



## Frequency of Meningitis in Neonates Presented with Late Onset Sepsis

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### Declaration

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### ABSTRACT

**Objective:** To determine the frequency of meningitis among neonates with late onset sepsis (LOS) and identify associated risk factors. **Study design:** cross-sectional study. **Study place and period:** Department of Pediatrics, Hameed Latif Hospital, Lahore, over six months from August 2024 to February 2025. **Methods:** A total of 120 neonates were enrolled with LOS and lumbar puncture was performed. Meningitis was diagnosed based on cerebrospinal fluid criteria: glucose <50% of plasma glucose, white cell count >10/mm<sup>3</sup>, protein >80 mg/dL, and/or positive culture. Demographic, clinical, and laboratory data were analyzed using SPSS v26.0, with p-value ≤ 0.05 significant. **Results:** Meningitis was identified in 38.3% (46/120) of neonates with LOS. Mean birth weight (2314.34 ± 380.32 g vs. 3013.10 ± 434.05 g; p-value < 0.001) and APGAR scores (6.50 ± 1.04 vs. 7.59 ± 0.99; p-value < 0.001) were significantly lower in the meningitis group. Preterm delivery (<37 weeks) was more common among affected neonates (63% vs. 44.6%; p-value = 0.049). No significant associations were found with gender, feeding patterns, residence, or delivery mode (p-value > 0.05). **Conclusion:** Meningitis complicates 38.3% of LOS neonates, with low birth weight and prematurity as significant risk factors. Routine lumbar puncture must be considered in all neonates with LOS for timely diagnosis and management, particularly in resource-limited clinical settings.

### INTRODUCTION

A bloodstream infection in newborns younger than 28 days is known as neonatal sepsis. It is still one of the main causes of newborn morbidity and mortality, particularly in middle- and lower-income nations. Depending on when the patient presents after delivery, it is classified as either early-onset sepsis or late-onset sepsis. Various experts use 72 hours or less than 7 days as the cutoff.<sup>(1)</sup> Neonatal meningitis is a potentially fatal illness that can have severe long-term effects. Bacterial meningitis still has a 20–60% poor outcome rate, despite improvements in critical care and preventive treatment.<sup>(2,3)</sup>

Because the pathogens vary depending on the patient's gestational age at birth, age at presentation, and geographic location, the clinical presentation is often subtle, and the results from infected individuals are inconsistent, it is still challenging to diagnose, even though the incidence and mortality have decreased over the past few decades.<sup>(4)</sup> Meningitis is more common during the neonatal era than at any other age. Newborns are more susceptible to meningitis because of their developing immune systems and the blood-brain barrier's permeability. It is still up for debate whether lumbar punctures should be used to acquire cerebrospinal fluid

(CSF) in infants born extremely preterm as part of an evaluation for late-onset sepsis.<sup>(5)</sup>

Rationale of this study is to determine the frequency of meningitis in neonates presented with late onset sepsis. Literature showed that frequency of meningitis is not so high in internationally reported study. But the rate is three times higher in Pakistani studies. Therefore, it is important to conduct a study confirm and resolve this ambiguity in local literature. Therefore, we have planned to conduct this study to get evidence for local population. This will help us to improve our knowledge and practice and in future, we will implement findings in local setting. The object of this study is to determine the frequency of meningitis in neonates presented with late onset sepsis

### METHODOLOGY

This cross-sectional study was conducted in the Department of Pediatrics at Hameed Latif Hospital, Lahore, from August 2024 to February 2025, following approval from ethical review committee (ERC letter number with date). The sample size was calculated by using the WHO calculator at a 95% confidence level, 6% margin of error, and an estimated meningitis prevalence of 12.5%<sup>(6)</sup>. Consecutive non-probability sampling was

employed for participant selection.

**Inclusion Criteria**

The study included 120 neonates aged 7-28 days diagnosed with late-onset sepsis, with Infants meeting the inclusion criteria were enrolled through the pediatric emergency department after obtaining informed consent from parents.

**Exclusion Criteria**

Comprised neonates previously treated for early-onset sepsis, those with neural tube defects (e.g., spina bifida, anencephaly), and critically ill infants unresponsive to initial stabilization.

Demographic and clinical data including age, gender, weight, symptom duration, birth weight, gestational age, Apgar score, delivery mode, feeding pattern, residence, and socioeconomic status were recorded. Lumbar puncture was performed on enrolled infants, and cerebrospinal fluid (CSF) samples were analyzed in the hospital laboratory. Meningitis was diagnosed based on predefined criteria: CSF glucose <50% of plasma glucose, white cell count >10/mm<sup>3</sup>, protein >80 mg/dL, and/or positive CSF culture. Neonates diagnosed with meningitis received standard management.

Data were analyzed using SPSS version 26.0. The Shapiro-Wilk test assessed data normality. Continuous variables (e.g., age, weight) were reported as mean ± SD, while categorical variables (e.g., gender, feeding pattern) were summarized as frequencies and percentages. Post-stratification by demographic and clinical factors, meningitis prevalence across subgroups was compared using the chi-square test, with statistical significance set at p-value ≤ 0.05.

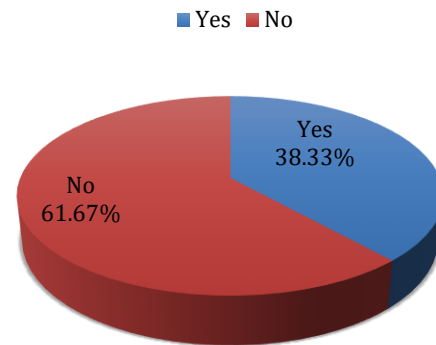
**RESULTS**

Out of a total of 120 neonates presenting with late-onset sepsis, 46 cases (38.3%) were diagnosed with meningitis. Comparative analysis between neonates with and without meningitis revealed no statistically significant differences in demographic or clinical characteristics (all p-values > 0.05) except birth weight and APGAR score. The mean age of neonates with meningitis was 17.80 ± 7.54 days, slightly higher than the 17.15 ± 5.77 days observed in those without meningitis. Mean birth weight in the meningitis group was 2314.34±380.32 grams, and mean current weight was 3124.41 ± 1243.59 grams. Gestational age at birth was also similar between groups, averaging 34.22 ± 4.05 weeks in neonates with meningitis. The mean duration of symptoms before presentation was 5.87 ± 3.04 days in this group. APGAR scores showed substantial variation (mean: 6.50±1.04 in the meningitis group). Among the neonates with meningitis, 56.5% (n=26) were male, and 43.5% (n=20) were female. Regarding place of residence, 39.1% were from rural areas, 30.4% from semi-urban areas, and 30.4% from urban areas. In terms of socioeconomic status, 37% of affected neonates belonged to low-income households, 30.4% to middle-income, and 32.6% to high-income families. Feeding patterns were relatively evenly distributed among meningitis cases: 34.8% were exclusively breastfed, 32.6% were bottle-fed, and 32.6% received both. Concerning the mode of delivery, 37% of neonates with meningitis were delivered via

spontaneous vaginal delivery (SVD), 47.8% via cesarean section, and 15.2% through induced labor. Frequency of neonates with birth weight <2500 g was significantly higher as compared to those without meningitis.

**Figure 1**

*Frequency of Meningitis in Neonates Presented with Late Onset Sepsis*



**Table 1**

*Comparison of Neonatal Characteristics in Relation to Meningitis Status*

	Meningitis		Total	p-value
	Yes	No		
	46	74	120	
Age	17.80±7.54	17.15±5.77	17.40±6.48	0.615
Weight	3124.41±1243.59	3202.82±1210.41	3172.76±1281.62	0.733
Birth Weight	2314.34±380.32	3013.10±434.05	2745.25±535.40	<0.001
Gestational age at Birth	34.22±4.05	35.31±3.50	34.89±3.74	0.120
Duration of Symptoms	5.87±3.04	5.65±2.75	5.73±2.85	0.682
APGAR Score	6.50±1.04	7.59±0.99	7.17±1.14	<0.001
Gender				
Male	26(56.5%)	38(51.4%)	64(53.33%)	0.581
Female	20(43.5%)	36(48.6%)	56(46.67%)	
Residence				
Rural	18(39.1%)	25(33.8%)	43(35.83%)	0.446
Semi Urban	14(30.4%)	31(41.9%)	45(37.50%)	
Urban	14(30.4%)	18(24.3%)	32(26.67%)	
Socioeconomic status				
Low	17(37%)	19(25.7%)	36(30%)	0.175
Middle	14(30.4%)	35(47.3%)	49(40.83%)	
High	15(32.6%)	20(27%)	35(29.17%)	
Feeding Pattern				
Breast feeding	16(34.8%)	26(35.1%)	42(35%)	0.864
Bottle Feeding	15(32.6%)	21(28.4%)	36(30%)	
Both	15(32.6%)	27(36.5%)	42(35%)	
Model of delivery				
SVD	17(37%)	27(36.5%)	44(36.67%)	0.197
Cesarean	22(47.8%)	26(35.1%)	48(40%)	
Induced	7(15.2%)	21(28.4%)	28(23.33%)	
Gestational Age				
<37 weeks	29(63%)	33(44.6%)	62(51.7%)	0.049
≥37 weeks	17(37%)	41(55.4%)	58(48.3%)	
Birth Weight				
<2500 g	28(60.9%)	6(8.1%)	34(28.3%)	<0.001
≥2500 g	16(39.1%)	68(91.9%)	86(71.7%)	

**DISCUSSION**

In this study, the frequency of meningitis among neonates with late-onset sepsis (LOS) was found to be 38.3%, aligning closely with earlier findings from tertiary care hospitals in Pakistan. This result underscores the importance of routine evaluation for meningitis in

neonates presenting with LOS, particularly in settings where clinical signs are often subtle and diagnostic delays can worsen outcomes. Our findings are consistent with the study by Saleem et al. at Gangaram Hospital, Lahore, which reported a meningitis frequency of 39.5% in neonates with LOS.<sup>(7)</sup>

Similarly, Khan et al. from MTI DHQ Dera Ismail Khan found an even higher frequency of 53.7%.<sup>(8)</sup> Mohit Baja from India reported the frequency of meningitis in late onset sepsis in newborn as 30.3%.<sup>(9)</sup> Both studies affirm the clinical overlap between sepsis and meningitis in the neonatal population, suggesting that lumbar puncture (LP) should be routinely considered in all neonates presenting with sepsis after 72 hours of life. In contrast, Naveed et al. reported a lower prevalence (22.4%) in a Lahore-based study, which may reflect differences in local protocols for LP or variability in clinical judgment when suspecting central nervous system (CNS) involvement.<sup>(10)</sup>

Ahmed L from Bangladesh reported the frequency of meningitis among neonates with late onset sepsis as 21.7%.<sup>(11)</sup> Despite variations in meningitis frequency across studies, most identify male gender, low birth weight, prematurity, and poor feeding as commonly associated factors. International studies, however, report variable prevalence. Umate et al. in Western India observed a 12.5% frequency of meningitis among 208 neonates with LOS<sup>(6)</sup>. Similarly Wondimu et al. from Ethiopia identified meningitis in 16.8% of neonates with LOS.<sup>(12)</sup> Lower rates in developed regions may reflect early intervention, better infection control, and consistent diagnostic practices, particularly the timely use of lumbar puncture. In our study, while males constituted a slightly larger proportion (56.5%) among neonates with meningitis, gender was not statistically significant ( $p$ -value= 0.581). This is comparable to findings by Khan et al. and Nafis et al., where male predominance was observed but not always statistically significant.<sup>(8, 13)</sup>

Contrary to these findings a local study from Peshawar reported significant association of male gender with meningitis.<sup>(14)</sup> The absence of statistically significant gender-based risk highlights the need to maintain a high index of suspicion for both sexes. This dominance of male gender might be due to a sex-linked genetic susceptibility to meningitis in males.<sup>(15)</sup> Regarding neonatal characteristics, our study did not find any significant associations with birth weight, gestational age, or duration of symptoms. The mean birth weight among meningitis cases was 2792.63±700.46 grams, and gestational age averaged 34.21±4.04 weeks, which are higher than figures reported by Nafis et al., where the average weight was 2.61 kg and preterm births were more common.<sup>(13)</sup>

Similarly, Ahmed et al. from Karachi identified low birth weight as a significant risk factor ( $p$ -value= 0.024), whereas our findings did not replicate this association.<sup>(16)</sup> This may suggest demographic or institutional differences in patient populations and referral patterns. A key observation in our dataset was the lack of significant relationships between meningitis and feeding pattern, delivery mode, socioeconomic status, or residence. While these variables may indirectly impact neonatal health outcomes, they were not individually predictive of meningitis in this cohort. Conversely, other studies have

emphasized the association between top feeding and poor outcomes. For instance, a Lahore-based study at Sharif Medical City Hospital found that exclusively breastfed infants had better recovery rates (94.5%) compared to top-fed neonates (77%).<sup>(17)</sup>

However, our data did not establish a meaningful difference in meningitis prevalence based on feeding methods ( $p$ -value= 0.864). Interestingly, our study revealed that the majority of neonates with meningitis had been delivered via cesarean section (47.8%). This contrasts with findings from Saleem et al., where vaginal delivery was slightly more common. Nonetheless, our analysis did not identify the mode of delivery as a statistically significant risk factor ( $p$ -value= 0.197), aligning with the broader literature, which often treats cesarean delivery as a background variable unless linked with prolonged hospitalization or infection risk.<sup>(7)</sup> A particularly relevant comparison can be drawn with the study by Afridi et al. from Hayatabad Medical Complex, Peshawar, which reported a meningitis prevalence of 52.4% in neonates with sepsis. That study also highlighted raised total leukocyte count (TLC) and C-reactive protein (CRP) as strong laboratory predictors, yet our dataset lacked these parameters for evaluation.<sup>(14)</sup>

Similarly, Khan et al. found lethargy and prior antibiotic use to be significantly associated with meningitis ( $p$ -value= 0.024 and  $p$ -value= 0.034, respectively).<sup>(8)</sup> Since our current analysis did not incorporate these clinical symptoms in the statistical comparison, future research should consider including laboratory and symptom-based indicators to strengthen predictive modeling.

According to an Indonesian study gestational age <37 weeks (Odds ratio=4.75,  $p$ -value=0.01) and birth weight <2500 g (Odds ratio=2.12,  $p$ -value=0.27) poses a significant risk for bacterial meningitis among late onset neonates sepsis.<sup>(18)</sup> Similar trend was seen in this study as among neonates with meningitis 60.9% had birth weight <2500 g and 63% gestational age at birth was <37 weeks. Similar findings were reported by Mohit Bajaj as per his findings 54.05% neonates with meningitis had birth weight 1.4-249 kg and 56.75% had preterm delivery.<sup>(9)</sup> Similar findings were reported by another study showing higher frequency of low birth weight (<2.5 kg: 63.1%) and preterm delivery (57.8%) among neonates with meningitis makes these parameters as significant risk factors.<sup>(19)</sup> Low birth weight is a well-known factor that increases susceptibility to infections in neonates. These infants often have underdeveloped immune systems, making them more prone to bacterial infections, including meningitis.<sup>(19)</sup>

Preterm neonates (<37 weeks) are at an elevated risk for meningitis, as their immune system and the blood-brain barrier are still developing. This has been documented in several studies, which show that preterm infants have a higher incidence of infections due to the incomplete maturation of key protective systems.<sup>(18, 19)</sup> Our results reinforce the diagnostic challenge posed by late-onset meningitis due to its non-specific presentation. The mean age of affected neonates was 17.8 days, comparable to the mean age in studies by Naveed et al. (17.7 days)<sup>(10)</sup> and Nafis et al. (16.2 days)<sup>(13)</sup>, supporting the idea that meningitis in LOS typically manifests during the third

week of life. This time window highlights the importance of timely LP within this critical period for suspected sepsis cases. Regional differences may be influenced by pathogen profiles.

This study had several limitations. First, it was conducted at a single center with a relatively small sample size, which may limit the generalizability of the findings. Second, the study did not include clinical symptomatology or laboratory markers such as CRP and TLC, which are frequently associated with meningitis risk. Additionally, the absence of microbiological data (e.g., CSF culture results) restricts our ability to comment on etiology and antibiotic resistance patterns. Finally, being a cross-sectional study, causal relationships could not be established. Future research should consider multicenter longitudinal designs, incorporate symptom-based and laboratory predictors, and assess long-term neurological outcomes

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## CONCLUSION

This study highlights that meningitis occurs in 38.3% of neonates diagnosed with late-onset sepsis (LOS), underscoring its critical role as a co-existing condition in this patient group. The results indicate that low birth weight and prematurity are significant risk factors for meningitis, with affected neonates having a substantially lower mean birth weight and APGAR scores. Despite no significant associations found with other clinical factors like gender, feeding pattern, or delivery mode, the findings emphasize the unpredictable nature of neonatal meningitis. These results reinforce the need for routine lumbar puncture in all neonates with LOS to ensure timely diagnosis and management, particularly in settings where clinical presentation may be subtle. The study calls for standardized protocols in resource-limited environments to improve diagnostic accuracy and prevent adverse outcomes, particularly for high-risk neonates.