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FREQUENCY OF MENINGITIS IN NEONATES WITH SEPSIS

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Abstract

Objectives: *To determine frequency of meningitis in neonates labelled to be suffering from neonatal sepsis.*

Study design: *Cross-sectional study.*

Place and Duration of the study: *Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from November-2024 to May-2025.*

Methodology: *A total of 146 term neonates admitted with the working diagnosis of neonatal sepsis were included. All the neonates were assessed for presence of meningitis as a cause of sepsis in neonates. Meningitis frequency as a sepsis cause in neonates was stratified by various confounding variables and post-stratification analysis was performed using Chi-square test. Data was analyzed using SPSS version 22.*

Results: *Median age of neonate was 12.00 (15.00) days. There were 88 (60.30%) male and 58 (39.70%) female neonates. Median gestational age was 39.50 (3.00) weeks. Median birth weight was 3.10 (0.30) kg. Among all NS cases, 41 (28.10%) were labelled as having EOS while 105 (71.90%) were labelled as case of LOS. Frequency of meningitis among neonates of present study who were originally labelled as a case of NS at the time of admission was 27 (18.50%).*

Conclusion: *In neonates admitted with the diagnosis of neonatal sepsis, frequency of meningitis was 18.50%.*

INTRODUCTION

Neonatal sepsis (NS) is a clinical phenomenon characterised by systemic sickness and bacteremia within the first month of life[1]. An estimate indicates that the global prevalence of newborn sepsis is 12.79% annually, with a fatality rate of 12.93% each year, which is considerable. [2] Early-onset sepsis (EOS) is a critical illness in neonates resulting from vertical transfer from mother to infant during parturition, manifesting within the initial 72 hours of life. Conversely, late-onset sepsis (LOS) manifests after 72 hours and is mostly contracted from the infant's surroundings, but it may occasionally arise from a delayed start of infections passed by the mother.[3] Numerous bacteria are recognized as causative agents of neonatal sepsis, including Acinetobacter, Klebsiella species, Salmonella paratyphi, Escherichia coli, Serratia species, Staphylococcus aureus, Group A Streptococcus, and Pseudomonas species. These bacteria are frequently recognized in instances of neonatal sepsis (NS). [4, 5]

When it comes to diagnostic evaluation of NS, in order to make a definitive diagnosis, best test that can be performed is blood culture that not only confirms the diagnosis but also provide information regarding the culprit organism along with its drug susceptibility. [6] However, it takes a lot of time for

which clinical assessment is crucial to correctly diagnose NS as well as the causative condition leading to NS. Signs and symptoms of neonatal sepsis are highly nonspecific, and this may result in failure to effectively find the underlying infectious process mimicking the clinical picture of NS, therefore, early and correct diagnosis of this potentially fatal condition remains a challenge. [7] Interestingly, studies have found that meningitis may be present with a clinical picture of NS, thus there is a possibility that the diagnosis of this infectious process may get delayed, potentially increasing the likelihood of developing long term neurological complications. [8] In this instance, a study found that the frequency of meningitis in neonates labelled originally to be suffering from NS was 19.3% with 22.8% in early NS type and 16.8% in late NS type. [8] Similarly, in another study, it was found that among neonates diagnosed with NS, meningitis was diagnosed to be actual infectious pathology in 16.25% of the neonates. [9]

Meningitis, if not treated promptly and appropriately, can result in development of various disabling long term complication in children including include seizures, hearing and vision loss, cognitive impairment, neuromotor disability and memory or behavioural changes. [10] Many cases of meningitis often get misdiagnosed as NS and thus have the potential to be treated inappropriately leading to high likelihood of developing neurological complication. Present study thus focuses on determining frequency of meningitis in neonates labelled to be suffering from NS.

METHODOLOGY

After getting institutional ethical committee clearance, this cross-sectional study was carried out at the Children Hospital, Pakistan Institute of Medical Sciences, Islamabad, from November 2024 to May 2025 (Ref No: F.1-1/2015/ERB/SZABMU/1340 dated 20-11-2024). The Raosoft ® sample size calculator was used to calculate the sample size using the following formula:

$$n = \frac{z^2_{1-\alpha/s} P(1-P)}{d^2}$$

Sample size calculation was performed by using confidence level 95%, precision of 6% and anticipated frequency of meningitis in neonatal sepsis of 16.25%. [9] This gave a sample size of 146. Non-probability consecutive sampling technique was used to select the sample.

Term neonates, aged 1-28 days, male and female, who were admitted at neonatal intensive care unit (NICU) with the working diagnosis of neonatal sepsis (NS) were included. Neonates with history of foetal anomalies detected on anomaly scan at 20 weeks, congenital neurological anomalies and chromosomal abnormality syndromes were excluded. All patients meeting the requirements for enrolment were enrolled in the study following acceptance of the study proposal from ethics committee and informed consent of the parents of participants. Baseline characteristics including age of neonate, gender, birth weight, gestational age at birth and type of neonatal sepsis (either early or late) were documented. A neonate was labelled to have the diagnosis of NS by presence of three of more of the following clinical signs including hyperthermia, hypothermia, hypoxaemia needing supplemented oxygen, tachycardia, bradycardia and hypotension. If the age of neonate was seventy two hours or less from time of birth, NS was classified as early while in case of neonatal age of more than seventy two hours, NS was classified as late. All these neonates were assessed for presence of meningitis by taking a 2ml sample of cerebrospinal fluid (CSF) obtained by performing lumbar puncture (LP) under aseptic conditions. The neonate was labelled to have meningitis in case of presence of > 30 leukocytes/mm, CSF protein > 200mg/dl and/or CSF sugar < 40mg/dl or 2/3rd of the blood glucose levels. In case meningitis was diagnosed in a neonate originally labelled as a case of NS, appropriate management was provided as per standard institutional guidelines.

Data was analysed using Statistical Package for Social Sciences (SPSS) version 22. Quantitative variables normality was checked by Shapiro-Wilk test which showed that age of neonate, gestational age at birth and birth weight were not distributed normally and were thus presented as median interquartile range (IQR). Qualitative variables (gender, type of neonatal sepsis and presence of meningitis) was presented as

frequency and percentages. Frequency of meningitis in neonates originally labelled as NS was stratified by age, gender, birth weight and type of neonatal sepsis and post-stratification comparative analysis was performed using Chi-square test. A p-value of ≤ 0.05 was considered as statistically significant.

RESULTS

In this study, 146 term neonates were included. Median age of neonate was 12.00 (15.00) days. There were 88 (60.30%) male and 58 (39.70%) female neonates. Median gestational age was 39.50 (3.00) weeks. Median birth weight was 3.10 (0.30) kg. Among all NS cases, 41 (28.10%) were labelled as having EOS while 105 (71.90%) were labelled as case of LOS. Patient demographics are given in Table-I:

Table-I: Patient demographics (n = 146)

Demographics	Median (IQR); n (%)
Median age of neonate	12.00 (15.00) days
1-14 days	88 (60.30%)
15-28 days	58 (39.70%)
Gender	
Male	88 (60.30%)
Female	58 (39.70%)
Median gestational age at birth	39.50 (3.00) weeks
Birth weight	3.10 (0.30) kg
< 3kg	45 (30.80%)
≥ 3kg	101 (69.20%)
Type of NS	
EOS	41 (28.10%)
LOS	105 (71.90%)

Abbreviations: IQR = Interquartile range, NS = Neonatal sepsis, EOS = Early onset sepsis, LOS = Late onset sepsis

Frequency of meningitis among neonates of present study who were originally labelled as a case of NS at the time of admission was 27 (18.50%). This frequency of meningitis in neonates originally labelled as NS is given in Table-II:

Table-II: Frequency of meningitis in neonates originally labelled as neonatal sepsis (n = 146)

Meningitis	n (%)
Yes	27 (18.50%)
No	119 (81.50%)

Stratification of frequency of meningitis in neonates originally labelled as NS by age, gender, birth weight and type of neonatal sepsis is given in Table-III:

Table-III: Stratification of frequency of meningitis in neonates originally labelled as neonatal sepsis by confounding variables (n = 146)

Stratification by age			
	1-14 days (n = 88)	**15-28 days (n = 58)**	**p-value**
Meningitis	18 (20.45%)	9 (15.52%)	0.452*
Stratification by gender			
	Male (n = 88)	**Female (n = 58)**	**p-value**
Meningitis	17 (19.32%)	10 (17.24%)	0.752*
Stratification by birth weight			
	< 3 kg (n = 45)	**≥ 3 kg (n = 101)**	**p-value**

Meningitis	9 (20.00%)	18 (17.82%)	0.754*
Stratification by type of NS			
	EOS (n = 41)	**LOS (n = 105)**	**p-value**
Meningitis	11 (26.83%)	16 (15.24%)	0.105*

Abbreviations: NS = Neonatal sepsis, EOS = Early onset sepsis, LOS = Late onset sepsis. * = Chi-square test.

DISCUSSION

Neonatal age is one of the most risk prone period in the life of a human being in which there is high propensity of developing a myriad of morbidities particularly the infections that can threaten the life of a new born due to immaturity of the immune system. [11, 12] Present study focused on one such type of infection which may be mislabelled as NS, i.e., meningitis. In present study, average age of the neonate admitted with the diagnosis of infectious aetiology was twelve days with majority of the labelled NS cases being of the younger age group. The possible reason behind this trend of younger neonates to be more susceptible to sepsis compared to older neonates can be attributed to the progressive development of the immune system as the baby grows making their immunity relatively stronger to fight off infectious agents. [13]

Upon assessment of the gender distribution of the septic neonates, it was observed that more than half of the neonates were male constituting 60.3% of the total population. Similar to this, a study was conducted by Nguyen et al. [14] in which similar dominance of males to be septic as compared to female neonates was observed, with males constituting 54.1% of septic neonates. Similarly, Yu et al. [15] found the similar trend of male neonates to be more affected by NS making up 56.2% of the septic neonates. This higher propensity of males to get infected can be attributed to the higher metabolic demand of the male babies since their growth rate is much more accelerated for which if there is even a slightest reduction in the oxygen delivery during pregnancy, birthing process or post-natal period leads to lacticacidaemia and higher chances of contracting an infection. [16]

When it comes to analysis of the frequency of neonates to have meningitis who were originally admitted with the working diagnosis of NS was 18.50%. Compared to this, a study was conducted by Wondimu et al. [8] in which it was observed that the frequency of meningitis among neonates labelled to have NS was 19.3%. Similarly, in another study which was conducted by Ahmad et al. [9] in which they assessed neonates who were considered to have diagnosis of NS, it was found that meningitis was present in 16.25% of the neonates. In another study, it was observed that the frequency of patients who actually had meningitis but were originally labelled as clinically suspected cases of NS was 20.56%. [17] Similarly, in another study conducted by Parmar et al. [18], meningitis was found to be affecting 20% of the neonates who were admitted as clinically suspected cases of NS. Frequencies reported in these studies were almost similar and comparable to the frequency of this condition in NS labelled cases being found in present study. Contrarily, a study was conducted by Hussain et al. [19] in which much higher frequency of meningitis in neonates labelled to be suffering from NS was found and was reported at 34.5%. The exact reason for such differences between various previously conducted studies and present study regarding meningitis frequency could not be found but possible reasons include differences in the sample size, demographics, neonatal clinical presentation and diagnostic facilities.

Upon analysis of the stratification of the meningitis frequency by various confounding variables, it was found that there was no significant difference of frequency of this condition in neonates labelled as NS cases in different age groups (p = 0.452), gender (p = 0.752), birth weight (p = 0.754) and type of NS (p = 0.105). Similar to this, a study was conducted by Naveed et al. [20] found no significant difference regarding meningitis frequency distribution (p = 0.816) among genders. Contrarily, a study was conducted by Kumar et al. [21] in which this distribution of meningitis across different types of NS showed a significant difference (p = 0.006) which was not the case in present study.

Based on the results of present study, it is evident that meningitis can be present at quite a high

frequency in neonates who are often labelled as cases of NS, therefore, practice of screening patients with NS for presence of meningitis is strongly recommended to be adopted as standard of care. There were no limitations of present study.

CONCLUSION

In conclusion, among neonates admitted with the working diagnosis of neonatal sepsis, frequency of meningitis was 18.50%.

CONFLICT OF INTEREST

None.

INFORMED CONSENT

Obtained from the parent in written form.

ETHICAL APPROVAL

Obtained from the institution (Ref No: F.1-1/2015/ERB/SZABMU/1340 dated 20-11-2024).

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