Original Article

Bacteriological Profile, Antimicrobial Susceptibility, and Clinical Outcomes of Neonatal Bloodstream Infections in a Tertiary Care Centre in Central India: A Prospective Cohort Study

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Abstract

Background: Neonatal sepsis is a major cause of morbidity and mortality, especially in low- and middle-income countries, where the emergence of multidrug-resistant (MDR) pathogens complicates empirical treatment. Accurate, region-specific epidemiological data are critical to guide antimicrobial therapy and enhance survival rates. The study aimed to determine the bacteriological profile of blood-culture-proven neonatal sepsis, determine the antimicrobial susceptibility patterns of the isolated pathogens, and evaluate the associated clinical outcomes in a tertiary care setting. **Material and Methods:** A one-year, observational, prospective cohort study was conducted at a Special Newborn Care Unit (SNCU) in central India, enrolling 150 neonates with culture-proven bacterial bloodstream infections. Demographic, clinical, and laboratory parameters were systematically recorded. Pathogen identification and antibiotic susceptibility testing were performed following standard Clinical and Laboratory Standards Institute (CLSI) protocols. **Results:** The majority (75.3%) were preterm, and 47.3% very low birth weight with early-onset sepsis as most common presentation (65.3%). The isolate profile consisted of mainly resistant Gram-negatives (68.7%), primarily driven by Acinetobacter spp. (22.0%) and Klebsiella pneumoniae (21.3%), which are highly multidrug-resistant to first-line agents but only moderately sensitive to colistin (50.5%) and had a 3.3% pandrug-resistance rate, with case fatality rate overall at 21.3%, the major cause being Gram-negative infections or extreme prematurity. **Conclusion:** Neonatal sepsis in this region is critically burdened by extensively resistant Gram-negative bacteria. The alarming emergence of pan-resistant strains demands immediate implementation of rigorous antimicrobial stewardship and targeted infection control bundles in neonatal units.

Keywords: Neonatal sepsis, antimicrobial resistance, Klebsiella pneumoniae, Acinetobacter, Pandrug-resistance.

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Introduction

Neonatal sepsis, clinically defined as a systemic blood infection that occurs within the first 28 days of life, is a major global health problem.[1] It is the leading cause of neonatal morbidity and mortality and contributes to around 3 million cases of disease each year.[2] While progress in peri-natal and intensive care has improved in high income regions, the burden of disease remains disproportionately concentrated in low and middle income countries (LMICs).[1] The clinical classification of neonatal sepsis is based on the chronological onset of symptoms: early-onset sepsis (EOS) occurs within 72 hours of birth and is usually due to vertical transmission, while late-onset sepsis (LOS) occurs later and is mainly acquired in the postnatal setting.[3] Historically, high income countries have reported Streptococcus group B as the primary pathogen of EOS.[4] By contrast, the LMICs show a pervasive predominance of Gram-negative enteric bacteria in both EOS and LOS presentations.[5] The rapid global increase in antimicrobial resistance compounds this epidemiological divergence.[6] Neonatal intensive care units (NICUs) are increasingly reporting widespread resistance to standard empirical regimens (such as ampicillin and aminoglycosides), leaving vulnerable infants exposed to multidrug-resistant (MDR) and pandrug-resistant pathogens.[6,7] Empirical treatment protocols must be based on current, local susceptibility data to minimize mortality and prevent the overuse of reserve antibiotics. For these reasons, the aim of this study was to characterize the bacteriological etiology, antimicrobial resistance profile, and clinical outcomes of neonatal bloodstream infections in a high-volume tertiary care center in central India.

Materials and Methods

Study Design and Setting: This was a prospective, observational cohort study conducted over a 12-month period in

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the Special Newborn Care Unit (SNCU) of the Department of Pediatrics at M.T.H., Maharaja Yashwantrao Hospital, an institution affiliated with M.G.M. Medical College, Indore, India.

Study Population and Sampling: The study population consisted of all neonates admitted to the SNCU with clinical signs of sepsis, and 150 neonates were enrolled using consecutive sampling, with the strict inclusion criterion of a blood-culture positive for a bacterial pathogen; neonates with fungal growth or cultures flagged as environmental contaminants were excluded. The sample size was determined through mathematical calculations using Cochran's formula, with a minimum of 115 subjects to account for 2% prevalence in institutional records, 15% attrition, and consecutive sampling.

Data Collection and Laboratory Procedures: After obtaining written informed parental consent, detailed maternal, perinatal, and neonatal data were recorded using a standardized proforma. Venous blood (0.5–1.0 mL) was collected under aseptic conditions and cultured, processed by the Department of Microbiology for bacterial identification, and subjected to antimicrobial susceptibility profiling via the Kirby-Bauer disc diffusion technique and interpreted strictly according to current Clinical and Laboratory Standards Institute (CLSI) guidelines.

Operational Definitions

- **Neonatal Sepsis:** A systemic bacterial infection confirmed by a positive blood culture that occurs within the first 28 days of life.[1]
- **Early-Onset Sepsis (EOS) & Late-Onset Sepsis (LOS):** EOS was defined as culture-proven sepsis presenting at or prior to 72 hours of life; onset occurring beyond 72 hours was classified as LOS.[3]
- **Multidrug-Resistant (MDR) Organism:** A bacterial isolate that is non-susceptible to at least one agent in three or more antimicrobial classes.
- **Pandrug-Resistant (Pan-resistant) Organism:** An isolate showing complete resistance to all tested antimicrobial agents across all available therapeutic classes.

Statistical Analysis: Data were aggregated and analyzed using OpenEpi to generate descriptive statistics of continuous variables (mean ± SD) and categorical data (frequencies and percentages); inferential statistics (Chi-square or Fisher's exact tests) assessed associations among categorical variables, and p-value significance was set at <0.05.

Results

[Table 1] shows the basic demographics of the study population, which had a high prevalence of preterm and low-birth-weight infants (75.3% and 47.3% of subjects, respectively) and a high incidence of early-onset sepsis (65.3%), which far exceeded the incidence of late-onset infections, suggesting that the early postnatal period may be a particularly vulnerable period for bacterial invasion at this facility.

Table 1: Baseline Socio-Demographic and Perinatal Characteristics (N=150)

Characteristic	Category	Frequency (n)	Percentage (%)
Gender	Male	68	45.3
	Female	82	54.7
Gestational Age	Preterm (≤ 37 weeks)	113	75.3
	Term (> 37 weeks)	37	24.7
Birth Weight	Extremely Low (< 1.0 kg)	17	11.3
	Very Low (1.0–1.4 kg)	71	47.3
	Low (1.5–2.4 kg)	46	30.7
	Normal (≥ 2.5 kg)	16	10.7
Mode of Delivery	Normal Vaginal Delivery	132	88.0
	Caesarean Section (LSCS)	18	12.0
Onset of Sepsis	Early-Onset (EOS)	98	65.3
	Late-Onset (LOS)	52	34.7

Table 2: Bacteriological Profile of Blood Culture Isolates (N=150)

Pathogen Category	Specific Organism	Frequency (n)	Percentage (%)
Gram-Negative (Total: 103, 68.7%)	Acinetobacter spp.	33	22.0
	Klebsiella pneumoniae	32	21.3
	Pseudomonas aeruginosa	15	10.0
	Morganella morganii	6	4.0
	Enterobacter spp.	6	4.0
	Other Gram-negative bacilli	11	7.3
Gram-Positive (Total: 47, 31.3%)	Staphylococcus aureus (MSSA)	22	14.7
	Staphylococcus aureus (MRSA)	14	9.3
	Enterococcus spp.	6	4.0
	Coagulase-negative Staph (CoNS)	4	2.7
	Unspecified Gram-positive cocci	1	0.7

[Table 2 and Figure 1] summarize the microbiology of the neonatal infections; Gram-negative bacilli clearly predominated, accounting for 68.7% of septic episodes, followed by Acinetobacter spp. (22.0%) and Klebsiella pneumoniae (21.3%), and 31.3% caused by Gram-positive cocci, primarily methicillin-sensitive Staphylococcus aureus (14.7%) and its methicillin-resistant counterpart (MRSA, 9.3%).

The high rate of antimicrobial resistance found in the SNCU is summarized in [Table 3]. Resistance to first-line empiric

therapies (aminoglycosides and cephalosporins) was high (71.8% and 53.4%, respectively) in Gram-negative organisms, and 33.0% of Gram-negative strains were carbapenem-resistant. Five Gram-negative isolates were pan-resistant (resistant to all tested therapeutic classes). Gram-positive pathogens also showed high levels of resistance to standard therapies but remained susceptible to reserve glycopeptides and oxazolidinones.

[Table 4] demonstrates the clinical manifestations and routine laboratory screening results of the infected neonates. The most significant clinical sign was respiratory distress (78.7% of the cohort), which requires close clinical attention. Biochemically, systemic inflammatory cascades were also evident, with 76.7% of the neonates testing positive for C-Reactive Protein and exactly two-thirds (66.7%) developing some degree of sepsis-induced thrombocytopenia.

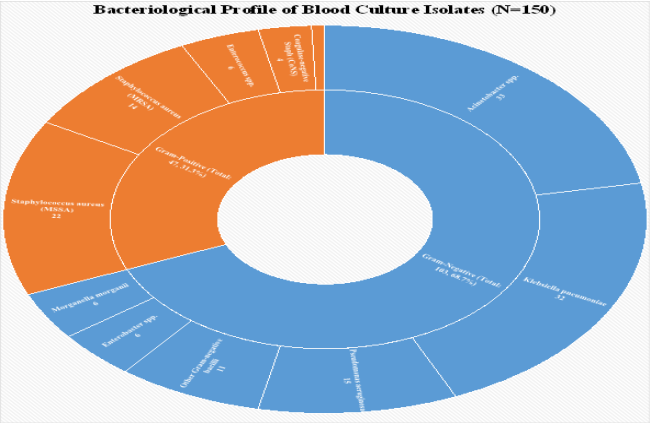

Figure 1: Bacteriological Profile of Blood Culture Isolates (N=150)

Table 3: Antimicrobial Resistance Patterns of Major Isolates (N=150)

Antibiotic Class	Gram-Negative Resistance (%)	Gram-Positive Resistance (%)
Aminoglycosides	71.8%	53.2%
Cephalosporins (e.g., Ceftriaxone)	53.4%	55.3%
Fluoroquinolones	46.6%	23.4%
Carbapenems	33.0%	6.4%
β-lactam + β-lactamase inhibitors	30.1%	53.2%
Glycopeptides (Vancomycin)	1.9%	8.5%
Pan-resistant isolates	4.9% (5 isolates)	0.0%

Table 4: Primary Clinical Presentation and Inflammatory Markers (N=150)

Parameter	Category	Frequency (n)	Percentage (%)
Clinical Presentation	Respiratory Distress	118	78.7
	Dehydration	18	12.0
	Seizures	13	8.7
	Septic Shock/Advanced Sepsis	9	6.0
Laboratory Screen	C-Reactive Protein (Positive)	115	76.7
	Thrombocytopenia (Mild to Severe)	100	66.7
	Leukocytosis (>30,000/µL)	43	28.7

Table 5: Clinical Outcomes Stratified by Birth Weight and Pathogen Class (N=150)

Variable	Survival (Discharged) n (%)	Mortality (Death) n (%)	Total (n)
Birth Weight			
ELBW (<1.0 kg)	11 (64.7%)	6 (35.3%)	17
VLBW (1.0–1.4 kg)	56 (78.9%)	15 (21.1%)	71
LBW (1.5–2.4 kg)	37 (80.4%)	9 (19.6%)	46
Normal (≥2.5 kg)	14 (87.5%)	2 (12.5%)	16
Organism Type			
Gram-Negative	77 (74.8%)	26 (25.2%)	103
Gram-Positive	41 (87.2%)	6 (12.8%)	47

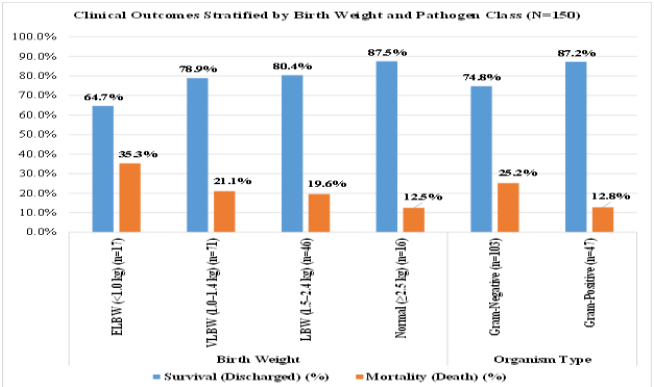

Figure 2: Clinical Outcomes Stratified by Birth Weight and Pathogen Class (N=150)

The clinical outcome metrics are shown on Table 5 and Figure 2. Mortality data for overall cohort were as follows: Overall, there was a significant inverse relationship between birth weight and mortality risk; ELBW infants had the highest case fatality rate at 35.3%. Moreover, survival depended strongly upon pathogen class: Gram-negative bacilli were associated with 26 of 32 deaths (81%) and group-specific mortality of 25.2%, compared to a lower but still significant Gram-positive infection-associated mortality risk of 12.8%; all infants infected by pan-resistant Klebsiella pneumoniae died from septic shock and multi-organ failure.

Discussion

This prospective cohort study describes the bacteriological

etiology, resistance profiles, and clinical course of neonatal sepsis at a high-volume tertiary center in central India, where the cohort was primarily made up of preterm (75.3%) and very low birth weight (47.3%) infants. The predominance of early-onset sepsis (65.3%) is consistent with physiological immune immaturity and perinatal risk factors.

The present study data show a clear predominance of Gram-negative pathogens (68.7%), with Acinetobacter spp. dominating the group. and Klebsiella pneumoniae. This bacterial distribution reflects the epidemiological changes observed in different regional analyses. Ahirwar et al. documented a similar prevalence of Gram-negative bacteria (50.5%), often isolating Klebsiella and coagulase-negative Staphylococci in Central India.[8] Similarly, Jyothi et al. identified Klebsiella and Acinetobacter as the predominant pathogens in North Karnataka.[9] On the contrary, Thakur et al. reported a 60% prevalence of Gram-positive bacteria in the sub-Himalayan region and stressed that the bacterial landscape is characterised by significant geographical diversity, which requires highly localised surveillance.[10]

The burden of antimicrobial resistance observed in this study is significant. Resistance to aminoglycosides and cephalosporins in Gram-negative isolates was greater than 70 and 50 percent, rendering traditional empirical regimens clinically obsolete. In Nepal, Klebsiella species showed massive resistance to standard therapies, with reserve antibiotics like colistin being the only remaining viable options, with comparable multi-resistance reported by Pokhrel et al.[11] A staggering 33% of our Gram-negative isolates were carbapenem-resistant, and 4.9% were completely pandrug-resistant. Isolation of pan-resistant Klebsiella pneumoniae, associated with 100% mortality, underscores an emergency in NICU infection control and reflects the MDR empiric failure warnings issued by Verma et al. regarding the devastating impact of MDR empiric failure.[12]

The most common clinical presentation was respiratory distress (78.7%), and the overall case fatality rate was 21.3%. Mortality was inversely related to birth weight, with the highest mortality in ELBW infants, and Gram-negative infections were more lethal than Gram-positive infections (25.2% vs 12.8% mortality).Mahich et al. also found the same prognostic markers, reporting far worse survival and higher complication rates in neonates with Gram-negative septicemia.[13] Similarly, Jatsho et al. also confirmed this, directly linking low APGAR scores, extreme prematurity, and highly resistant Gram-negative strains to severe septic shock and high mortality.[14]

Conclusion

Neonatal sepsis in this tertiary centre is mainly a condition of premature, low birth weight babies, driven mainly by Gram-negative bacteria resistant to multiple antibiotics, such as Acinetobacter and Klebsiella pneumoniae. The emergence of lethal pan-resistant strains, together with a 21.3 percent mortality rate, calls for an immediate clinical shift from unnecessary empirical regimens to targeted surveillance-based antimicrobial prescribing.

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Conflicts of interest

There are no conflicts of interest.

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