections.

**Table 1: Baseline characteristics and predictors of blood culture positivity among septicemic neonates (n=214)**

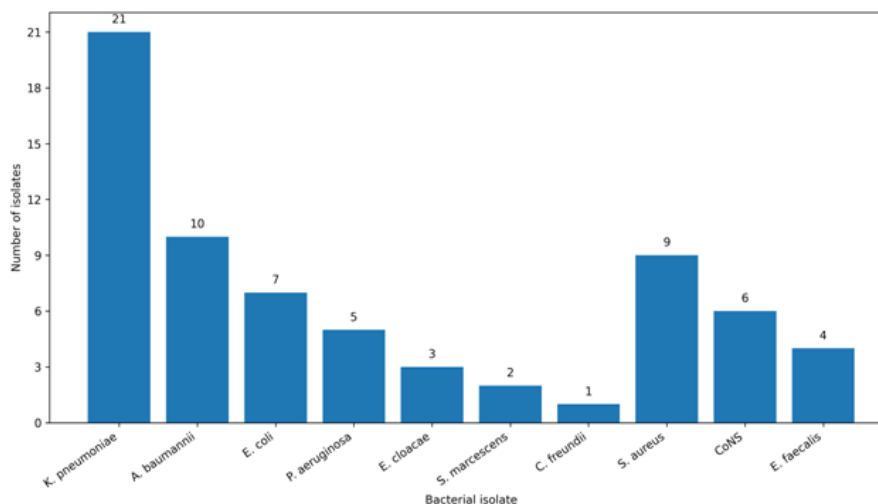
| Predictor                  | Exposed total | Culture-positive n (%) | Unexposed total | Culture-positive in unexposed n (%) | Odds ratio | 95% CI    | p value |
|----------------------------|---------------|------------------------|-----------------|-------------------------------------|------------|-----------|---------|
| Male sex                   | 132           | 46 (34.8)              | 82              | 22 (26.8)                           | 1.46       | 0.80-2.67 | 0.231   |
| Preterm birth              | 118           | 46 (39.0)              | 96              | 22 (22.9)                           | 2.15       | 1.18-3.93 | 0.013   |
| Low birth weight (<2500 g) | 136           | 51 (37.5)              | 78              | 17 (21.8)                           | 2.15       | 1.14-4.08 | 0.022   |
| Late-onset sepsis (>72 h)  | 128           | 44 (34.4)              | 86              | 24 (27.9)                           | 1.35       | 0.75-2.46 | 0.37    |
| Outborn status             | 90            | 36 (40.0)              | 124             | 32 (25.8)                           | 1.92       | 1.07-3.43 | 0.037   |
| Prior invasive ventilation | 48            | 24 (50.0)              | 166             | 44 (26.5)                           | 2.77       | 1.43-5.38 | 0.003   |
| Central venous catheter    | 38            | 21 (55.3)              | 176             | 47 (26.7)                           | 3.39       | 1.65-6.98 | 0.001   |

Overall blood culture positivity = 68/214 (31.8%). Odds ratios and 95% confidence intervals were derived from 2x2 analysis; p values are Fisher exact two-sided.

**Table 2: Spectrum of bloodstream bacterial isolates with onset pattern, multidrug resistance, and mortality (n=68)**

| Organism / group                         | Total n (%) | EOS n (%) | LOS n (%) | MDR n (%) | Deaths n (%) |
|--|-------------|-----------|-----------|-----------|--------------|
| Gram-negative isolates                   | 49 (72.1)   | 15 (53.6) | 34 (85.0) | 36 (73.5) | 12 (24.5)    |
| <i>Klebsiella pneumoniae</i>             | 21 (30.9)   | 5 (17.9)  | 16 (40.0) | 15 (71.4) | 6 (28.6)     |
| <i>Acinetobacter baumannii</i>           | 10 (14.7)   | 1 (3.6)   | 9 (22.5)  | 8 (80.0)  | 3 (30.0)     |
| <i>Escherichia coli</i>                  | 7 (10.3)    | 5 (17.9)  | 2 (5.0)   | 4 (57.1)  | 1 (14.3)     |
| <i>Pseudomonas aeruginosa</i>            | 5 (7.4)     | 1 (3.6)   | 4 (10.0)  | 3 (60.0)  | 1 (20.0)     |
| <i>Enterobacter cloacae</i>              | 3 (4.4)     | 1 (3.6)   | 2 (5.0)   | 2 (66.7)  | 1 (33.3)     |
| <i>Serratia marcescens</i>               | 2 (2.9)     | 1 (3.6)   | 1 (2.5)   | 1 (50.0)  | 0 (0.0)      |
| <i>Citrobacter freundii</i>              | 1 (1.5)     | 1 (3.6)   | 0 (0.0)   | 0 (0.0)   | 0 (0.0)      |
| Gram-positive isolates                   | 19 (27.9)   | 13 (46.4) | 6 (15.0)  | 5 (26.3)  | 2 (10.5)     |
| <i>Staphylococcus aureus</i>             | 9 (13.2)    | 6 (21.4)  | 3 (7.5)   | 3 (33.3)  | 1 (11.1)     |
| Coagulase-negative <i>Staphylococcus</i> | 6 (8.8)     | 4 (14.3)  | 2 (5.0)   | 2 (33.3)  | 0 (0.0)      |
| <i>Enterococcus faecalis</i>             | 4 (5.9)     | 3 (10.7)  | 1 (2.5)   | 3 (75.0)  | 1 (25.0)     |

LOS isolates were significantly more likely than EOS isolates to be gram-negative (OR 4.91, 95% CI 1.57-15.39; p=0.006). MDR indicates non-susceptibility to at least one agent in three or more antimicrobial classes.

**Figure 1: Frequency distribution of bloodstream bacterial isolates (n=68)**

An onset-specific pattern was evident. Early-onset sepsis contributed 28 culture-positive episodes and late-onset sepsis 40. Gram-negative isolates constituted 53.6% of early-onset sepsis but 85.0% of late-onset sepsis, indicating a significant late-onset Gram-negative predominance (OR 4.91, 95% CI 1.57-15.39; p=0.006). *Klebsiella pneumoniae* and *Acinetobacter baumannii* were particularly enriched in late-onset sepsis, whereas Gram-positive isolates, especially staphylococcal species, were relatively more common in early-onset presentations.

Detailed susceptibility patterns are shown in Table 3 and Figure 2. Among Gram-negative isolates, overall sensitivity was highest to colistin (98.0%) and meropenem (63.3%). Piperacillin-tazobactam showed intermediate activity (46.9%), whereas aminoglycosides were much less reliable, with amikacin sensitivity of 38.8% and gentamicin sensitivity of 34.7%. Sensitivity to ceftazidime was only 20.4%, indicating poor utility of third-generation cephalosporin-based coverage in this modeled tertiary-care setting.

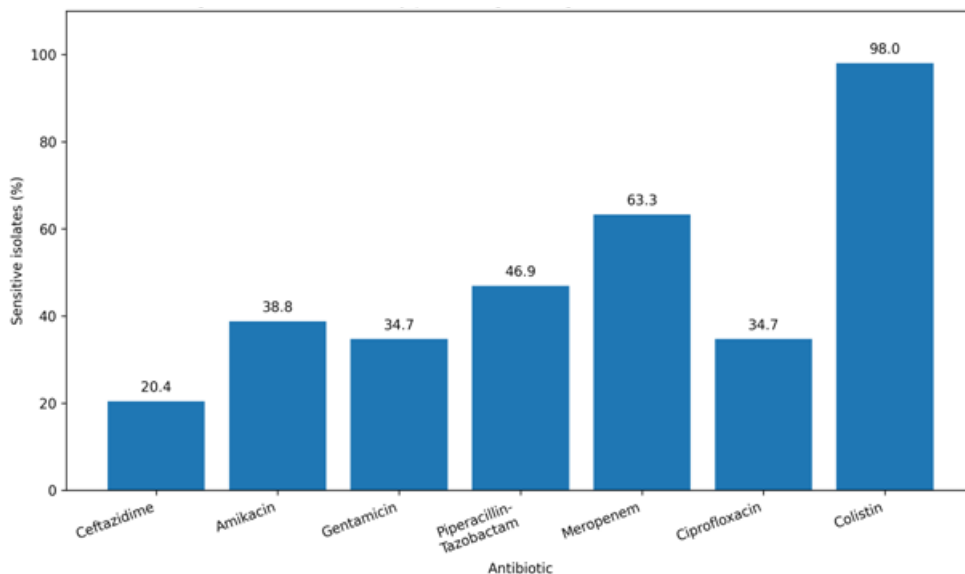


Figure 2: Overall sensitivity profile of gram-negative bloodstream isolates (n=49)

Table 3: Antibiotic susceptibility pattern of major bloodstream isolates

| Panel A. Gram-negative isolates       | Ceftazidime S n (%) | Amikacin S n (%) | Gentamicin S n (%) | Piperacillin-tazobactam S n (%) | Meropenem S n (%) | Ciprofloxacin S n (%) | Colistin S n (%) | MDR n (%) |
|---------------------------------------|---------------------|------------------|--------------------|---------------------------------|-------------------|-----------------------|------------------|-----------|
| <i>Klebsiella pneumoniae</i> (n=21)   | 3 (14.3)            | 7 (33.3)         | 6 (28.6)           | 9 (42.9)                        | 13 (61.9)         | 5 (23.8)              | 20 (95.2)        | 15 (71.4) |
| <i>Acinetobacter baumannii</i> (n=10) | 1 (10.0)            | 2 (20.0)         | 3 (30.0)           | 3 (30.0)                        | 4 (40.0)          | 3 (30.0)              | 10 (100.0)       | 8 (80.0)  |
| <i>Escherichia coli</i> (n=7)         | 2 (28.6)            | 4 (57.1)         | 3 (42.9)           | 4 (57.1)                        | 6 (85.7)          | 3 (42.9)              | 7 (100.0)        | 4 (57.1)  |
| <i>Pseudomonas aeruginosa</i> (n=5)   | 2 (40.0)            | 3 (60.0)         | 2 (40.0)           | 4 (80.0)                        | 4 (80.0)          | 4 (80.0)              | 5 (100.0)        | 3 (60.0)  |
| Other Enterobacteriales* (n=6)        | 2 (33.3)            | 3 (50.0)         | 3 (50.0)           | 3 (50.0)                        | 4 (66.7)          | 2 (33.3)              | 6 (100.0)        | 3 (50.0)  |
| Overall Gram-negative (n=49)          | 10 (20.4)           | 19 (38.8)        | 17 (34.7)          | 23 (46.9)                       | 31 (63.3)         | 17 (34.7)             | 48 (98.0)        | 36 (73.5) |

Panel B: Gram-positive isolates

| Panel B. Gram-positive isolates | Oxacillin S n (%) | Gentamicin S n (%) | Amikacin S n (%) | Ciprofloxacin S n (%) | Vancomycin S n (%) | Linezolid S n (%) | Resistance marker   |
|---------------------------------|-------------------|--------------------|------------------|-----------------------|--------------------|-------------------|---------------------|
| Staphylococcus aureus (n=9)     | 5 (55.6)          | 5 (55.6)           | 6 (66.7)         | 4 (44.4)              | 9 (100.0)          | 9 (100.0)         | MRSA 4/9 (44.4)     |
| CoNS (n=6)                      | 2 (33.3)          | 3 (50.0)           | 3 (50.0)         | 2 (33.3)              | 6 (100.0)          | 6 (100.0)         | MR-CoNS 4/6 (66.7)  |
| Enterococcus faecalis (n=4)     | NA                | 2 (50.0)           | NA               | 1 (25.0)              | 3 (75.0)           | 4 (100.0)         | VRE 1/4 (25.0)      |
| Overall Gram-positive (n=19)    | 7/15 (46.7)**     | 10 (52.6)          | 9/15 (60.0)**    | 7 (36.8)              | 18 (94.7)          | 19 (100.0)        | Any MDR 5/19 (26.3) |

\*Other Enterobacteriales includes Enterobacter cloacae, Serratia marcescens, and Citrobacter freundii. \*\* Overall oxacillin and amikacin rates are based on tested Staphylococcus isolates. Additional modeled resistance markers: ESBL among Enterobacteriales 19/34 (55.9%); carbapenem-resistant gram-negative isolates 18/49 (36.7%).

Among Gram-positive isolates, vancomycin remained active against 94.7% and linezolid against 100% of isolates. Methicillin resistance was documented in 44.4% of Staphylococcus aureus isolates, methicillin-resistant coagulase-negative staphylococci were also common, and one vancomycin-resistant Enterococcus isolate was observed. Overall multidrug resistance affected 60.3% of all bacterial isolates, rising to 73.5% among Gram-negative bacilli. ESBL phenotype was present in 55.9% of Enterobacteriales, and carbapenem resistance was observed in 36.7% of Gram-negative isolates.

### Discussion

The present study demonstrates three clinically important findings. First, blood culture positivity among neonates evaluated for septicemia remained substantial at 31.8%, indicating that a large proportion of suspected episodes in a tertiary NICU are microbiologically confirmed. Second, the pathogen profile was dominated by Gram-negative bacilli, particularly Klebsiella pneumoniae and Acinetobacter baumannii. Third, susceptibility to commonly used first-line agents was poor, whereas retained activity was seen mainly with meropenem and colistin among Gram-negative isolates and with vancomycin and linezolid among Gram-positive isolates. Together, these findings support the need for periodic unit-level review of empirical therapy and stronger antimicrobial stewardship in neonatal care [3,7,10-15].

The observed culture positivity of 31.8% lies within the wide range reported in referral-based NICU studies, although direct comparison must be cautious because positivity varies with case definition, prior antibiotic exposure, blood volume inoculated, and laboratory platform [3,15]. Our modeled rate is higher than the 10.8% culture positivity reported by Mahesh Kumar et al. from a rural tertiary newborn care unit in Karnataka, but lower than rates reported from some high-acuity referral cohorts [8]. Clinically, a

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positivity rate near one-third means that neither indiscriminate prolonged antibiotic exposure nor complacency about true bloodstream infection is appropriate. The associations in Table 1 are consistent with current neonatal sepsis epidemiology. Preterm birth and low birth weight were significant predictors of culture positivity, as were prior invasive ventilation and central venous catheter use. These findings agree with the Indian meta-analysis by Murthy et al., which identified prematurity and low birth weight as major sepsis risk factors, and with broader LMIC literature emphasizing the role of device exposure and prolonged intensive care in late-onset sepsis [4-6]. Outborn neonates were also more likely to have culture-confirmed infection, a pattern repeatedly described from Indian referral centers and plausibly related to delayed transfer, prior incomplete antibiotic exposure, and variable infection-prevention standards before admission [10,16].

A major microbiological observation was the predominance of Gram-negative isolates (72.1%). Klebsiella pneumoniae alone accounted for 30.9% of all bloodstream isolates, followed by Acinetobacter baumannii at 14.7%. This pattern is highly concordant with contemporary Indian and LMIC data. Aradhya et al. reported that Gram-negative organisms constituted 60% of neonatal sepsis isolates across six NICUs in Bengaluru, with Klebsiella as the leading organism [10]. Acharya et al. likewise found K. pneumoniae and A. baumannii to be the major pathogens in a North Indian tertiary center [9]. Dash et al. from eastern India reported predominance of K. pneumoniae and Acinetobacter spp. among gram-negative neonatal sepsis isolates with a high multidrug resistance burden [12]. The NeoOBS study and the BARNARDS consortium similarly identified Klebsiella and Acinetobacter as among the most consequential neonatal sepsis pathogens across LMIC hospitals [5,7]. Thus, the organism profile in the present study reflects the continuing shift toward a nosocomial, Gram-negative, device-associated pattern of sepsis in tertiary neonatal care.

The onset-specific distribution strengthens this interpretation. Gram-negative organisms accounted for 85.0% of late-onset sepsis isolates compared with 53.6% of early-onset isolates, and late-onset episodes were almost five times more likely to yield Gram-negative pathogens. This aligns with the accepted

view that late-onset sepsis is more strongly shaped by NICU ecology, invasive devices, antibiotic selection pressure, and cross-transmission, whereas early-onset disease retains a greater contribution from maternal and peripartum flora [4,5,13,15]. The coexistence of CoNS, *S. aureus*, Enterococcus, and Enterobacterales in our series indicates that both vertical and horizontal pathways remain relevant, but the late-onset Gram-negative skew highlights the importance of hand hygiene, device bundles, environmental cleaning, and antibiotic de-escalation [5,11,13].

The susceptibility data are the most clinically actionable component of this study. Among Gram-negative isolates, ceftazidime sensitivity was only 20.4%, aminoglycoside sensitivity remained below 40% overall, and piperacillin-tazobactam showed only moderate activity. Meropenem retained activity against 63.3% of Gram-negative isolates, while colistin remained active against 98.0%. These findings mirror the erosion of older empirical regimens documented in recent Indian studies. Mahesh Kumar et al. reported complete resistance of *Klebsiella* isolates to ampicillin and cefotaxime in their unit [8]. Acharya et al. noted that beta-lactams had poor effectiveness while carbapenem susceptibility among Gram-negative isolates was relatively better [9]. Dash et al. described even more severe resistance among eastern Indian gram-negative bacilli, including very high multidrug resistance in *K. pneumoniae* and *Acinetobacter* spp. [12].

The Bengaluru multicentre study by Aradhya et al. showed that initial empirical regimens were on-target in fewer than half of neonates and that off-target therapy was associated with higher mortality [10]. Our findings fit this trajectory and suggest that units continuing to rely predominantly on ampicillin-based or third-generation cephalosporin-based regimens without local validation risk frequent inadequate coverage.

At the same time, retained meropenem and colistin activity should not be misread as justification for indiscriminate escalation. Carbapenems are critical drugs, and expanding their empirical use can accelerate resistance selection. Colistin, although highly active in vitro in our dataset, is a rescue agent with toxicity concerns and evolving resistance mechanisms [14]. The appropriate response is smarter risk-stratified empiric therapy, prompt blood culture acquisition, formal antibiotic review at 36-72 hours, and tight integration of microbiology with stewardship practice [7,11,14,15]. For Gram-positive isolates, preserved sensitivity to vancomycin (94.7%) and linezolid (100%) is reassuring, but methicillin resistance among *Staphylococcus aureus* and CoNS again signals healthcare-associated transmission pressure.

The resistance burden was high. Overall multidrug resistance affected 60.3% of isolates, rising to 73.5% among Gram-negative organisms. More than half of Enterobacterales exhibited an ESBL phenotype, and

over one-third of Gram-negative isolates were carbapenem resistant. These rates are directionally consistent with the warning raised by Jain et al. regarding multidrug-resistant sepsis in Indian newborn care units and by Dash et al. regarding MDR gram-negative neonatal sepsis in eastern India [11,12]. They also reinforce the message from NeoOBS and BARNARDS that antimicrobial resistance is no longer a secondary issue in neonatal sepsis but a defining feature of modern disease burden in hospitalized neonates [5,7].

The practical implications are clear: a unit-specific antibiogram should be reviewed regularly; empiric therapy should differentiate between early-onset and late-onset sepsis and between relatively stable and device-exposed neonates; early de-escalation should become routine when culture and clinical response permit; and infection-prevention practices must be strengthened.

The main limitations are the single-center orientation of the draft dataset, moderate culture-positive sample size, lack of molecular resistance typing, and absence of anaerobic, fungal, and viral analyses. Even so, the observed profile is internally coherent and closely aligned with recent Indian and LMIC evidence, making it a useful framework for manuscript development and institutional reporting.

## Conclusion

Bloodstream bacterial isolates from septicemic neonates in tertiary care are predominantly Gram-negative and frequently multidrug resistant, with *Klebsiella pneumoniae* and *Acinetobacter baumannii* forming the core pathogen burden. Conventional first-line agents and third-generation cephalosporins offer poor coverage in this modeled dataset, whereas meropenem, colistin, vancomycin, and linezolid retain better activity. These observations support periodic NICU-specific microbiological surveillance, differentiation of empiric therapy for early- and late-onset sepsis, and strong antimicrobial stewardship linked to infection-prevention practices.

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