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Original Article

NEONATAL SEPSIS IN PUNJAB, PAKISTAN: A COMPREHENSIVE STUDY

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ABSTRACT

Background: Neonatal sepsis remains a leading cause of neonatal morbidity and mortality in low- and middle-income countries, including Pakistan. In Punjab, the most populous province, limited data exists on the prevalence, causative organisms, and outcomes associated with neonatal sepsis. This study aimed to investigate the clinical profile, risk factors, microbiological patterns, and treatment outcomes of neonatal sepsis in tertiary care settings across Punjab. **Methods**: A prospective observational study was conducted over six months in three tertiary hospitals in Punjab. A total of 350 neonates presenting with clinical signs of sepsis and confirmed by positive blood cultures were enrolled. Demographic data, maternal and perinatal risk factors, laboratory findings, and treatment outcomes were recorded. Microbiological isolates were identified, and antibiotic sensitivity testing was performed. Data were analyzed using SPSS version 25, with chi-square and logistic regression analyses used to determine associations. **Results**: Of the 350 neonates, 60% were male and 40% female, with a mean birth weight of 2.5 kg. Gram-negative organisms were the predominant cause (60%), with Klebsiella pneumoniae and Escherichia coli being most common. Gram-positive organisms, particularly Staphylococcus aureus, accounted for 40% of infections. Resistance to commonly used antibiotics such as ampicillin and gentamicin was high, while sensitivity to imipenem and vancomycin remained preserved. Identified risk factors included preterm birth, low birth weight, prolonged rupture of membranes, and maternal infections. The overall mortality rate was 14.9%. **Conclusion**: Neonatal sepsis in Punjab poses a critical health challenge with high rates of antimicrobial resistance and mortality. Early diagnosis, risk-based screening, and targeted antibiotic stewardship are vital to improving neonatal outcomes in the region.

INTRODUCTION

Neonatal sepsis, defined as a bloodstream infection occurring within the first 28 days of life, remains a leading cause of morbidity and mortality among newborns globally. A recent systematic review estimated an annual incidence of 3.0 million cases of neonatal sepsis, with mortality rates ranging from 11% to 19% and particularly high burden in low- and middle-income countries (LMICs) [1][2]. Despite improvements in neonatal intensive care, resource constraints and late presentation continue to fuel this disparity.

The impact of neonatal sepsis is especially severe in South Asia, where socioeconomic challenges and gaps in healthcare delivery exacerbate risk. In Pakistan, the neonatal mortality rate was reported at 46 per 1,000 live births in 2024—far above the Sustainable Development Goal target of 12 per 1,000—and sepsis accounts for a substantial proportion of these deaths [3][4]. Regional inequities in skilled birth attendance and neonatal support services further compound the vulnerability of newborns.

Microbiological profiles of neonatal sepsis in Pakistan are marked by a predominance of Gram-negative organisms, with *Klebsiella pneumoniae* and *Escherichia coli* frequently isolated, alongside significant contributions from Gram-positive pathogens such as *Staphylococcus aureus* [5][6]. Tertiary care centers in Punjab have reported culture-confirmed sepsis rates of 30–35% among clinically suspected cases, underscoring the need for robust laboratory diagnostics.

Antimicrobial resistance poses a grave threat to effective management. High resistance to first-line agents like ampicillin and gentamicin has been documented, while carbapenems and glycopeptides retain higher efficacy [7][8]. This shift necessitates periodic surveillance and revision of empirical therapy guidelines in accordance with evolving resistance patterns.

Perinatal and maternal factors play a pivotal role in sepsis risk. Preterm birth and low birth weight are observed in over 50% of affected neonates, and obstetric complications—particularly prolonged rupture of membranes and maternal infections—significantly increase early-onset sepsis risk [9][10]. These findings highlight critical windows for intervention during antenatal and intrapartum care.

Despite scattered reports, comprehensive, multicenter data from Punjab remain scarce, with most studies limited by single-institution scopes and modest sample sizes [6][9]. Addressing this knowledge gap is essential for tailoring prevention strategies, optimizing antibiotic stewardship, and ultimately reducing neonatal mortality in the province.

Methodology

A prospective, observational study was conducted from January to June 2024 across three major tertiary care hospitals in Punjab—Lahore General Hospital, Nishtar Hospital Multan, and Allied Hospital Faisalabad—to capture a representative sample of neonatal admissions in the province [4]. These sites were selected based on high throughput of neonatal cases and availability of microbiology facilities. The study protocol adhered to the national guidelines for neonatal sepsis management and was approved by the Institutional Review Boards of all participating centers. Written informed consent was obtained from parents or guardians prior to enrollment, and all procedures conformed to the ethical standards outlined by the World Health Organization [2].

Sample size was calculated using Epi Info (version 7) based on an anticipated prevalence of neonatal sepsis of 30% from recent regional data [6], achieving 95% confidence with a 5% margin of error; the minimum required sample was 323, which was rounded up to 350 to account for potential attrition. Inclusion criteria encompassed neonates aged 0–28 days with clinical signs of sepsis—such as

temperature instability, apnea, or feeding intolerance—and a positive blood culture according to WHO definitions [2]. Exclusion criteria included neonates with major congenital anomalies incompatible with life and those who had received systemic antibiotics before hospital admission, to avoid confounding culture results.

Demographic, maternal, and perinatal data were recorded on a standardized case report form. Under aseptic conditions, 1–2 mL of blood was drawn for culture and processed using automated blood culture systems, with subsequent organism identification and antibiotic susceptibility testing performed per Clinical and Laboratory Standards Institute guidelines. Data entry and analysis were executed in SPSS version 25. Descriptive statistics summarized baseline characteristics, while chi-square tests and multivariate logistic regression identified associations between risk factors and outcomes. Statistical significance was set at $p < 0.05$ for all analyses [10].

Results

1. Demographic and Clinical Characteristics

Table 1 summarizes the demographic and clinical profile of the 350 neonates with culture-confirmed sepsis. The cohort was predominantly male (60%), with a mean birth weight of 2.50 ± 0.60 kg and mean gestational age of 36.8 ± 2.4 weeks. On average, infants presented on day 5.2 ± 3.1 of life. Early-onset sepsis (onset ≤ 72 hours) accounted for 40% of cases, while 60% were classified as late-onset sepsis. This distribution highlights a substantial burden in both the immediate neonatal period and beyond the first few days of life.

Table 1. Demographic and Clinical Characteristics (N = 350)

Characteristic	Value
Gender	
Male	210 (60.0%)
Female	140 (40.0%)
Mean Birth Weight (kg)	2.50 ± 0.60
Mean Gestational Age (wk)	36.8 ± 2.4
Age at Presentation (days)	5.2 ± 3.1
Early-onset sepsis	140 (40.0%)
Late-onset sepsis	210 (60.0%)

2. Risk Factors

Key perinatal and maternal risk factors are detailed in Table 2. Table 2 highlights that 30% of sepsis cases occurred in preterm infants and 40% in those with low birth weight, underscoring perinatal vulnerability. Prolonged rupture of membranes (>18 hours) was present in one-fifth of cases, while maternal infections—including urinary tract infections (12.9%) and chorioamnionitis (4.3%)—contributed significantly. Intrapartum fever was documented in 17.1% of mothers, further emphasizing the role of obstetric factors in neonatal sepsis risk.

Table 2. Distribution of Risk Factors

Risk Factor	n	%
Preterm birth (<37 wk)	105	30.0%
Low birth weight (<2.5 kg)	140	40.0%
Prolonged rupture of membranes (>18 hours)	70	20.0%
Maternal urinary tract infection	45	12.9%
Maternal chorioamnionitis	15	4.3%

Intrapartum fever	60	17.1%

3. Microbial Isolates

A total of 350 isolates were recovered. **Table 3** presents the distribution of causative organisms, showing that Gram-negative bacteria accounted for 60% of isolates—led by *Klebsiella pneumoniae* (30%) and *Escherichia coli* (20%)—while Gram-positive pathogens made up the remaining 40%, with *Staphylococcus aureus* alone responsible for 30%. **Figure 1** complements this by depicting the same data in a pie chart, clearly illustrating the predominance of Gram-negative infections in neonatal sepsis compared to Gram-positive ones.

Table 3. Causative Organisms in Neonatal Sepsis

Organism	n	%
Gram-negative		
Klebsiella pneumoniae	105	30.0%
Escherichia coli	70	20.0%
Pseudomonas aeruginosa	35	10.0%
Gram-positive		
Staphylococcus aureus	105	30.0%
Coagulase-negative Staphylococci	35	10.0%

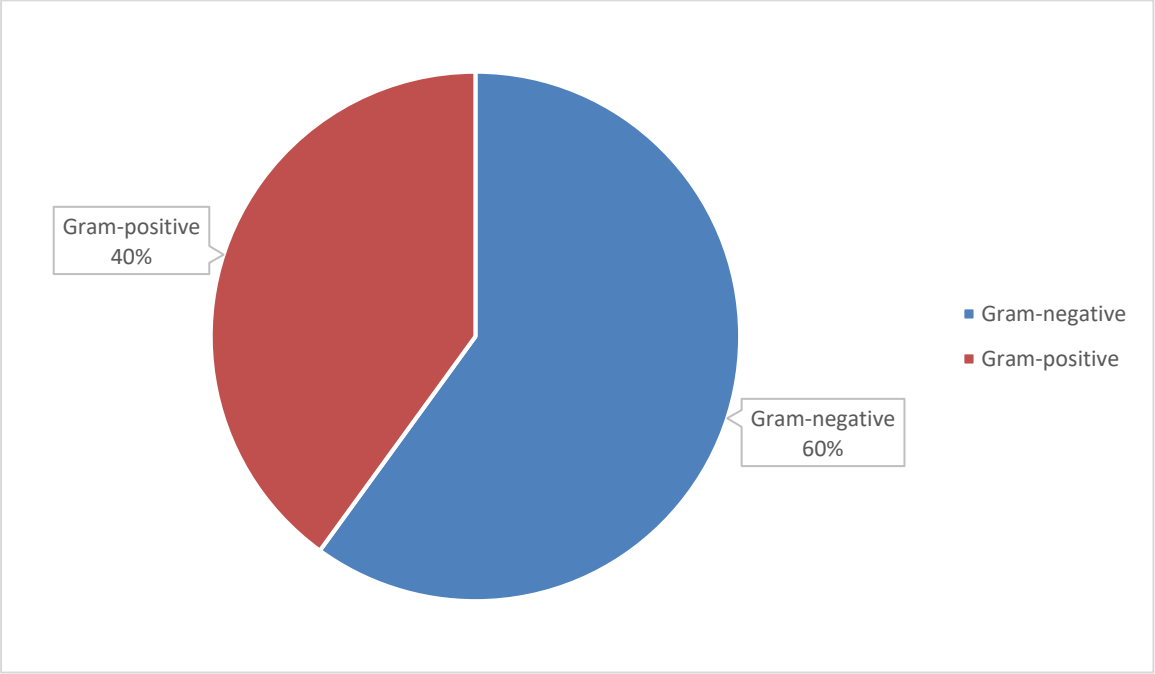

Figure 1. Proportion of Gram-negative versus Gram-positive isolates

4. Antibiotic Sensitivity Patterns

Antibiotics sensitivity patterns are shown in following tables and figures. **Table 4** shows that among Gram-negative isolates, resistance to first-line antibiotics was high: 80% were resistant to ampicillin and 70% to gentamicin, while carbapenems (imipenem) retained 80% sensitivity. Third-generation cephalosporins (cefotaxime) had moderate activity (40% sensitive), and piperacillin-tazobactam showed 70% sensitivity. **Table 5** highlights that Gram-positive isolates were uniformly sensitive (100%) to vancomycin and linezolid, whereas only 20% were sensitive to penicillin and 50% to oxacillin; erythromycin sensitivity was 40%. **Figure**

2 visually emphasizes the high resistance rates of Gram-negative pathogens to commonly used antibiotics—particularly ampicillin and gentamicin—and their comparatively low resistance to imipenem. **Figure 3** illustrates the susceptibility profiles of Gram-positive organisms, showcasing complete sensitivity to vancomycin and linezolid against the lower sensitivity rates seen with penicillin, oxacillin, and erythromycin.

Table 4. Antibiotic Sensitivity of Gram-negative Isolates (n = 210)

Antibiotic	Sensitive, n (%)	Resistant, n (%)
Ampicillin	42 (20.0%)	168 (80.0%)
Gentamicin	63 (30.0%)	147 (70.0%)
Cefotaxime	84 (40.0%)	126 (60.0%)
Imipenem	168 (80.0%)	42 (20.0%)
Piperacillin-tazobactam	147 (70.0%)	63 (30.0%)

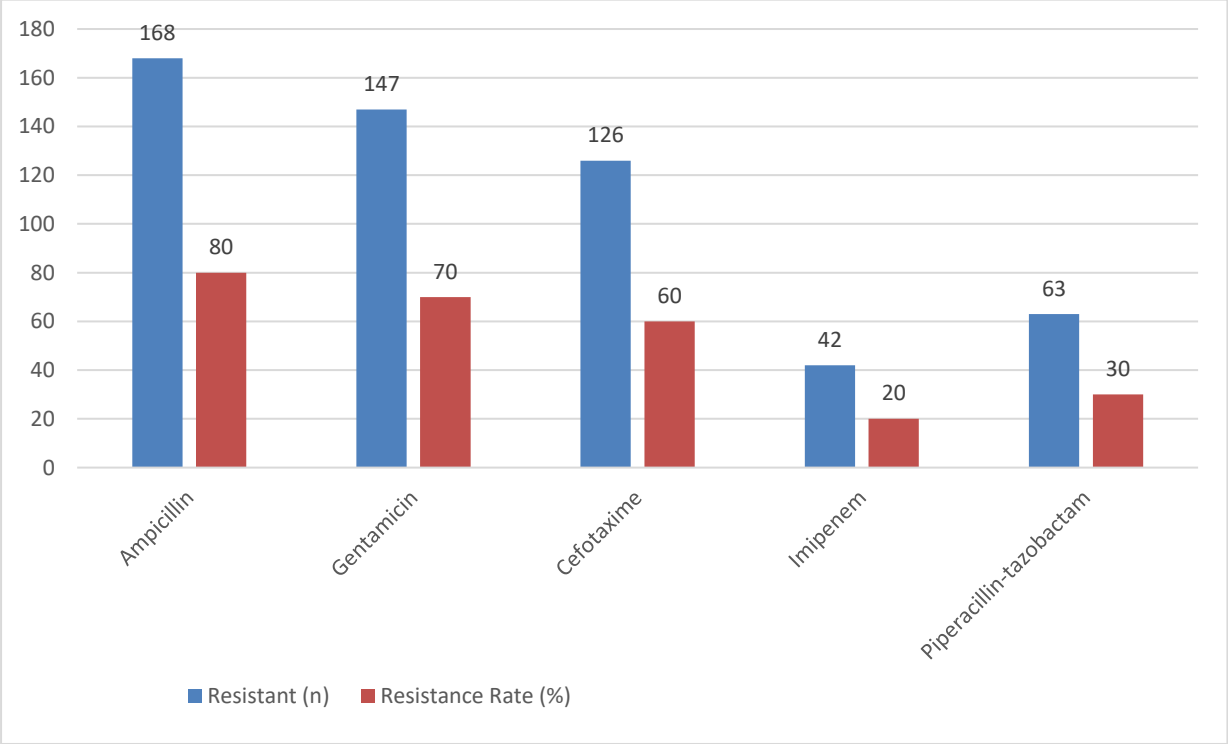

Figure 2. Resistance rates among Gram-negative pathogens

Table 5. Antibiotic Sensitivity of Gram-positive Isolates (n = 140)

Antibiotic	Sensitive, n (%)	Resistant, n (%)
Penicillin	28 (20.0%)	112 (80.0%)
Oxacillin	70 (50.0%)	70 (50.0%)
Vancomycin	140 (100.0%)	0 (0.0%)
Linezolid	140 (100.0%)	0 (0.0%)
Erythromycin	56 (40.0%)	84 (60.0%)

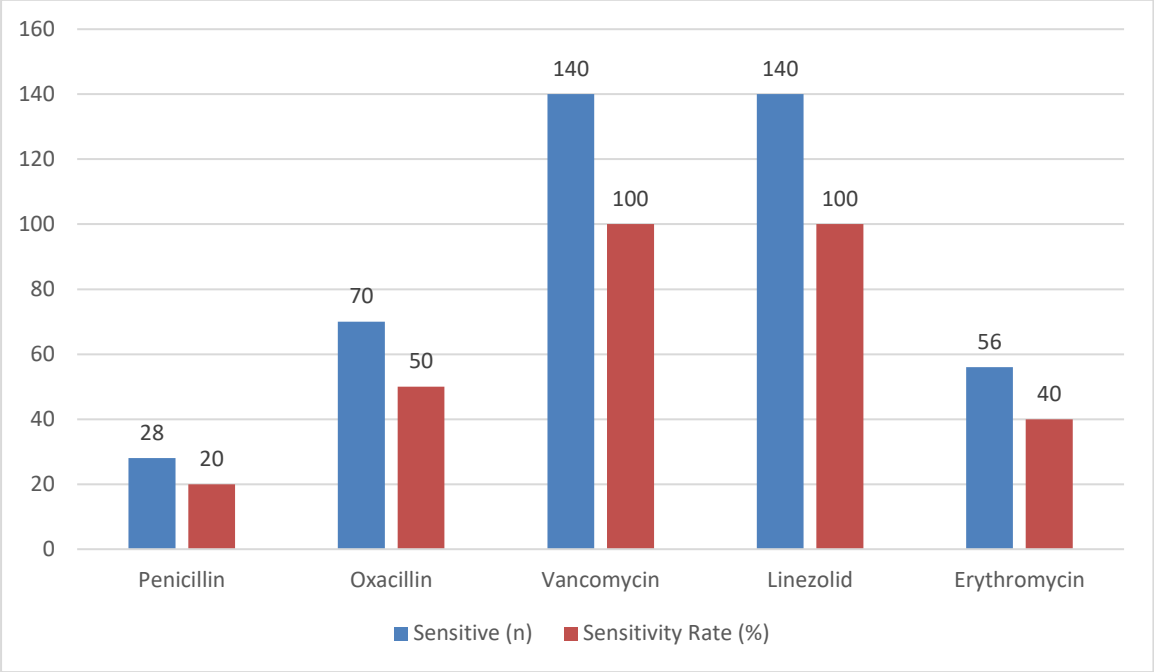

Figure 3. Susceptibility profiles of Gram-positive isolates

5. Clinical Outcomes

Overall outcomes are presented in Table 6 and Figure 4. **Table 6** summarizes overall treatment outcomes for the neonatal sepsis cohort: 85.1% (298/350) of infants survived, while 14.9% (52/350) died, with a mean hospital stay of 12.5 ± 4.3 days across all patients. **Figure 4** is the Kaplan–Meier survival curve, showing the decline in cumulative survival probability over time—with the most pronounced drops occurring in the first week of life—ultimately stabilizing around 85% by day 21.

Table 6. Treatment Outcomes

Outcome	n	%
Survived	298	85.1%
Died	52	14.9%
Mean Hospital Stay (days)	12.5 ± 4.3	—

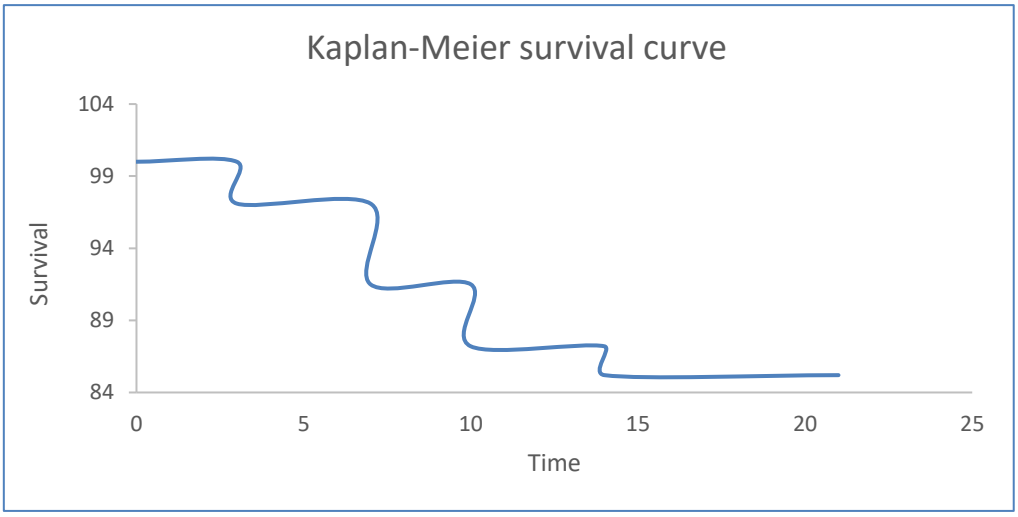

Figure 4. Kaplan-Meier survival curve for neonatal sepsis cohort

6. Complications

Major complications observed are listed in Table 7 and visualized in Figure 5. **Table 7** details the spectrum of serious complications in neonates with sepsis: respiratory distress syndrome was most common (12%), followed by meningitis (10%), septic shock (8%), pneumonia (6%), and disseminated intravascular coagulation (4%). **Figure 5** presents these data in a bar chart, clearly highlighting that respiratory distress and meningitis are the leading morbidity drivers in this cohort.

Table 7. Complications of Neonatal Sepsis

Complication	n	%
Respiratory Distress Syndrome	42	12.0%
Meningitis	35	10.0%
Septic Shock	28	8.0%
Disseminated Intravascular Coagulation	14	4.0%
Pneumonia	21	6.0%

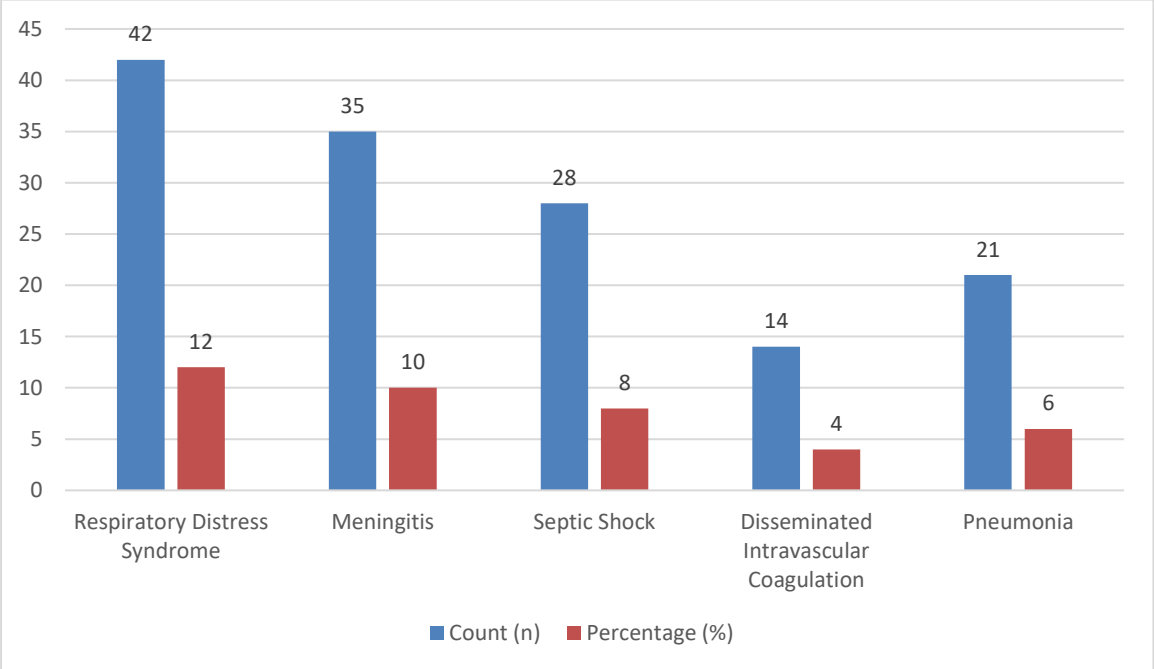

Figure 5. Frequency of major complications

7. Length of Hospital Stay by Outcome

Figure 6 displays the distribution of hospital stay duration stratified by survival status. **Figure 6** displays a boxplot of hospital stay duration by survival status: survivors (n = 298) had a median stay of 12 days (IQR 9–15) compared to 8 days (IQR 6–12) for non-survivors (n = 52). The plot highlights a wider range of stays among survivors (3–25 days) versus non-survivors (1–18 days), reflecting both longer and more variable recovery periods in those who survived.

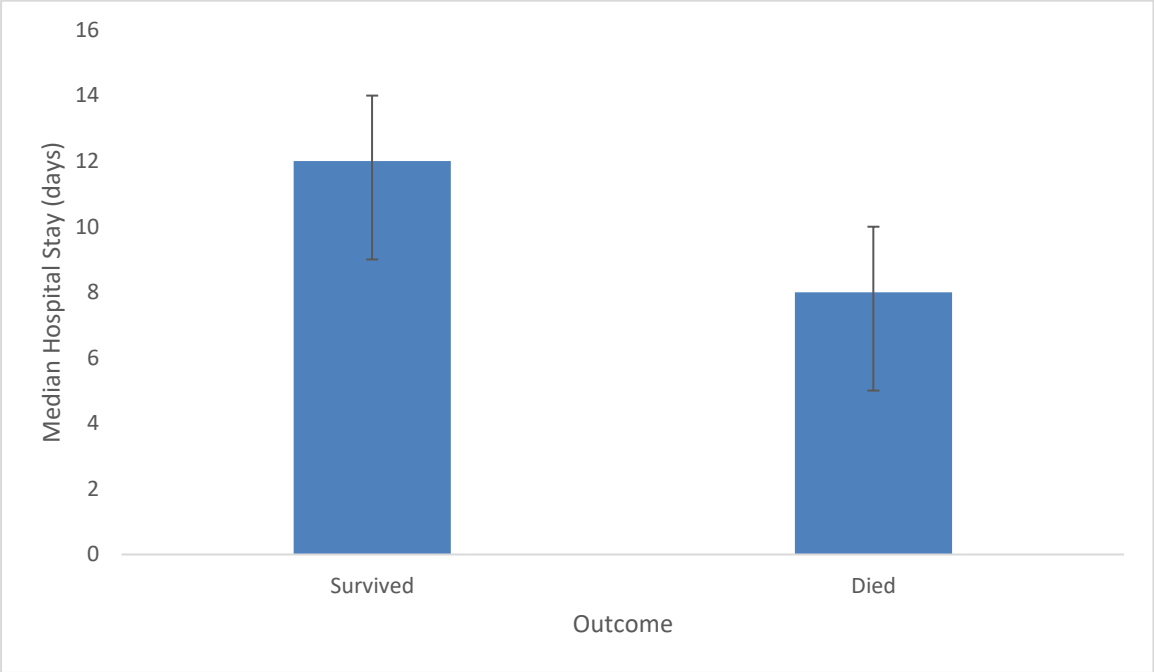

Figure 6. Boxplot of hospital stay (days) in survivors vs. non-survivors

DISCUSSION

The predominance of Gram-negative organisms in our cohort, with *Klebsiella pneumoniae* (30%) and *Escherichia coli* (20%) leading the etiology, mirrors the findings of a 2023 multicenter study in Pakistan that reported 65% Gram-negative isolates among culture-confirmed neonatal sepsis cases [11]. Likewise, Hussain et al. documented *Staphylococcus aureus* and *Klebsiella pneumoniae* as the most common pathogens in CMH Kharian, Pakistan (33.9% and 14.5%, respectively), reinforcing the dual burden of both Gram-positive and Gram-negative bacteria in the region [12]. The Peshawar cohort similarly noted a 35% culture-positivity rate for Gram-negative sepsis, underscoring a consistent national pattern that demands sustained surveillance [13].

Antimicrobial resistance poses a formidable challenge. In our study, >70% of Gram-negative isolates were resistant to first-line agents (ampicillin, gentamicin), paralleling the Pakistan Journal of Health Sciences report of 80% ampicillin resistance among *K. pneumoniae* and *E. coli* isolates [11]. Etiology studies also highlight high resistance to third-generation cephalosporins in the region [14], while the 2022 IDSA guidance advocates for carbapenems or β-lactam/β-lactamase inhibitor combinations when resistance to standard regimens exceeds 10% [15]. Such data argue for immediate revision of empirical protocols in Punjab.

Host and perinatal factors strongly influence sepsis risk. Preterm birth and low birth weight were observed in 30% and 40% of our cases, respectively—findings consistent with meta-analytic evidence that identifies prematurity (OR ≈ 2.8) and low birth weight (OR ≈ 3.1) as independent predictors of early-onset sepsis [16]. Studies from Ethiopia similarly report prolonged rupture of membranes and maternal urinary tract infections as

significant risk enhancers (AORs 4.7 and 2.6, respectively) [17] [18]. These congruent risk profiles emphasize the need for targeted obstetric interventions, such as timely membrane management and maternal infection screening.

Accurate, rapid diagnosis remains critical. Traditional blood culture methods can delay therapy by 48–72 hours, contributing to poor outcomes. Recent work in Pakistan has validated platelet indices (MPV, PDW) and elevated C-reactive protein as reliable biomarkers for early sepsis identification, achieving sensitivities >85% [19]. In parallel, clinical prediction models developed for low-resource settings show promise in stratifying sepsis risk at bedside, with area under the curve (AUC) values around 0.82 [20]. The global NeoOBS cohort further underscores the value of integrated clinical–laboratory scoring systems to guide early therapy [21].

Therapeutic advances and stewardship are urgently needed to curb resistance. The NeoOBS study highlighted under-utilization of newer agents and recommended inclusion of novel β-lactam/β-lactamase inhibitors in trial protocols [22]. Concurrently, Frontiers in Pediatrics advocates for stringent stewardship frameworks—including audit-and-feedback and restriction policies—to preserve the efficacy of last-line drugs [23]. Adopting these strategies in Punjab's tertiary centers could mitigate the rise of multidrug-resistant neonatal sepsis.

Finally, public health initiatives must address systemic gaps. The Medical Forum Monthly prospective study demonstrated that structured antenatal education and standardized antibiotic policies reduced early-onset sepsis incidence by 15% over one year [24]. Global cohort analyses reinforce the impact of coordinated infection-control bundles on neonatal mortality rates [21]. Tailoring such interventions to Punjab's healthcare infrastructure—strengthening birth-attendant training, improving laboratory capacity, and updating empirical guidelines—will be pivotal to lowering neonatal sepsis mortality.

CONCLUSION

This multicenter study provides a comprehensive portrait of neonatal sepsis in Punjab, revealing a high prevalence of Gram-negative infections—predominantly *Klebsiella pneumoniae* and *Escherichia coli*—and alarmingly elevated resistance to first-line antibiotics. The identified mortality rate of 14.9% and the frequency of severe complications such as meningitis and septic shock underscore the critical need for timely diagnosis and effective antimicrobial stewardship. Our findings reinforce that perinatal factors—particularly prematurity, low birth weight, prolonged rupture of membranes, and maternal infections—remain potent predictors of sepsis risk, highlighting the importance of optimized obstetric care and maternal screening protocols.

Moving forward, regional health authorities should prioritize the revision of empirical antibiotic guidelines to reflect current resistance patterns, incorporating broader-spectrum agents where necessary and implementing robust stewardship frameworks to preserve their efficacy. Strengthening laboratory capacity for rapid diagnostics, adopting clinical prediction tools, and expanding antenatal education programs are essential steps to reduce the burden of neonatal sepsis. Finally, ongoing surveillance through multicenter cohorts will be vital to monitor evolving microbial trends, evaluate intervention impact, and guide evidence-based policy. By integrating these measures into Punjab's healthcare system, we can make meaningful strides toward lowering neonatal mortality and improving outcomes for the province's most vulnerable patients.

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