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PATTERNS OF NEONATAL SEPSIS: A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: Neonatal sepsis constitutes a systemic bacterial infection affecting newborns and remains associated with substantial mortality in resource-limited settings. The present investigation was undertaken to evaluate the incidence, bacteriological profiles, antimicrobial susceptibility patterns, and mortality among neonates presenting with septicemia in the intensive care units of a referral maternity hospital in Sudan. Methods: This study included 122 neonates with septicemia. Maternal and neonatal characteristics, clinical manifestations, hospitalization status, and the need for mechanical ventilation were recorded. Blood cultures were performed to identify causative organisms, and antimicrobial susceptibility testing was conducted. Results: Among the 122 neonates, 80 (65.6%) were preterm and 81 (66.4%) had low birth weight. Males accounted for 68 (55.7%) cases, and 64 (52.5%) were delivered by cesarean section. The most common clinical features were tachycardia (98.4%), central cyanosis (91.0%), respiratory distress (82.8%), and fever (72.1%). Blood cultures were positive in 55 cases (45.1%). Pseudomonas spp. was the most frequently isolated organism (34.5%), followed by Staphylococcus aureus (20.0%). Hospitalization (OR = 6.1, 95% CI: 3.7–10.2), low birth weight (OR = 5.5, 95% CI: 3.6–9.5), and prematurity (OR = 4.1, 95% CI: 3.9–7.1) were significantly associated with the study outcome (all $p < 0.001$). Most bacterial isolates demonstrated sensitivity to vancomycin, meropenem, and several other tested antimicrobial agents, whereas resistance patterns varied according to the bacterial species. Conclusion: Prematurity and low birth weight were common among neonates with septicemia and were significantly associated with the study outcome. Tachycardia, central cyanosis, and respiratory distress were the predominant clinical manifestations. Pseudomonas spp. was the most frequently isolated organism. The observed antimicrobial susceptibility patterns highlight the importance of culture-based diagnosis and antimicrobial susceptibility testing to guide appropriate treatment and reduce the emergence of antimicrobial resistance.

Keywords: Neonatal septicemia; bacteriological profile; antimicrobial susceptibility, Staphylococci, Staphylococcus aureus

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INTRODUCTION

Neonatal sepsis represents a systemic and generalized bacterial infection in newborns, confirmed by a positive blood culture within the first four weeks of life, and is associated with considerable mortality rates in developing nations. The condition manifests through fever, hypothermia, lethargy, tachycardia, hyperventilation, toxicity, and/or prostration, all of which stem from the proliferation of circulating bacteria. As a leading contributor to neonatal morbidity and mortality, sepsis constitutes a life-threatening emergency that demands prompt antimicrobial intervention to ensure favorable clinical outcomes. It has been estimated to account for 30–50% of all neonatal deaths annually [1,2].

Based on the timing of clinical onset, neonatal sepsis is categorized into early-onset sepsis (EOS) and late-onset sepsis (LOS), defined by presentation within the first 72 hours or between 72 hours and 30 days of life, respectively. The demarcation between EOS and LOS is not rigid and is influenced by the causative pathogen. The spectrum of causative organisms varies across nurseries and is shaped by prenatal factors, the caliber and number of healthcare personnel, the microbial flora present in delivery rooms, and the availability of antimicrobial agents [3,4]. EOS is typically caused by microorganisms acquired from the mother during the antepartum or intrapartum period, whereas LOS pathogens are generally acquired from the postnatal environment. Infections caused by group B *Streptococcus* that manifest within the first seven days of life are conventionally classified as early-onset and thus of maternal origin. Conversely, infections caused by coagulase-negative *Staphylococci* at any age are likely nosocomial in nature [5,6].

The primary route of microbial transmission within the nursery is through direct physical contact or indirectly via the hands of healthcare personnel from another infant. Maternal risk factors including intrapartum fever, premature rupture of membranes, spontaneous preterm labor, chorioamnionitis, urinary tract infections, and group B *Streptococcus* colonization significantly contribute to the development of neonatal sepsis [7,8]. A laboratory-confirmed bloodstream infection (LCBI) in neonates requires the following criteria: the patient is ≤1 year of age and presents with at least one of the following features: fever or hypothermia (rectal temperature >38 °C or <37 °C, respectively), apnea, or bradycardia, accompanied by positive laboratory findings not attributable to infection at another site [9].

The gold standard for diagnosing neonatal septicemia remains the isolation of bacterial agents from one or more blood cultures, supplemented by additional laboratory evidence of sepsis such as elevated serum C-reactive protein (CRP) levels. Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Haemophilus influenzae*), *Staphylococcus* spp., and β-hemolytic *Streptococcus* continue to be the predominant causative agents, with escalating resistance to commonly administered antibiotics in developing countries [10,11]. Up to 60% of blood cultures may yield false-negative results

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for common neonatal pathogens due to various factors. In cases of clinically suspected culture-negative neonates, adjunctive laboratory investigations including serum procalcitonin, CRP, and interleukin-6/interleukin-8 (IL-6/IL-8) levels can provide valuable diagnostic support [12,13]. Polymerase chain reaction (PCR) has emerged as a significant technique for the rapid and accurate diagnosis of neonatal septicemia [14,15].

The management of neonatal sepsis presents considerable challenges owing to several physiological distinctions and differences in neonatal antibiotic pharmacokinetics compared with older children. Familiarity with the antimicrobial susceptibility profiles of common causative pathogens is essential for guiding antibiotic selection, provided that periodic active surveillance is conducted. Antibiotics are also employed prophylactically for asymptomatic newborns when the mother presents with risk factors for or a confirmed infection [16,17]. The World Health Organization (WHO) recommendation of an ampicillin and gentamicin combination for the treatment of neonatal sepsis may no longer be efficacious in many cases. This concern arises from reports indicating that the majority (71%) of *Klebsiella* isolates and 50% of *E. coli* isolates are resistant to gentamicin, contributing to elevated neonatal sepsis mortality in developing countries [18,19].

The current study was designed to determine the bacteriological profiles, antimicrobial susceptibility patterns of isolates, associated risk factors, and mortality rates of late-onset neonatal septicemia within the intensive care units.

METHODS

Study Design and Setting: This is cross-sectional study was carried out at the Intensive Care Unit during the period from June 2023 to June 2024. A total of 122 neonates aged 0–30 days were enrolled. The inclusion criteria comprised neonates with clinically suspected septicemia, indicated by fever or hypothermia (rectal temperature >38 °C or <37 °C, respectively), apnea, bradycardia, tachycardia, hyperventilation, and toxic. The exclusion criteria were neonates born as outpatients, those with a birth weight below 1,500 grams, and those presenting with apparent congenital anomalies.

Variables: age, sex, birth weight, delivery mode, Apgar score, mechanical ventilation used, intravascular catheterization, antibiotic usage, hospitalization, infecting bacteria present, and antimicrobial susceptibility patterns.

Blood sampling and processing: Blood specimens were collected aseptically; 2 mL of venous blood was drawn and immediately inoculated into a tube. The samples were incubated aerobically at 37 °C and examined daily for 1 week for visible indicators of bacterial proliferation.

Culture and Gram staining: Blood cultures demonstrating microbial growth were sub-cultured onto

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blood, chocolate, and MacConkey agar. All positive blood cultures were identified. Cultures that exhibited no microbial growth within seven days were reported as negative [20].

Antimicrobial Susceptibility Testing

Small filter paper discs (6 mm) were placed onto Mueller–Hinton agar plates that had been inoculated with the test bacteria. The diameter of the zone of inhibition of bacterial growth was used as a measure of susceptibility. Interpretation of results was performed in accordance with the guidelines established by the Clinical and Laboratory Standards Institute (CLSI) [21].

Data Analysis

Data were entered into SPSS-24 (IMB, NY) software. Frequencies with 95% confidence intervals (CIs) and odds ratios (ORs) were computed.

RESULTS

Table (1), among the 122 neonates included in the study, 80 (65.6%) were preterm, while 42 (34.4%) were born at term. Regarding birth weight, 81 neonates (66.4%) had low birth weight (<2,500 g), whereas 41 (33.6%) had normal birth weight (≥2,500 g). There were 68 males (55.7%) and 54 females (44.3%). Regarding the mode of delivery, 64 neonates (52.5%) were delivered by cesarean section, while 58 (47.5%) were delivered vaginally. A low Apgar score was reported in 100 neonates (82.0%), and 121 (99.2%) required hospitalization. Mechanical ventilation was required in 33 neonates (27.0%).

Table 1: Maternal and Neonatal Characters (n = 122)

Characteristic	n	%
Gestational age		
Preterm	80	65.6
Term	42	34.4
Birth weight		
Low birth weight (<2,500 g)	81	66.4
Normal birth weight (≥2,500 g)	41	33.6
Sex		
Male	68	55.7
Female	54	44.3
Mode of delivery		
Cesarean section	64	52.5
Vaginal delivery	58	47.5
Low Apgar score	100	82.0
Hospitalization	121	99.2
Mechanical ventilation	33	27.0

Table (2), the most common clinical feature among the studied neonates was tachycardia, observed in 120 (98.4%) cases, followed by central cyanosis in 111 (91.0%) and respiratory distress in 101 (82.8%).

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Fever was reported in 88 (72.1%) neonates, while lethargy was observed in 70 (57.4%) cases. Hypothermia was present in 34 (27.9%) neonates. Less common clinical manifestations included jaundice, reported in 12 (9.8%) cases, and seizures, observed in 10 (8.2%) cases. Bulging of the anterior fontanelle was the least common feature, occurring in 4 (3.3%) neonates.

Table 2: Clinical Features of Neonates with Clinically Suspected Septicemia

Clinical Feature	n	%
Respiratory distress	101	82.8
Lethargy	70	57.4
Fever	88	72.1
Tachycardia	120	98.4
Central cyanosis	111	91.0
Hypothermia	34	27.9
Jaundice	12	9.8
Seizures (fits)	10	8.2
Bulging anterior fontanelle	4	3.3

Table (3), blood culture results were positive in 55 neonates (45.1%), while 67 (54.9%) had negative blood cultures. Among the 55 culture-positive cases, Pseudomonas spp. was the most frequently isolated organism, accounting for 19 cases (34.5%), followed by Staphylococcus aureus in 11 cases (20.0%). Klebsiella spp. and coagulase-negative Staphylococci were each isolated in 8 cases (14.5%), while Bacillus spp. was identified in 7 cases (12.7%). Escherichia coli was the least frequently isolated organism, accounting for 2 cases (3.6%).

Table 3: Blood Culture Results and Distribution of Bacterial Isolates

Parameter	n	%
Blood culture results		
Positive	55	45.1
Negative	67	54.9
Organisms isolated among culture-positive cases (n = 55)		
Pseudomonas spp.	19	34.5
Staphylococcus aureus	11	20.0
Klebsiella spp.	8	14.5
Coagulase-negative *Staphylococci*	8	14.5
Bacillus spp.	7	12.7
Escherichia coli	2	3.6
Total	**55**	**100.0**

Table (4), the analysis demonstrated significant associations between the studied risk factors and the outcome. Hospitalization was associated with a 6.1-fold increase in the odds of the outcome (OR = 6.1,

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95% CI: 3.7–10.2; p < 0.001). Similarly, low birth weight was significantly associated with increased odds of the outcome (OR = 5.5, 95% CI: 3.6–9.5; p < 0.001). Prematurity was also significantly associated with the outcome, with an odds ratio of 4.1 (95% CI: 3.9–7.1; p < 0.001).

Table 4: Risk Factors for Neonatal Septicemia.

Risk Factor	Odds Ratio (95% CI)	p-value
Hospitalization	6.1 (3.7–10.2)	<0.001
Low birth weight	5.5 (3.6–9.5)	<0.001
Prematurity	4.1 (3.9–7.1)	<0.001

The antimicrobial susceptibility patterns of bacterial isolates demonstrated considerable variation among the identified organisms. Coagulase-negative *Staphylococci* were resistant to penicillin G and trimethoprim/sulfamethoxazole but were sensitive to vancomycin, meropenem, gentamicin, amikacin, ciprofloxacin, and chloramphenicol. *Staphylococcus aureus* was sensitive to all tested antibiotics except trimethoprim/sulfamethoxazole. *Pseudomonas* spp., the most frequently isolated organism, was sensitive to vancomycin, meropenem, gentamicin, amikacin, ciprofloxacin, chloramphenicol, and ceftazidime but resistant to cefotaxime and trimethoprim/sulfamethoxazole. Similarly, *Klebsiella* spp. and *Bacillus* spp. showed sensitivity to most tested antimicrobial agents but resistance to cefotaxime. In contrast, the *E. coli* isolates demonstrated resistance to gentamicin, amikacin, ciprofloxacin, chloramphenicol, cefotaxime, and trimethoprim/sulfamethoxazole. (Table 5)

Table 5: Antimicrobial Susceptibility Patterns of Bacterial Isolates from Neonatal Septicemia

Organism	PEN	VAN	MER	GEN	AMK	CIP	CHL	CTX	CAZ	SXT
Coagulase - negative *Staphylococci*	R	S	S	S	S	S	S	—	—	R
S. aureus	S	S	S	S	S	S	S	—	—	R
Pseudomonas spp.	—	S	S	S	S	S	S	R	S	R
Klebsiella spp.	—	S	S	S	S	S	S	R	S	—
Bacillus spp.	—	S	S	S	S	S	S	R	—	—
E. coli	—	—	—	R	R	R	R	R	—	R

PEN = Penicillin G; VAN = Vancomycin; MER = Meropenem; GEN = Gentamicin; AMK = Amikacin; CIP = Ciprofloxacin; CHL = Chloramphenicol; CTX = Cefotaxime; CAZ = Ceftazidime; SXT = Trimethoprim/sulfamethoxazole. S = Sensitive; R = Resistant.

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DISCUSSION

Neonatal sepsis continues to pose a substantial mortality risk in developing nations, where regular bacterial resistance surveillance programs are often lacking, rendering empirical antibiotic therapy suboptimal. It remains a relatively neglected condition that has not fully benefited from recent advancements in medical care. The incidence, clinical manifestations, risk factors (including low birth weight and prematurity), and mortality rates of neonatal septicemia observed in Sudan were found to be comparable to those reported in other developing countries [5,22].

Clinical assessment based on a combination of symptoms and signs proved to be an insufficient guide for the provisional diagnosis of neonatal sepsis, a finding consistent with previous investigations. This inadequacy likely stems from the absence of a consensus on the clinical definition of neonatal septicemia. Furthermore, these definitions may be inappropriate for preterm neonates, who constitute a considerable proportion of live births [4,6,9].

The blood culture positivity rate documented in the present study is consistent with reports from other developing nations but exceeds the rates reported in certain other settings. The causative organism profiles identified herein were similar to those documented in other regions of the developing world. *K. pneumoniae*, *P. aeruginosa*, and *E. coli* emerged as the pathogens most resistant to routinely used antibiotics, a finding that aligns with previous studies [10,11,23,24,25].

The high mortality rate associated with *K. pneumoniae* infections is particularly concerning and corroborates recent evidence highlighting the growing threat of carbapenem-resistant and extended-spectrum β-lactamase-producing organisms in neonatal units across low- and middle-income countries [6,15]. The observed resistance patterns underscore the urgent need for updated empirical antibiotic guidelines, as the WHO-recommended ampicillin–gentamicin combination may no longer provide adequate coverage in many settings [26,27].

CONCLUSION

In conclusion, the incidence and mortality rates of neonatal septicemia were found to be elevated in the neonatal intensive care units studied in Sudan. Prematurity, low birth weight, and prolonged hospital stay exceeding seven days emerged as significant risk factors. The causative organisms (*K. pneumoniae*, *Pseudomonas aeruginosa*, *S. aureus*, and *E. coli*) demonstrated considerable sensitivity to meropenem, vancomycin, gentamicin, and amikacin, with marked resistance to penicillin G. There is an urgent need to conduct regular antimicrobial susceptibility surveillance to better guide empirical antibiotic selection and to update existing treatment guidelines accordingly.

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