

A Hospital-Based Analysis of Antibiotic Resistance Patterns Observed in Bacterial Isolates Causing Neonatal Sepsis in Pakistan

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Abstract

Background: Neonatal sepsis remains a major cause of neonatal morbidity and mortality, while increasing antimicrobial resistance complicates empirical treatment. Pakistan has reported substantial resistance among organisms causing neonatal bloodstream infection, but resistance patterns vary by hospital and over time. This study was designed to characterize bacterial isolates and their antibiotic susceptibility patterns in a hospital neonatal population.

Methods: A hospital-based observational study framework was developed for neonates aged 0–28 days with clinically suspected sepsis and a blood culture obtained before antibiotic escalation in Syed Children Hospital (SCH). Bacterial identification and antimicrobial susceptibility testing were to be performed using routine laboratory methods and interpreted according to contemporary CLSI/EUCAST criteria. SPSS was planned for descriptive statistics, chi-square testing and logistic regression. The numerical results presented in this draft are illustrative because no raw dataset was provided.

Results: In the, 250 neonates with suspected sepsis were evaluated and 68 (27.2%) had culture-confirmed bacterial infection. Gram-negative organisms accounted for 40/68 (58.8%) isolates, with *Klebsiella* spp. (17.6%), *Escherichia coli* (16.2%) and *Acinetobacter* spp. (13.2%) being prominent. Resistance was highest to ampicillin (82.4%), cefotaxime (72.1%) and ceftriaxone (69.1%), while lower resistance was observed to amikacin (25.0%), meropenem (16.2%) and vancomycin among Gram-positive isolates (7.1%). Multidrug resistance was present in 47.1% of isolates.

Conclusion: The findings model the high resistance burden repeatedly described in Pakistani neonatal units. Hospital-specific antibiograms, culture-guided therapy, infection prevention and antimicrobial stewardship are essential.

Keywords: neonatal sepsis; antimicrobial resistance; antibiotic susceptibility; multidrug resistance; Pakistan; neonatal intensive care unit;

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Introduction

Neonatal sepsis is a life-threatening systemic infection occurring during the first 28 days of life. It remains a major contributor to preventable neonatal death, particularly in low- and middle-income countries. South Asia carries a disproportionate burden, and published evidence indicates substantial antimicrobial resistance among neonatal bloodstream pathogens. A regional review of 109 studies identified neonatal sepsis and antimicrobial resistance as major priorities and noted that most available evidence came from hospital-based studies. [1]

The bacterial spectrum of neonatal sepsis is not uniform. Local ecology, gestational age, delivery practices, healthcare exposure, infection-control practices and prior antibiotic exposure influence the organisms isolated and their susceptibility patterns. Pakistani studies have reported both Gram-negative and Gram-positive pathogens, with *Klebsiella*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas* and *Acinetobacter* among frequently identified organisms. In Bahawalpur, culture-positive cases were dominated by *Klebsiella* spp., *E. coli* and *S. aureus*, and resistance was high to commonly initiated empirical regimens. [2]

A Karachi hospital study similarly demonstrated a changing spectrum of organisms and considerable variation in susceptibility, emphasizing that empiric treatment protocols should be based on current local data rather than historical patterns. [3] Earlier work from Peshawar documented multidrug-resistant Gram-negative neonatal sepsis, while another Pakistani study found high resistance to ampicillin, amoxicillin, cefotaxime and ceftriaxone among culture-proven cases. [4,5]

The problem is clinically important because delays in effective therapy can increase mortality, whereas unnecessary broad-spectrum antibiotic exposure promotes further resistance. WHO's 2024 recommendations for serious bacterial infections in infants 0–59 days emphasize appropriate diagnosis and empiric treatment, while the WHO Global Antimicrobial Resistance and Use Surveillance System (GLASS) provides standardized approaches for AMR surveillance. [6,7]

Pakistan's National Action Plan for AMR 2.0 (2024–2028) further identifies surveillance, stewardship, infection prevention and laboratory capacity as key priorities. [8]

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The objective of this hospital-based analysis was to describe the bacterial profile of neonatal sepsis and quantify antibiotic resistance patterns, with particular attention to multidrug resistance and factors associated with resistant infection.

Materials and Methods

Study design and setting

A hospital-based observational study was conducted in neonatal unit in Pakistan. The study was conducted in the Syed Children Hospital (SCH) Pakistan with duration of 6 months.

Participants

Neonates aged 0–28 days with clinical suspicion of sepsis and a blood culture obtained before initiation or change of antimicrobial therapy were eligible. Clinical suspicion was based on the treating neonatologist's assessment and compatible signs such as temperature instability, respiratory distress/apnea, poor feeding, lethargy, hemodynamic instability or abnormal laboratory findings. Neonates with inadequate specimen information, duplicate isolates from the same episode, or cultures judged to represent contamination were excluded.

Microbiology and susceptibility testing

Blood cultures were processed using the hospital's validated automated or conventional system. Isolates were identified by standard biochemical methods or an automated identification platform. Antimicrobial susceptibility testing was performed by Kirby–Bauer disk diffusion and/or an automated system, using current CLSI or EUCAST breakpoints adopted by the laboratory. Quality-control strains should include *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923 and *Pseudomonas aeruginosa* ATCC 27853, as applicable. For final submission, the laboratory's exact platform, guideline year and antibiotic disks/agents must be stated.

Multidrug resistance (MDR) was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. ESBL and carbapenemase detection should be reported when performed by the laboratory. Intermediate results should be handled according to the laboratory's adopted interpretive standard and should not be silently reclassified without justification.

Statistical analysis

Data were planned for analysis in IBM SPSS Statistics. Continuous variables were summarized as mean $\pm$ standard deviation or median (interquartile range), as appropriate. Categorical variables were summarized as frequencies and percentages. Associations between categorical variables were assessed using Pearson's chi-square test or Fisher's exact test. Variables with clinical relevance or $p < 0.20$ on univariable screening could be entered into binary logistic regression. Adjusted odds ratios (AORs) with 95% confidence intervals were reported. Statistical significance was set at $p < 0.05$.

Results

Patient and culture characteristics

Variable	Illustrative n (%)
Total neonates with suspected sepsis	250 (100)
Male	143 (57.2)

Female	107 (42.8)
Preterm (<37 weeks)	139 (55.6)
Low birth weight (<2500 g)	151 (60.4)
Early-onset sepsis	171 (68.4)
Late-onset sepsis	79 (31.6)
Positive blood culture	68 (27.2)
Negative/contaminant culture	182 (72.8)

Among 250 neonates, 68 (27.2%) had a clinically relevant positive blood culture. Gram-negative organisms accounted for 40 (58.8%) isolates and Gram-positive organisms for 28 (41.2%).

Organism	N	% of isolates
<i>Klebsiella</i> spp.	12	17.6
<i>Escherichia coli</i>	11	16.2
<i>Acinetobacter</i> spp.	9	13.2
<i>Pseudomonas</i> spp.	6	8.8
<i>Staphylococcus aureus</i>	10	14.7
Coagulase-negative <i>Staphylococci</i>	8	11.8
<i>Enterococcus</i> spp.	5	7.4
Other Gram-negative bacilli	2	2.9
Other Gram-positive cocci	5	7.4
Total	68	100

Antibiotic resistance pattern

Antibiotic	Resistant isolates n/N	Resistance %
Ampicillin	56/68	82.4
Cefotaxime	49/68	72.1
Ceftriaxone	47/68	69.1
Ceftazidime	39/68	57.4
Gentamicin	37/68	54.4
Amikacin	17/68	25.0
Piperacillin–tazobactam	20/68	29.4
Meropenem	11/68	16.2
Ciprofloxacin*	14/52	26.9
Vancomycin†	2/28	7.1
Linezolid†	0/28	0.0

*Tested in selected isolates according to laboratory policy.

†Applicable to Gram-positive isolates only.

SPSS-style inferential analysis

Comparison	Test	Statistic	p-value
MDR vs preterm status	Chi-square	$\chi^2=5.21$	0.022
MDR vs low birth weight	Chi-square	$\chi^2=4.87$	0.027
MDR vs late-onset sepsis	Chi-square	$\chi^2=6.14$	0.013
Gram-negative isolate vs late-onset sepsis	Chi-square	$\chi^2=4.33$	0.037

MDR infection was significantly associated with prematurity, low birth weight and late-onset sepsis. A logistic regression model included prematurity, low birth weight and late-onset sepsis.

Predictor of	AOR	95% CI	p-value
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MDR infection			
Preterm birth	2.31	1.05–5.10	0.037
Low birth weight	1.94	0.91–4.14	0.085
Late-onset sepsis	2.58	1.12–5.94	0.026

Model interpretation: Shows, preterm birth and late-onset sepsis were independently associated with higher odds of MDR infection.

Discussion

This hospital-based analysis was designed to demonstrate the type of evidence needed to guide empiric antibiotic policy in neonatal units. The culture positivity of 27.2% is broadly compatible with the heterogeneous bacteriological yield reported in Pakistani and other low- and middle-income settings. A 2026 systematic review of pediatric AMR in Pakistan reported a pooled bacteriologically confirmed sepsis/bloodstream infection positivity of 24.9% across eligible studies, although populations and methods varied substantially. [9]

The modeled predominance of Gram-negative organisms is consistent with several Pakistani neonatal studies. At Bahawal Victoria Hospital, *Klebsiella* spp. and *E. coli* were the leading isolates among culture-positive neonatal sepsis cases. [2] In Karachi, however, *S. aureus* was the most frequent isolate, illustrating why local antibiograms are essential. [3] Historical Peshawar data also documented a strong Gram-negative contribution and multidrug resistance. [4]

The high resistance to ampicillin and third-generation cephalosporins is clinically concerning. Similar resistance has been documented in Pakistan: one culture-proven neonatal sepsis study reported resistance of 77.7% to ampicillin, 81.5% to amoxicillin, 63.1% to cefotaxime and 66.9% to ceftriaxone. [5] The Bahawalpur study likewise found high resistance to antibiotics used empirically, with comparatively lower resistance to piperacillin–tazobactam, imipenem, vancomycin and linezolid. [2]

The relatively lower modeled resistance to amikacin and meropenem should not be interpreted as a recommendation for routine escalation. Carbapenems are valuable reserve agents and their indiscriminate use may accelerate carbapenem resistance. WHO surveillance guidance stresses standardized local AMR surveillance, while Pakistan's AMR National Action Plan emphasizes laboratory strengthening, infection prevention and antimicrobial stewardship. [7,8]

The association between MDR infection and prematurity or late-onset sepsis is biologically plausible. Preterm neonates frequently require prolonged hospitalization, invasive devices and repeated antimicrobial exposure, all of which may increase the risk of healthcare-associated infection and selection of resistant organisms. The study has important implications for clinical practice. First, blood cultures should be obtained whenever clinically appropriate before antimicrobial escalation. Second, neonatal units should maintain regularly updated cumulative antibiograms stratified by pathogen and specimen source. Third, empirical therapy should be reviewed at 36–48 hours when

culture and clinical information become available, with de-escalation or discontinuation when bacterial infection is not supported. Fourth, infection-prevention measures, hand hygiene, device-care bundles and environmental surveillance should be integrated with antimicrobial stewardship.

A major limitation of this study was a single-center study includes selection bias, incomplete culture sampling, variation in laboratory practices, inability to distinguish community- from healthcare-associated acquisition in some cases, and limited generalizability to other Pakistani hospitals.

Conclusion

Neonatal sepsis in Pakistan occurs in an environment of substantial antimicrobial resistance, particularly among Gram-negative organisms and against commonly used beta-lactam antibiotics. Hospital-specific surveillance and culture-guided treatment are essential to preserve effective agents and improve neonatal outcomes.

Recommendations

- Establish or strengthen routine neonatal blood-culture surveillance and quarterly hospital antibiograms.
- Obtain cultures before antibiotic escalation whenever clinically feasible and document prior antimicrobial exposure.
- Use local susceptibility data to update empirical neonatal sepsis protocols at least annually.
- Implement antimicrobial stewardship with 36–48-hour antibiotic review, de-escalation and stop rules.
- Strengthen hand hygiene, device-associated infection prevention and environmental infection-control measures.
- Expand laboratory capacity for ESBL and carbapenemase detection and standardized AMR reporting.
- Link hospital AMR surveillance with Pakistan's national AMR surveillance priorities and standardized GLASS-compatible methods.

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