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(RESEARCH ARTICLE)

ASSOCIATION OF PRETERM LOW BIRTH WEIGHT WITH BLOOD CULTURE POSITIVITY AND ANTIMICROBIAL SENSITIVITY PATTERNS IN NEONATES WITH CLINICALLY SUSPECTED SEPSIS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Neonatal sepsis is a leading cause of neonatal morbidity and mortality in low- and middle-income countries. Prematurity and low birth weight (LBW) are recognized risk factors for invasive infection, but their combined effect on blood culture positivity and the antimicrobial sensitivity of the causative organisms is incompletely characterized in this setting.

Objective: To determine the association between preterm LBW and blood culture positivity in neonates with clinically suspected sepsis, and to describe the bacterial profile and antimicrobial sensitivity patterns of the isolated organisms.

Methods: This cross-sectional analytical study enrolled 180 neonates with clinically suspected sepsis admitted to the neonatal unit of Dhaka Central International Medical College & Hospital, Dhaka, Bangladesh over 12 months. Under aseptic precautions, 1–2 mL of blood was collected before antibiotic administration and processed by aerobic culture; organism identification and antimicrobial susceptibility testing were performed by the modified Kirby–Bauer disc-diffusion method interpreted per CLSI guidelines. Data were analyzed in SPSS v27; the chi-square test and odds ratios (OR) with 95% confidence intervals (CI) were used, with $p < 0.05$ taken as significant.

Results: Blood culture was positive in 54/180 (30.0%) neonates. Positivity was significantly higher among preterm LBW neonates than among term normal-birth-weight neonates (39.6% vs 19.0%; OR 2.78, 95% CI 1.42–5.47; p = 0.003). Gram-negative organisms predominated (72.2%), led by Klebsiella pneumoniae (29.6%), Acinetobacter spp. (16.7%) and Escherichia coli (14.8%). Gram-negative isolates were largely resistant to ampicillin and third-generation cephalosporins but retained sensitivity to carbapenems and colistin; gram-positive isolates were uniformly sensitive to vancomycin and linezolid.

Conclusion: Preterm LBW is significantly associated with a higher rate of blood culture positivity in neonatal sepsis. The predominance of multidrug-resistant gram-negative organisms underscores the need for local antibiogram-guided empirical therapy and strengthened antimicrobial stewardship.

Keywords: Neonatal sepsis; Preterm; Low birth weight; Blood culture; Antimicrobial sensitivity; Klebsiella pneumoniae.

1 INTRODUCTION

Neonatal sepsis remains a critical contributor to morbidity and mortality among infants born with low birth weight, necessitating precise diagnostic accuracy to guide timely clinical interventions (1). While blood culture remains the gold standard for diagnosis, the sensitivity of this method is frequently constrained in preterm populations due to low initial bacteremia levels and the prior administration of empiric antimicrobial therapy (2). Furthermore, the frequent occurrence of gut dysbiosis in very-low-birth-weight infants may facilitate bacterial translocation, potentially altering the microbial profile identified in bloodstream infections (3). Despite these physiological challenges, preterm infants continue to experience high rates of both early- and late-onset sepsis, necessitating a rigorous evaluation of how gestational maturity influences pathogen recovery from standard diagnostic protocols (4). This diagnostic limitation is further compounded by the high prevalence of health care–associated infections, which often require robust surveillance to differentiate from transient or contamination-related findings (5). Specifically, the diagnostic yield in this vulnerable cohort is often limited by the minimal blood volumes typically drawn from smaller neonates, which significantly diminishes the likelihood of pathogen detection (6). Consequently, the threshold for defining systemic infection in extremely-low-birth-weight infants often necessitates a reliance on secondary inflammatory biomarkers to augment the limited sensitivity of conventional microbiological analysis (7,8). This diagnostic gap is particularly pronounced in resource-limited settings, where the challenge of accurately identifying causative organisms is exacerbated by variable access to advanced diagnostic infrastructure (9). This study aims to evaluate the correlation between preterm low birth weight and the sensitivity of blood cultures, providing a critical analysis of diagnostic accuracy within neonatal intensive care settings (10). By examining the discordance between culture-negative clinical presentations and underlying systemic inflammatory responses, we seek to elucidate how immature immune function and anatomical factors inherent to preterm infants impede reliable microbiological confirmation (11,12). Specifically, we investigate whether the volume-dependent limitations of automated culture systems contribute to a disproportionate rate of false-negative results in infants weighing less than 1,500 grams compared to their more mature counterparts (13,14). Given that the recovery of pathogens is inherently restricted by the limited total blood volume attainable from these infants, the diagnostic sensitivity is further challenged by age-dependent variations in immune maturity and the rapid onset of sepsis characteristics in the preterm population (15). Moreover, the current reliance on conventional blood cultures often leads to a high frequency of "culture-negative" sepsis, which complicates clinical decision-making regarding the initiation and duration of antimicrobial therapy (16,17). In these instances, over half of septic newborns exhibit low-colony count bacteremia, with up to 60% of samples yielding falsely negative results due to insufficient blood volumes (18). Such constraints necessitate a critical reassessment of current diagnostic protocols, as the long incubation times and limited sensitivity of these cultures frequently delay the discontinuation of unnecessary empirical antibiotics (19,20). To mitigate these limitations, research is increasingly focusing on the integration of specific biomarkers, such as procalcitonin and interleukin-6, which may offer higher positive predictive values during the early stages of disease progression (21,22).

2 MATERIAL AND METHODS

2.1 Study design and setting

This was a hospital-based cross-sectional analytical study conducted in the neonatal ward / neonatal intensive care unit (NICU) in collaboration with the Department of Microbiology of Dhaka Central International Medical College & Hospital, Dhaka, Bangladesh.

2.2 Study period

The study was carried out over a period of 12 months, from Month Year to Month Year.

2.3 Study population and eligibility

Neonates (0–28 days of age) admitted with clinically suspected sepsis during the study period were considered for enrolment. Inclusion criteria: neonates with clinically suspected sepsis (presence of recognised clinical features and/or a positive sepsis screen) whose guardians provided informed written consent, and in whom blood for culture was drawn before initiation of antibiotics. Exclusion criteria: neonates with major congenital malformations, those who had already received antibiotics before blood sampling, samples with evidence of gross contamination, and cases where consent was declined.

2.4 Sample size

The sample size was estimated using the formula for a single proportion, $n = Z^2pq / d^2$, where Z = 1.96 (95% confidence level), p = expected proportion of culture-positive sepsis taken from a previous study (p = 0.30), q = 1 − p, and d = absolute precision (0.07). The calculated minimum sample size was ≈165; a total of 180 neonates were finally enrolled by consecutive sampling.

2.5 Operational definitions

Neonate: an infant aged 0–28 completed days. Preterm: gestational age < 37 completed weeks (assessed from the last menstrual period and/or the New Ballard Score). Low birth weight (LBW): birth weight < 2500 g. Preterm LBW: a neonate who is both preterm and low birth weight; the comparison group comprised term neonates of normal birth weight (≥ 2500 g). Clinically suspected sepsis: presence of one or more clinical features (e.g., lethargy, poor feeding, temperature instability, respiratory distress, apnoea) supported by the perinatal history and/or sepsis screen. Early-onset sepsis: onset < 72 hours of life; late-onset sepsis: onset ≥ 72 hours. Culture-proven sepsis: growth of a recognised pathogen on blood culture.

2.6 Data collection

Relevant maternal and neonatal variables (sex, gestational age, birth weight, mode of delivery, age at onset, and perinatal risk factors) were recorded on a pre-tested structured proforma by direct examination and from clinical records.

2.7 Blood culture and antimicrobial susceptibility testing

Under strict aseptic precautions, 1–2 mL of venous blood was collected before the administration of antibiotics and inoculated into paediatric blood-culture medium (conventional brain–heart-infusion broth / automated BACT/ALERT bottle). Cultures were incubated at 37 °C and monitored for up to 7 days. Subcultures were made on blood agar and MacConkey agar; isolates were identified by colony morphology, Gram staining and standard biochemical reactions (or an automated identification system). Antimicrobial susceptibility testing was performed by the modified Kirby–Bauer disc-diffusion method on Mueller–Hinton agar, and results were interpreted according to the current Clinical and Laboratory Standards Institute (CLSI) breakpoints. Appropriate reference strains were used for quality control.

2.8 Statistical analysis

Data were compiled and analysed using SPSS (version 27.0). Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. The chi-square test (or Fisher's exact test where expected cell counts were small) was used to test associations between neonatal characteristics and blood culture positivity. Odds ratios with 95% confidence intervals were calculated to quantify the strength of association. A p-value < 0.05 was considered statistically significant.

2.9 Ethical considerations

The study protocol was approved by the Institutional Ethical Review Committee of institution (approval no. IRB/DCIMC/8/2026). Informed written consent was obtained from a parent or legal guardian of each neonate. Confidentiality of all records was maintained, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

3 RESULTS

A total of 180 neonates with clinically suspected sepsis were studied. Males accounted for 104 (57.8%) and females for 76 (42.2%). 108 (60.0%) neonates were preterm and 114 (63.3%)were of low birth weight; 96 (53.3%) were both preterm and low birth weight. Early-onset sepsis was recorded in 122 (67.8%) and late-onset in 58 (32.2%) neonates. The baseline characteristics of the study population are summarised in Table 1.

Table 1: Baseline characteristics of the study neonates (N = 180).

Characteristic	Frequency (n)	Percentage (%)
Sex		
Male	104	57.8
Female	76	42.2
Gestational age		
Preterm (< 37 weeks)	108	60.0
Term (≥ 37 weeks)	72	40.0
Birth weight		
Low birth weight (< 2500 g)	114	63.3
Normal (≥ 2500 g)	66	36.7
Preterm LBW status		
Preterm and LBW	96	53.3
Term, normal birth weight	84	46.7
Age at onset		
Early-onset (< 72 h)	122	67.8
Late-onset (≥ 72 h)	58	32.2
Mode of delivery		
Vaginal	98	54.4
Caesarean section	82	45.6
Perinatal risk factors		
Prolonged rupture of membranes (> 18 h)	46	25.6
Maternal fever / urinary tract infection	34	18.9
Perinatal asphyxia	30	16.7
Prolonged / obstructed labour	28	15.6

LBW, low birth weight. Categories may overlap for perinatal risk factors.

Overall, blood culture was positive in 54 of 180 (30.0%) neonates. Culture positivity increased with decreasing gestational age and birth weight and was highest in neonates who were both preterm and low birth weight. Preterm LBW neonates had a significantly higher positivity rate than term normal-birth-weight neonates (39.6% vs 19.0%; OR 2.78, 95% CI 1.42–5.47; p = 0.003). Positivity was also higher with preterm status and with low birth weight individually, and among late-onset cases, whereas sex showed no significant association (Table 2).

Table 2: Association of neonatal characteristics with blood culture positivity (N = 180).

Variable	Total (n)	Culture positive, n (%)	OR (95% CI)	p-value
Preterm LBW status				
Preterm and LBW	96	38 (39.6)	2.78 (1.42–5.47)	0.003
Term, normal weight (ref.)	84	16 (19.0)	1.00	—
Gestational age				
Preterm (< 37 wk)	108	40 (37.0)	2.44 (1.21–4.90)	0.011
Term (ref.)	72	14 (19.4)	1.00	—
Birth weight				

LBW (< 2500 g)	114	42 (36.8)	2.63 (1.26–5.46)	0.008
Normal (ref.)	66	12 (18.2)	1.00	—
Age at onset				
Late-onset (≥ 72 h)	58	24 (41.4)	2.16 (1.11–4.20)	0.021
Early-onset (ref.)	122	30 (24.6)	1.00	—
Sex				
Male	104	33 (31.7)	1.22 (0.64–2.33)	0.545
Female (ref.)	76	21 (27.6)	1.00	—

OR, odds ratio; CI, confidence interval; LBW, low birth weight; ref., reference category. p-values from chi-square test.

Among the 54 positive cultures, gram-negative bacteria predominated, accounting for 39 (72.2%) isolates, followed by gram-positive bacteria 13 (24.1%) and Candida species 2 (3.7%). Klebsiella pneumoniae was the single most common isolate, followed by Acinetobacter species and Escherichia coli. Among gram-positive organisms, coagulase-negative staphylococci and Staphylococcus aureus were most frequent (Table 3).

Table 3: Distribution of organisms isolated from blood culture (n = 54 isolates).

Organism	Number (n)	Percentage (%)
Gram-negative bacteria	**39**	**72.2**
Klebsiella pneumoniae	16	29.6
Acinetobacter spp.	9	16.7
Escherichia coli	8	14.8
Enterobacter spp.	3	5.6
Pseudomonas spp.	3	5.6
Gram-positive bacteria	**13**	**24.1**
Coagulase-negative staphylococci	8	14.8
Staphylococcus aureus	5	9.3
Fungi	**2**	**3.7**
Candida spp.	2	3.7
Total	**54**	**100.0**

The antimicrobial sensitivity patterns of the gram-negative isolates are shown in Table 4. Most gram-negative organisms were highly resistant to ampicillin, amoxicillin–clavulanate and the third-generation cephalosporins, and showed reduced sensitivity to gentamicin. Higher sensitivity was retained to amikacin, piperacillin–tazobactam, and especially to the carbapenems (meropenem, imipenem) and colistin. Gram-positive isolates (Table 5) were poorly sensitive to penicillin but uniformly sensitive to vancomycin and linezolid.

Table 4: Antimicrobial sensitivity of major gram-negative isolates (% sensitive).

Antibiotic	K. pneumoniae (n=16)	Acinetobacter (n=9)	E. coli (n=8)	Overall GN (n=39)
Ampicillin	6	0	13	6
Amoxicillin–clavulanate	19	11	25	18
Ceftriaxone	13	11	25	15
Ceftazidime	19	11	25	18
Cefepime	25	22	38	28
Gentamicin	25	22	38	28

Amikacin	63	56	75	64
Ciprofloxacin	38	33	63	44
Piperacillin–tazobactam	56	44	75	59
Meropenem	81	78	88	82
Imipenem	88	78	88	85
Colistin	100	100	88	97

GN, gram-negative. Values are percentages of isolates testing sensitive by disc diffusion (CLSI).

Table 5: Antimicrobial sensitivity of gram-positive isolates (% sensitive).

Antibiotic	CoNS (n=8)	S. aureus (n=5)	Overall GP (n=13)
Penicillin	13	20	15
Cefoxitin / oxacillin	38	40	38
Gentamicin	50	60	54
Ciprofloxacin	50	60	54
Amikacin	63	60	62
Cotrimoxazole	38	40	38
Vancomycin	100	100	100
Linezolid	100	100	100

CoNS, coagulase-negative staphylococci; GP, gram-positive.

4 DISCUSSION

In this study of neonates with clinically suspected sepsis, blood culture was positive in 30.0% of cases, and positivity was significantly greater among neonates who were both preterm and of low birth weight than among term neonates of normal birth weight. This overall positivity rate is consistent with the range reported from other tertiary centres in Bangladesh and the wider South Asian region, where culture-positive proportions have varied broadly depending on case definitions, blood volume, culture technique and prior antibiotic exposure (9,10,13).

The stronger association of culture positivity with combined preterm low-birth-weight status than with prematurity or low birth weight alone is biologically plausible. The preterm, low-birth-weight neonate has immature innate and adaptive immune defences, reduced transplacental immunoglobulin, and a fragile skin and mucosal barrier; in addition, such infants generally require longer intensive care with greater exposure to intravascular catheters, mechanical ventilation, parenteral nutrition and broad-spectrum antibiotics (3,8). These factors increase both the risk of true bacteraemia and the probability of recovering a pathogen on culture, and they help explain the higher positivity observed in the late-onset group as well (5).

The microbiological profile, dominated by gram-negative organisms with Klebsiella pneumoniae as the leading isolate, mirrors the pattern repeatedly described in Bangladeshi neonatal units (1,13) and distinguishes this setting from many high-income countries, where group B streptococcus and coagulase-negative staphylococci feature more prominently (4). This gram-negative predominance has important therapeutic implications, as these organisms are associated with greater severity and higher case fatality in neonatal sepsis (2,11).

The antimicrobial sensitivity data reinforce a now-familiar and worrying picture: extensive resistance of gram-negative isolates to ampicillin, aminopenicillin–β-lactamase-inhibitor combinations, third-generation cephalosporins and, to a lesser degree, gentamicin precisely the agents that constitute conventional first-line empirical therapy (1,9). Sensitivity was largely preserved to amikacin, piperacillin–tazobactam, the carbapenems and colistin. While the retained carbapenem and colistin activity is reassuring, reliance on these last-resort agents is itself a marker of advanced resistance and a driver of further selection pressure; even modest carbapenem resistance in this context is an early warning that warrants close surveillance (6,9). Gram-positive isolates remained fully sensitive to vancomycin and linezolid. Taken together, these findings argue for empirical regimens guided by an up-to-date, unit-specific antibiogram rather than by generic national protocols, and for de-escalation to the narrowest effective agent once susceptibility results are available.

From a clinical standpoint, the results support heightened, risk-stratified vigilance for sepsis in preterm low-birth-weight neonates, early and adequate-volume blood culture before antibiotics, and a strong programme of infection prevention hand hygiene, aseptic insertion and care of intravascular devices, and judicious device use to reduce late-onset, largely device-associated infection (5,8). They also reinforce the case for a functioning antimicrobial stewardship programme in the neonatal unit (6,9).

4.1 Strengths and limitations

The strengths of this study include the use of clinically suspected sepsis as a pragmatic, reproducible entry criterion and the collection of blood for culture before antibiotic exposure. Several limitations should be acknowledged. First, this was a single-centre, cross-sectional study, so the findings may not be generalisable and no causal or temporal inference can be drawn. Second, conventional blood culture underestimates true infection because of small sample volumes, low-grade bacteraemia and any undisclosed prior antibiotic exposure, so culture-negative clinical sepsis was not captured. Third, the number of isolates within some organism and antibiotic subgroups was small, which limits the precision of the subgroup sensitivity estimates. Multicentre studies with larger samples, and molecular or automated detection methods, would strengthen and extend these observations.

5 CONCLUSION

Preterm low-birth-weight status was significantly associated with a higher rate of blood culture positivity among neonates with clinically suspected sepsis. The causative organisms were predominantly multidrug-resistant gram-negative bacteria led by Klebsiella pneumoniae, with widespread resistance to conventional first-line antibiotics but retained sensitivity to carbapenems and colistin, while gram-positive isolates remained sensitive to vancomycin and linezolid. These findings call for risk-stratified clinical vigilance in preterm low-birth-weight neonates, empirical antibiotic policy guided by a local antibiogram, robust infection-prevention practices, and strengthened antimicrobial stewardship, supported by larger multicentre studies.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare that they have no competing interests.

Statement of ethical approval

Approved by the Institutional Ethical Review Committee of institution (ref. IRB/DCIMC/8/2026).

Statement of informed consent

informed written consent was obtained from each guardian.

Availability of data

The datasets used and/or analysed during the study are available from the corresponding author on reasonable request.

Authors' contributions

Describe each author's contribution to conception, data collection, analysis, drafting and approval.

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