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Original Article

Frequency of Meningitis in Neonatal Late Onset Sepsis

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ABSTRACT

Objective: To determine the frequency of bacterial meningitis in neonate presenting with late onset sepsis at children's hospital Larkana.

Methodology: This cross-sectional research, undertaken at SMBBMU Larkana during the year 2022. The study encompassed the engagement of 250 neonates, aged from 7 to 27 days, representing both sexes, who exhibited symptoms indicative of late-onset sepsis. The diagnosis of bacterial meningitis was determined through the procedure of lumbar puncture, utilizing established cerebrospinal fluid (CSF) criteria. The collected data was analyzed by utilizing SPSS version 26.0. Descriptive statistics and Chi-square tests were used, with $p < 0.05$ considered significant.

Results: Among those 250 neonatal sepsis patients, mean age at diagnosis was 16.5 days; 125 (58.4%) of them were male. In 16% of cases meningitis was the diagnosis. The most common symptom was seizures, with a frequency of 88.8%. Meningitis was not significantly associated with blood culture positivity ($p=0.109$). There were also no statistically significant differences that were noted in mortality, hospital stay, and duration of antibiotic treatment ($p > 0.05$).

Conclusion: The prevalence of meningitis was found in a significant number of neonates with late-onset sepsis and suggests that there is an indication of early CSF assessment to ensure prompt diagnosis and treatment of meningitis. Lumbar puncture, in order to establish the involvement of the CNS, must be done routinely in suspected cases, irrespective of the outcome of the blood culture. These findings support integrating standard CSF analysis into neonatal sepsis protocols to improve clinical outcomes and reduce neurological complications.

Keywords: Bacterial meningitis, Neonates, Prevalence, Sepsis

INTRODUCTION

Neonatal sepsis remains a critical global health concern, particularly in low- and middle-income countries where limited resources and diagnostic challenges contribute to high neonatal morbidity and mortality rates[1,2]. Late-onset sepsis (LOS), defined as sepsis occurring after 72 hours of birth, is commonly associated with nosocomial infections, often resulting from prolonged hospitalization and invasive interventions in neonatal intensive care units (NICUs)[3]. Among its most severe complications is neonatal meningitis, which carries a high risk of mortality and long-term neurological sequelae, including hydrocephalus, cerebral palsy, hearing loss, and developmental delay[4,5].

Diagnosing meningitis in neonates is inherently difficult, as clinical signs such as poor feeding, temperature instability, irritability, apnea, or seizures are often subtle and nonspecific[6]. Relying solely on blood cultures may lead to underdiagnosis since central nervous system (CNS) involvement can exist even with sterile blood cultures[7]. Thus, cerebrospinal fluid (CSF) analysis remains essential for identifying meningitis in suspected LOS cases. However, lumbar puncture is frequently delayed or omitted, especially in critically ill neonates or in resource-limited settings, potentially resulting in missed diagnoses[8].

Reported frequencies of meningitis among neonates with LOS range from 10% to 30%, depending on geographic location, institutional protocols, and whether lumbar puncture is routinely performed[4,9]. Gram-negative bacteria, especially Klebsiella pneumoniae, Escherichia coli, and Acinetobacter species, are the predominant causative organisms in LOS-associated meningitis in many developing countries and are often multidrug resistant[10–12]. In Pakistan, there is a paucity of updated data on the frequency and microbiological profile of neonatal meningitis in LOS, although earlier reports have indicated a substantial burden[13,14].

This study was conducted to determine the frequency of meningitis among neonates with late-onset sepsis at a tertiary care centre. Through routine CSF examination in all LOS cases, the study aims to provide local evidence to support timely diagnosis and informed therapeutic decision-making.

METHODOLOGY

This descriptive cross-sectional study was performed in the department of pediatrics at Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU), Larkana, between January to July 2022, which lasted a period of 6 months. A total of 250 neonates were enrolled through a non-probability consecutive sampling methodology, in which eligible subjects were systematically recruited as they presented throughout the designated study timeframe. The sample size was determined utilizing the WHO sample size calculator, predicated on a previously documented prevalence of bacterial meningitis in late-onset sepsis (22.5%)[13], incorporating a margin of error of 6.1% and establishing a 95% confidence interval.

Inclusion criteria encompassed neonates of either gender, aged between 7 and 27 days, who presented with clinical features of late-onset sepsis. To ensure accuracy in CSF findings, neonates who had received antibiotics prior to enrollment were excluded to prevent potential alterations in laboratory parameters. Additional exclusion criteria included neonates with birth weight below 1000 grams, those receiving total parenteral nutrition (TPN), and infants with dysmorphic features, as these factors could introduce confounding

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variables due to their association with altered immune or metabolic responses.

Eligible neonates were identified upon presentation to the Pediatrics department, and written informed consent was obtained from the parents or guardians before enrollment. Ethical approval for the study was obtained from the institutional ethics review committee, and confidentiality was strictly maintained throughout the research process.

Demographic and clinical data—including age, gestational age, birth weight, and gender—were recorded using a structured proforma. Lumbar puncture was performed under aseptic conditions at the L3–L4 interspace to obtain cerebrospinal fluid (CSF) samples. Acute bacterial meningitis was diagnosed based on the following CSF criteria: leukocyte count >10/mm³ with neutrophilic predominance, protein level >45 mg/dL, and CSF glucose < two-thirds of the corresponding serum glucose level. All CSF specimens were sent to the microbiology and biochemistry laboratories for cytological, biochemical, and glucose analysis to assess the primary outcome variable—presence of bacterial meningitis.

Statistical analysis was performed using IBM SPSS version 26.0. Descriptive statistics were used to summarize demographic and clinical characteristics. The Chi-square test was applied to determine associations between categorical variables, with a p-value <0.05 considered statistically significant.

RESULTS

A total of 250 neonates diagnosed with late-onset sepsis were included in the study. As shown in **Table I**, 146 (58.4%) were male and 104 (41.6%) were female. The mean gestational age was 36.12 ± 2.05 weeks, with 136 (54.4%) neonates born preterm and 114 (45.6%) born at term. The average age of presentation was 16.48 ± 6.57 days; 42.4% of neonates presented between 7–14 days of life, while 57.6% presented after 14 days. The mean birth weight was 2.60 ± 0.75 kg, with 88.0% of neonates weighing between 1.6 and 3.0 kg.

Laboratory and clinical characteristics are summarized in **Table II**. The mean platelet count was 146,612 ± 63,512.8/mm³ and the mean white blood cell (WBC) count was 12,376 ± 4,120.9/mm³. The mean leukocyte count was 22,801.1 ± 8,563.6/mm³, while the average CRP level was 5.8 ± 1.3 mg/dL. Mean CSF protein and glucose levels were 128.9 ± 42.9 mg/dL and 34.1 ± 13.7 mg/dL, respectively. Blood cultures were positive in 85 (34.0%) neonates and negative in 165 (66.0%). In terms of clinical signs, seizures were reported in 222 (88.8%) neonates, respiratory distress in 178 (71.2%), lethargy in 170 (68.0%), and fever in 133 (53.2%). Other clinical features included temperature instability (34.8%), shock (22.0%), convulsions (14.4%), abdominal distension (14.0%), and reluctance to feed (25.0%).

Table III summarizes the clinical outcomes in neonates with and without meningitis. Among those with meningitis, 80.0% were discharged and 20.0% died, compared to 77.1% discharges and 22.9% deaths in the non-meningitis group (p = 0.691). Mean hospital stay was slightly longer in the meningitis group (20.7 ± 8.5 days vs. 19.3 ± 9.7 days; p=0.402). Antibiotic duration was similar between groups (p=0.803), indicating no significant differences in clinical outcomes.

Table I: Demographic Characteristics of Participants (n=250)

Characteristics	Frequency (%)
Gender	
Male	146 (58.4)
Female	104 (41.6)
Gestational Age (Mean ± SD) = 36.12 ± 2.05 (weeks)	
Gestation	
Preterm	136 (54.4)
Term	114 (45.6)
Age (Mean ± SD) = 16.48 ± 6.57 (days)	
7-14 days	106 (42.4)
>14 days	144 (57.6)
Weight (Mean ± SD) = 2.60 ± 0.75 (kg)	
1.6-3.0 kg	220 (88.0)
>3.0 kg	30 (12.0)

Table II: Clinical & Laboratory Findings in Neonatal Sepsis

Laboratory Parameters (Mean ± SD)		
Platelets		146612 ± 63512.8
WBC		12376 ± 4120.9
Leukocyte		22801.1 ± 8563.6
CRP		5.8 ± 1.3
Protein Level		128.9 ± 42.9
Glucose Level		34.1 ± 13.7
Blood Culture	Positive	85 (34.0)
	Negative	165 (66.0)
Clinical Signs and Symptoms		
Seizure		222 (88.8)
Fever		133 (53.2)
Abdomen Distension		35 (14.0)
Lethargy		170 (68.0)
Shock		55 (22.0)
Convulsions		36 (14.4)
Temperature Instability		87 (34.8)
Respiratory Distress		178 (71.2)
Reluctant to feed		15 (25.0)

Figure I: Isolated Microorganisms in Meningitis Patients

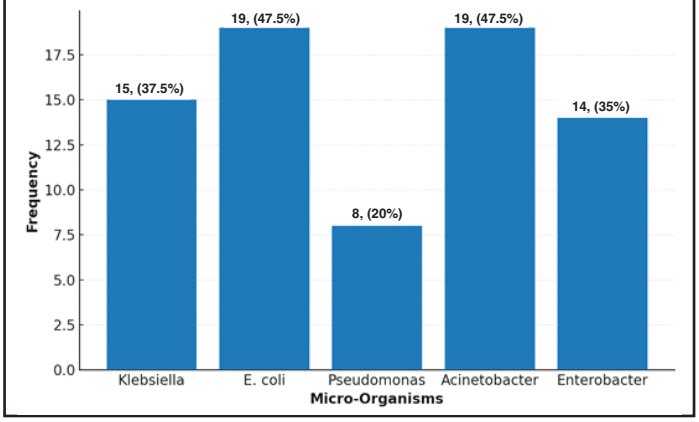

Table III: Comparison of In-Hospital Outcomes in Bacterial Meningitis Versus Non-Meningitis Patients (n=250)

In-Hospital Outcomes	Meningitis (n=40)	Non-Meningitis (n=210)	P-Value
Discharge	32 (80.0%)	162 (77.1%)	0.691
Mortality	8 (20.0%)	48 (22.9%)	
Hospital Stays (days)	20.7 ± 8.5	19.3 ± 9.7	0.402
Duration of Antibiotic Treatment (days)	9.7 ± 2.3	9.8 ± 2.3	0.803

DISCUSSION

Bacterial meningitis continues to be a severe complication of late-onset sepsis (LOS) in neonates, as demonstrated by its occurrence in 16% of affected cases in the current cohort. This frequency is consistent with rates reported in recent literature from similar clinical settings, where prevalence typically ranges between 10% and 30%, depending on diagnostic criteria and the extent of CSF analysis performed[4,9,13]. Early identification of meningitis through routine lumbar puncture is widely supported and remains crucial in guiding timely treatment, especially in resource-limited environments[8,17].

The demographic profile of the study population revealed a mean age of 16.48 days, aligning well with standard definitions of LOS, which typically occurs beyond 72 hours of life[3,5]. A male predominance (58.4%) was also observed, in agreement with previously published data suggesting increased susceptibility to neonatal infections among male infants, possibly due to immunological and hormonal factors[1,2]. These demographic patterns underscore the importance of considering both age and gender when stratifying risk in neonatal sepsis protocols.

Although clinical signs of meningitis in neonates are frequently non-specific, neurological manifestations such as seizures are widely recognized as a strong indicator of CNS involvement[5,6,15]. Given the poor sensitivity of blood cultures in isolation, reliance solely on hematologic findings may result in underdiagnosis[7]. Therefore, consistent with global best practices, lumbar puncture should be routinely performed in neonates presenting with LOS, even when blood cultures are negative[7,8].

The microbiological profile of meningitis in LOS is dominated by gram-negative pathogens, particularly Klebsiella pneumoniae, Escherichia coli, and Acinetobacter species, all of which are prevalent in South Asia and sub-Saharan Africa[10,11]. These organisms pose significant challenges due to rising antibiotic resistance, making empirical treatment increasingly difficult and often ineffective[12,14]. The findings align with those of Saleem et al. and Roshi et al., who reported similar trends in Pakistani tertiary hospitals[10,13]. Mukherjee et al. further reinforced the urgency of tailored antibiotic strategies based on local antibiograms[12].

While the uniform application of lumbar puncture in this study strengthens the reliability of findings, limitations must be acknowledged. These include the single-center nature of the study, modest sample size, and lack of long-term neurological outcome data. The absence of detailed antimicrobial sensitivity patterns also limits the ability to draw conclusions about treatment adequacy. Previous investigations by Ahmad et al. and Khaskheli et al. highlighted similar gaps, calling for broader, multicenter research[9,14].

Emerging global frameworks, such as those recommended by Fitchett et al. and Le Doare et al., emphasize the importance of region-specific data to improve neonatal infection outcomes, particularly in low- and middle-income countries[16,17]. Findings from this study contribute to that evidence base, reinforcing the value of early diagnostic workup in neonates with LOS and guiding appropriate antimicrobial stewardship.

Ultimately, the presence of meningitis in a considerable portion of neonates with LOS underlines the necessity of including CSF analysis in standard clinical protocols. Early detection through lumbar puncture, supported by locally relevant microbiological surveillance, remains essential to reducing both acute and long-term morbidity associated with neonatal meningitis.

CONCLUSION

The prevalence of meningitis was found in a significant number of neonates with late-onset sepsis and suggests that there is an indication of early CSF assessment to ensure prompt diagnosis and treatment of meningitis. Lumbar puncture, in order to establish the involvement of the CNS, must be done routinely in suspected cases, irrespective of the outcome of the blood culture. These findings support integrating standard CSF analysis into neonatal sepsis protocols to improve clinical outcomes and reduce neurological complications.

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