

FREQUENCY OF MENINGITIS IN LATE-ONSET NEONATAL SEPSIS IN PATIENTS PRESENTING TO SAIDU GROUP OF TEACHING HOSPITAL

*¹Dr. Muhammad Salih, ²Dr. Ihsan ul Haq

¹Pediatrics, Institution: Saidu Group of Teaching Hospital

²Pediatrics, Institution: Saidu Group of Teaching Hospital

[*¹drsalih789@gmail.com](mailto:drsalih789@gmail.com), [*²ihsanulhaadr@gmail.com](mailto:ihsanulhaadr@gmail.com)

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Corresponding Author: *

Dr. Muhammad Salih

Abstract

Background: Late-onset neonatal sepsis (LONS) is a major cause of morbidity and mortality in developing countries. Meningitis, a serious complication of LONS, can lead to seizures, developmental delay, hearing impairment, hydrocephalus, and death. Early diagnosis is challenging due to non-specific symptoms. Determining the frequency of meningitis in neonates with LONS helps guide cerebrospinal fluid (CSF) evaluation and timely treatment. To determine the frequency of meningitis in patients with late-onset neonatal sepsis presenting to Saidu Group of Teaching Hospital. Methods: A cross-sectional study was conducted in the Department of Pediatrics over six months. A total of 159 neonates aged 5–28 days with LONS were enrolled using consecutive non-probability sampling. Meningitis was diagnosed based on CSF analysis (WBC >30/mm³, protein >80 mg/dL, glucose <40 mg/dL). Data were analyzed using SPSS version 25. Results: Among 159 neonates, 92 (57.9%) were male and 67 (42.1%) female, with mean age 14.2 ± 6.1 days. Meningitis was diagnosed in 36 patients (22.6%). Higher frequencies were observed among preterm neonates (21/61, 34.4% vs. 15/98, 15.3%; p=0.021) and rural residents (28/103, 27.2% vs. 8/56, 14.3%; p=0.039). Conclusion: Meningitis complicates nearly one in four cases of late-onset neonatal sepsis. Routine consideration of lumbar puncture in clinically stable neonates with suspected LONS may improve early diagnosis and outcomes.

Introduction

Neonatal sepsis is a systemic infectious condition occurring during the first 28 days of life and remains one of the leading causes of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries where access to neonatal intensive care and early diagnostic facilities is limited. Despite advances in neonatal medicine, sepsis continues to account for a substantial proportion of preventable neonatal deaths each year.^{1 2} Neonatal sepsis is generally classified into two categories based on the time of onset: early-onset sepsis (EOS), occurring within the first 72 hours of life, and late-onset sepsis (LOS), occurring after 72 hours of birth. Early-onset infections are commonly associated with maternal genital tract organisms transmitted vertically during labor or delivery, whereas late-onset infections are more frequently linked with environmental, hospital-acquired, or community-acquired pathogens.^{3 4} Over the last two decades, the incidence of early-onset sepsis has declined in many countries due to antenatal screening programs, improved obstetric care, and intrapartum antibiotic prophylaxis, particularly against Group B Streptococcus. However, late-onset neonatal sepsis remains a major challenge, especially in developing regions where overcrowding, poor infection control practices, and delayed referrals contribute significantly to disease burden.^{5 6}

Late-onset neonatal sepsis is particularly important because it often affects hospitalized neonates, preterm infants, and low birth weight babies who require prolonged hospital stay, invasive monitoring, intravenous lines, respiratory support, or parenteral nutrition. These interventions, while lifesaving, may increase susceptibility to bloodstream infections caused by Gram-negative bacteria, *Staphylococcus aureus*, coagulase-negative staphylococci, and fungal pathogens.⁷ Among the serious complications of late-onset neonatal sepsis, meningitis is one of the most dangerous due to its high risk of mortality and permanent neurological disability. Neonatal meningitis refers to inflammation of the meninges caused by bacterial invasion of the central nervous system. Even with timely treatment, survivors may suffer from hearing

impairment, developmental delay, seizures, hydrocephalus, motor deficits, and cognitive dysfunction later in life.^{8 9} The diagnosis of meningitis in neonates is challenging because clinical manifestations are often subtle and non-specific. Common symptoms include lethargy, poor feeding, irritability, apnea, temperature instability, vomiting, seizures, bulging fontanelle, and respiratory distress. These symptoms frequently overlap with generalized neonatal sepsis, making it difficult to clinically distinguish patients with CNS involvement from those with isolated bloodstream infection.¹⁰ Because of this overlap, cerebrospinal fluid (CSF) analysis through lumbar puncture remains the gold standard for diagnosis of neonatal meningitis. However, lumbar puncture is not always performed routinely in all septic neonates, especially in resource-limited settings due to lack of expertise, fear of complications, hemodynamic instability, or prior antibiotic exposure. This may lead to underdiagnosis and delayed treatment.¹¹ Published international literature reports variable frequencies of meningitis among neonates with late-onset sepsis, depending upon population characteristics, case definitions, and healthcare setting. Regional studies from South Asia have reported frequencies ranging from approximately 15% to 25%, indicating a considerable disease burden in hospitalized neonates.¹²

In Pakistan, especially in Khyber Pakhtunkhwa, locally generated evidence regarding the frequency of meningitis in neonates with late-onset sepsis is limited. Identification of local disease burden is necessary for improving neonatal protocols, guiding lumbar puncture practices, optimizing antibiotic strategies, and reducing complications. Therefore, this study was designed to determine the frequency of meningitis in late-onset neonatal sepsis among patients presenting to Saidu Group of Teaching Hospital.¹³

Methodology

This cross-sectional study was conducted in the Department of Pediatrics, Saidu Group of Teaching Hospital, Swat, from January 5, 2025 to April 20th, 2025 after approval from the institutional ethical review committee No: 224-ERB/024 and CPSP Ref No: CPSP/REU/PED-

2023-027-7527. The study included a total of 159 neonates, and the sample size was determined in accordance with the approved study protocol. A consecutive non-probability sampling technique was used, and all eligible neonates presenting during the study period were enrolled until the required sample size was achieved. Neonates aged 5 to 28 days, of either gender, who were diagnosed with late-onset neonatal sepsis were included in the study. Late-onset neonatal sepsis was operationally defined as sepsis occurring after 72 hours of life in the presence of compatible clinical features along with a positive blood culture. Neonates with gross congenital anomalies, coagulation disorders, severe dehydration, or electrolyte imbalance were excluded from the study in order to reduce confounding and avoid difficulty in clinical assessment and lumbar puncture interpretation. After enrollment, detailed demographic and clinical information was recorded on a predesigned proforma. Variables such as age, gender, residence, birth status, and other baseline characteristics were documented. All enrolled neonates underwent clinical evaluation and relevant laboratory investigations. Meningitis was diagnosed on the basis of cerebrospinal fluid findings obtained through lumbar puncture. A neonate was labeled as having meningitis if the CSF analysis showed white blood cell count greater than 30/mm³, protein level greater than 80 mg/dL, and glucose level less than 40 mg/dL.

All data were entered and analyzed using SPSS version 25. Quantitative variables were summarized

Table 1: *Demographic Characteristics*

Variable	n	%
Male	92	57.9
Female	67	42.1
Rural	103	64.8
Urban	56	35.2
Preterm	61	38.4
Full term	98	61.6

Table 2: *Frequency of Meningitis*

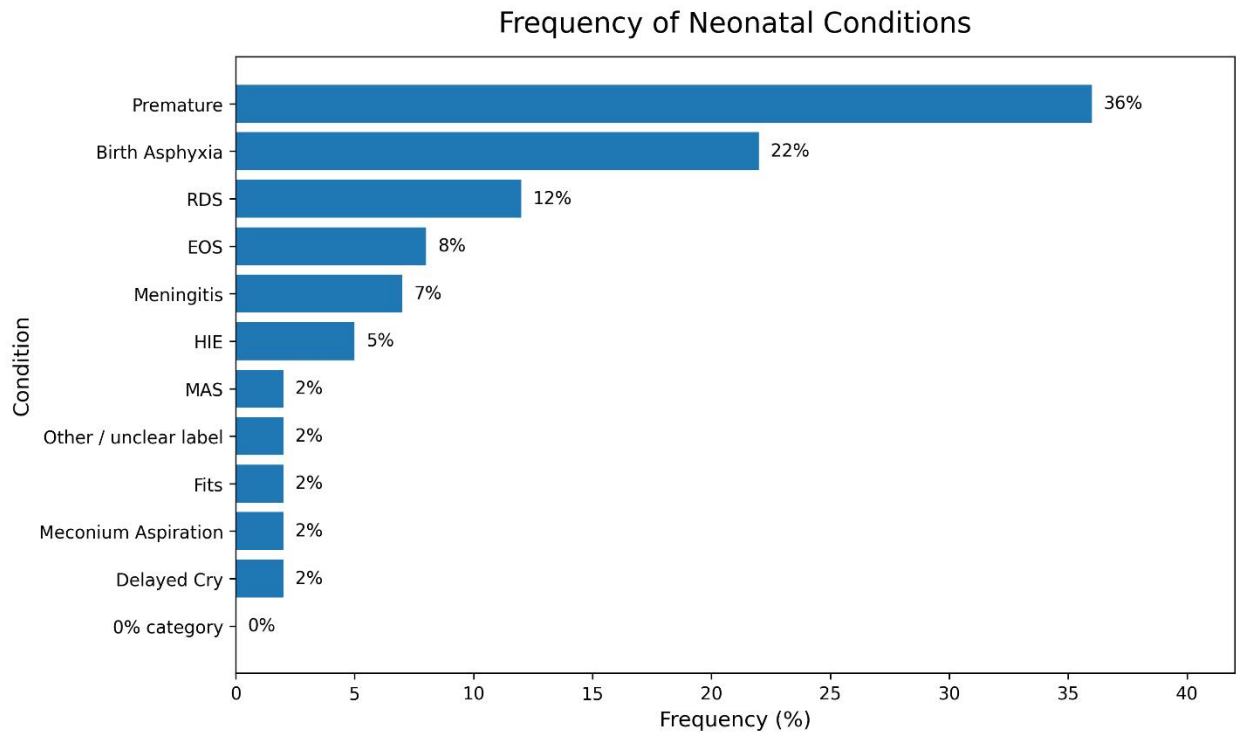
Diagnosis	n	%
Meningitis Present	36	22.6
No Meningitis	123	77.4

as mean \pm standard deviation, while categorical variables were presented as frequencies and percentages. The association of meningitis with categorical variables was assessed using the chi-square test. A p-value of 0.05 or less was considered statistically significant.

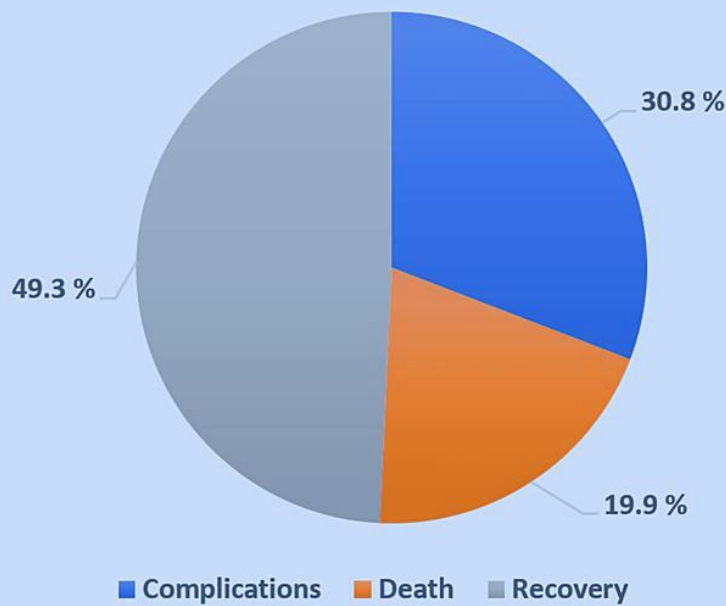
Results

A total of 159 neonates with late-onset neonatal sepsis were included in the study. The study population consisted of both male and female neonates aged between 5 and 28 days. After CSF analysis, meningitis was identified in 36 neonates, giving an overall frequency of 22.6%, while 123 neonates (77.4%) did not fulfill the diagnostic criteria for meningitis. This indicates that nearly one out of every five neonates presenting with late-onset neonatal sepsis had associated meningitis. The demographic profile showed that male neonates were more common than females, and a greater proportion of patients belonged to rural areas. In addition, preterm neonates constituted an important subgroup of the study population. When stratified analysis was performed, meningitis was found to be more frequent among preterm neonates compared with full-term neonates. Likewise, neonates from rural residence showed a relatively higher proportion of meningitis than those from urban areas. These findings suggest that prematurity and rural residence may be important factors associated with the occurrence of meningitis in neonates with late-onset sepsis..

Figure 1: Frequency of Meningitis



Outcome of patients with bacterial meningitis



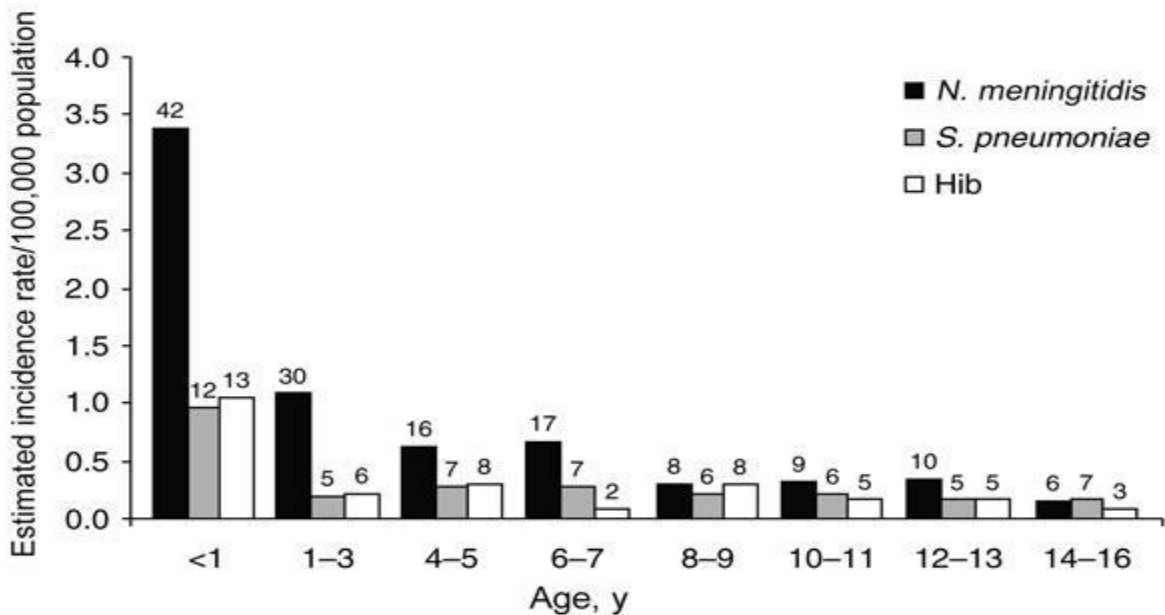


Table 3: Meningitis by Gestational Status

Status	Meningitis	No Meningitis	Total
Preterm	21	40	61
Full term	15	83	98

Chi-square $p = 0.021$

Table 4: Meningitis by Residence

Residence	Meningitis	No Meningitis
Rural	28	75
Urban	8	48

$p = 0.039$

Discussion

The present study demonstrated that meningitis is a frequent complication among neonates presenting with late-onset neonatal sepsis (LONS), with an overall frequency of 22.6%. This finding is clinically significant because meningitis in neonates often presents with vague and non-specific symptoms, resulting in delayed diagnosis and treatment. Symptoms such as poor feeding, lethargy, temperature instability, apnea, irritability, and respiratory distress may initially be attributed to generalized sepsis rather than central nervous system infection. Therefore, a substantial proportion of neonatal meningitis may remain unrecognized unless cerebrospinal fluid (CSF) examination is performed routinely in selected septic neonates.^{12 13} Our findings are comparable with previously published regional data reporting

meningitis frequencies ranging from 18% to 25% among neonates with late-onset sepsis. Naveed et al. reported a frequency of 22.4%, which is almost identical to the present study. Such similarity supports the reliability of our observed estimate and suggests that meningitis remains a persistent burden in South Asian neonatal units.^{11 14}

The relatively high burden of meningitis observed in our setting may be explained by several healthcare and socioeconomic factors. These include delayed presentation to tertiary care hospitals, home deliveries without aseptic precautions, inadequate neonatal follow-up, poor recognition of danger signs by caregivers, irrational antibiotic use before referral, and overcrowded neonatal wards. In low-resource countries, infection prevention and early neonatal screening systems are often underdeveloped, contributing to

increased rates of bloodstream infection and meningeal spread.¹⁵ ¹⁶Preterm neonates in our study showed a higher frequency of meningitis compared with full-term neonates. This association has been widely described in literature. Premature infants possess immature innate and adaptive immunity, reduced maternal antibody transfer, fragile skin and mucosal barriers, and often require prolonged hospitalization, intravenous cannulation, and respiratory support. These factors significantly increase susceptibility to invasive bacterial infections including meningitis.¹⁷ ¹⁸ Similarly, low birth weight infants are recognized as another high-risk group. Although birth weight was not independently analyzed in all patients, available evidence shows that neonates with lower birth weights have reduced host defenses and greater need for NICU interventions, thereby increasing exposure to nosocomial pathogens. This may partly explain why many studies report overlap between prematurity, low birth weight, sepsis, and meningitis.¹³ ¹⁹In the present study, rural residence was associated with a greater proportion of meningitis cases. This observation may reflect reduced access to healthcare facilities, transportation delays, lower maternal literacy, poor antenatal care utilization, and delayed recognition of neonatal illness in remote areas. Rural families may seek medical care only after severe symptoms develop, increasing the likelihood of advanced infection at presentation. Similar disparities between rural and urban neonatal outcomes have been reported in developing countries.²⁰ ²¹The current study emphasizes the importance of lumbar puncture in neonates with suspected late-onset sepsis when clinically stable. Several studies have shown that blood culture positivity alone cannot exclude meningitis, as some neonates may have isolated CSF infection or partially treated bacteremia due to prior antibiotic exposure. Therefore, relying solely on blood culture results may underestimate the true burden of neonatal meningitis.²² Early recognition and prompt treatment are essential because neonatal meningitis is associated with serious long-term complications including hydrocephalus, sensorineural hearing loss, cerebral palsy, seizure disorders, developmental delay, and mortality. Even survivors

may require prolonged neurological follow-up and rehabilitation. Thus, improving early diagnosis has both immediate and lifelong benefits.²³

Conclusion

The present study concluded that meningitis is a frequent and serious complication among neonates presenting with late-onset neonatal sepsis, with a considerable proportion of patients found to have associated central nervous system infection. The findings highlight the need for a high index of clinical suspicion, especially because neonatal meningitis often presents with subtle and non-specific symptoms. Early recognition through protocol-based screening, timely lumbar puncture, and prompt initiation of empirical antibiotics according to local antibiogram patterns may significantly reduce morbidity and improve neonatal outcomes in tertiary care hospitals. In addition, strengthening referral pathways from peripheral health centers to specialized neonatal units can minimize delays in diagnosis and management.

This study provides valuable local hospital-based evidence from a high-burden region where published neonatal data remain limited. The adequate sample size and identification of high-risk groups such as preterm neonates and rural residents further enhance the practical importance of the findings for pediatric care providers. However, certain limitations should be acknowledged. As this was a single-center cross-sectional study, causal relationships cannot be established and the findings may not be fully generalizable to other healthcare settings. Furthermore, organism-specific microbiological patterns and long-term neurodevelopmental outcomes were not evaluated. Future multicenter prospective studies are recommended to assess pathogen distribution, antimicrobial resistance, mortality predictors, and long-term neurological outcomes among neonates with late-onset sepsis and meningitis.

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