Frequency of Bacterial Meningitis in Neonates presenting with Sepsis to Department of Pediatrics, Sheikh Zayed Hospital, Rahim Yar Khan

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Abstract

Background: Bacterial meningitis is a devastating infection leading to high mortality and morbidity in neonates. Prompt diagnosis and treatment of bacterial meningitis are essential for achieving good outcomes in affected infants. Over the last several decades, overall incidence and mortality have declined, but morbidity associated with neonatal meningitis remains virtually unchanged.

Objective: To determine the frequency of Bacterial Meningitis in Neonates presenting with sepsis to the Department of Pediatrics, Sheikh Zayed Hospital, Rahim Yar Khan.

Methodology: It was a descriptive cross-sectional study conducted in the Pediatric ward, Sheikh Zayed Hospital, Rahim Yar Khan, from July 2021 to January 2022. A total of 120 neonates of either sex with age ≤28 days, who were diagnosed cases of sepsis, were included. Patients with Congenital Heart Disease i.e., ASD, VSD, AV malformations, TB Meningitis, and Bleeding disorders were excluded. Every patient fulfilling the criteria of sepsis as per the operational definition underwent lumbar puncture under full aseptic measures by a medical officer with at least one year of experience in the pediatric department and was labeled as bacterial meningitis.

Results: Mean age of neonates was 15.18±4.96 days. Out of the 120 patients, 79 (65.83%) were male and 41 (34.17%) were female, with a male-to-female ratio of 1.9:1. The frequency of Bacterial Meningitis in this study was 29 (24.17%) neonates presenting with sepsis.

Conclusion: The study found a high frequency of Bacterial Meningitis among neonates presenting with sepsis, highlighting the critical need for routine cerebrospinal fluid evaluation in septic neonates.

Keywords: Bacterial Meningitis, Neonates, Sepsis

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Introduction

Neonatal septicemia is a systemic infection occurring in neonates (≤28 days of life). It is one of the leading causes of morbidity and mortality in neonates.[1] It can further be divided into early and late onset sepsis. Early Onset Sepsis (EOS) is defined as bacteremia occurring at ≤72 hours of age in infants hospitalized in the neonatal intensive care unit (NICU). If it occurs>72 hours of age in NICU infants, then it is termed late-onset sepsis.[1,2]

Neonatal Sepsis (NS) is a worldwide problem. Previous studies showed that neonates are at risk for bacterial septicemia, having a worldwide prevalence of 1 to 10 per 1000 live births.[3,4] Similarly, different etiological agents have been found in different studies. The evidence from the literature found that the commonest etiological agent is Group B streptococcus (GBS), while Escherichia Coli (E. Coli) is the most common cause of mortality.[2] Min Lee found that E. Coli was the most commonly occurring in 11.8% of patients.[4] Similarly, in a study in Hayatabad, E. Coli was found to be the most common in (40.91%) cases, followed by Klebsiella (19.32%), Staphylococcus aureus (15.91%), Pseudomonas aeruginosa (13.63%), and Staphylococcus epidermidis (10.23%).[5] Neonatal sepsis is the most important cause of morbidity and mortality in neonates throughout the world, in both developing and developed countries, despite high hygienic measures, best health services in hospitals, access to antibiotics for prophylaxis, treatment, and best advanced intensive care facilities.[1] Bacterial meningitis in children is a neurological emergency that, despite advances in medical management, continues to lead to significant morbidity and mortality.[6]

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Although meningitis in neonates is a devastating infection associated with high mortality and morbidity. Due to prompt diagnosis and treatment, overall prevalence and deaths have declined over the last few decades, but morbidity associated with Bacterial Meningitis remains high. The incidence of culture-positive bacterial meningitis is estimated at 0.3 per 1000 live births, and mortality ranges from 10-15% in developed countries. Data is scarce regarding the developing countries.[6-8] There are various risk factors that share the same mechanisms for sepsis as well as for meningitis. Prematurity, indwelling catheters, delayed breastfeeding, and weight less than 1.5 kg are among the salient ones.[9] According to one study by Khurshid A et al, in their study on 73 neonates with sepsis, meningitis was seen in 20 (27.4%) of the cases.[10]

Sepsis, especially in neonates, can be life-threatening, especially where there is a complication like meningitis; as clinical symptoms are not as classical as in adults, and the management plan is definitely different, oriented to this than sepsis alone. Along with this presence of drug facilities and disease pattern is also difference across the globe due to variation of the local flora; that's why this study was planned to see the prevalence of this dreadful complication, so that if it is found high, it can be carried out on priority basis to rule out and manage to avoid significant degree of morbidity and mortality. The objective of this study was to determine the frequency of Bacterial Meningitis in neonates presenting with sepsis to the Department of Pediatrics, Sheikh Zayed Hospital, Rahim Yar Khan.

Methodology

This was a descriptive, cross-sectional study conducted in the Pediatric Ward of Sheikh Zayed Hospital, Rahim Yar Khan, over a period from July 2021 to January 2022. The sample size was calculated as 120 participants, based on a 95% confidence level, a 5% margin of error, and an anticipated prevalence of meningitis in neonates with sepsis of 27.4%, as reported in a previous study.[10] A non-probability consecutive sampling technique was used to enroll participants meeting the inclusion criteria. All neonates aged ≤28 days of either sex who were diagnosed with sepsis according to the operational definition were included in the study. Cases with documented Congenital Heart diseases (e.g., ASD, VSD, AV malformations), Tuberculosis Meningitis, or bleeding disorders were excluded based on medical records and history.

Neonatal sepsis was labeled as yes when all of the following were present for at least 1 day: temperature more than 100^{0}F, WBC count more than 11,000 or less than 4,000 mg/dl, and Blood culture positive within 72 hours, assessed by growth of bacteria on the basis of colony formation of any number. Bacterial Meningitis was labelled when the CSF picture showed all of the following: Polymorph Nuclear Pleocytosis (more than 500 neutrophils per cubic mm) with increased CSF protein (more than 100 mg/dl) and decreased CSF glucose concentration (less than 60% of the corresponding plasma level checked at the same time as CSF examined).

Data collection began after obtaining approval from the Institutional Review Board of Sheikh Zayed Medical College/ Hospital, Rahim Yar Khan (Ref. No. 27/IRB/SZMC/RYK, Dated: 13-06-2021). Informed consent was obtained from the parents or guardians of each participant. Neonates presenting to the pediatric emergency department or admitted to the ward, who fulfilled the inclusion criteria were enrolled in the study. Socio-demographic data, including age in days, weight in kilograms, and gender, were recorded on a pre-designed proforma. Additional information, such as duration of sepsis, presence of prematurity (yes/no), and breastfeeding status (yes/no), was also collected. Weight was measured using an electronic weighing machine. Each patient who met the operational criteria for sepsis underwent a lumbar puncture under full aseptic conditions performed by a medical officer with at least one year of experience in the pediatric department. Based on the results of cerebrospinal fluid (CSF) analysis, the patient was classified as having Bacterial Meningitis (yes/no) according to the defined operational criteria, and the findings were recorded on the same proforma. For data analysis, SPSS version 21 was used. Quantitative variables such as age, weight, white blood cell (WBC) count, and duration of sepsis were expressed as mean ± standard deviation (SD). Frequency and percentages were calculated for qualitative

variables, including gender, breastfeeding status, prematurity, and the outcome variable, i.e., detection of bacterial meningitis. Stratification was performed across potential effect modifiers such as age, weight, gender, duration of sepsis, breastfeeding, and prematurity to assess their influence on the outcome. Post-stratification chi-square tests were applied, and a p-value <0.05 was considered statistically significant.

Results

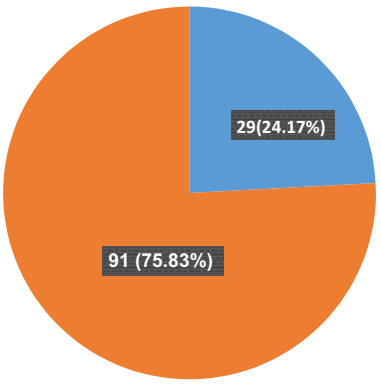
The mean age of neonates was 15.18±4.96 days. Out of the 120 patients, 79 (65.83%) were male and 41 (34.17%) were female, with a male-to-female ratio of 1.9:1. Mean duration of sepsis was 3.45±1.34 days. Mean weight was 5.75±0.71 kg. Out of 120 patients, 66 (55%) were breastfeeding. Out of the total 120 patients, 69 (57.5%) were of age up to 14 days. (Table I)

Table-I: Age distribution of the patients. (n=120)

Age (in days)	No. of Patients	Percentage
≤14	69	57.5
15-28	51	42.5
Total	120	100

Regarding gestational age 38 patients were premature. The frequency of bacterial meningitis in this study was 29 (24.17%) neonates presenting with sepsis. (Figure I)

Figure-I: Frequency of Bacterial Meningitis in Neonates presenting with Sepsis (n=120)



The distribution of Bacterial Meningitis among neonates was analyzed across various demographic and clinical variables. Among the 120 neonates, stratification by age group revealed that 17 out of 69 (24.64%) neonates younger than 14 days had Bacterial Meningitis compared to 12 out of 51 (23.53%) in the 15-28 days age group, with no statistically significant difference (p=0.883). When analyzed by gender, 13 out of 72 (18%) male neonates had meningitis compared to 16 out of 48 (33.33%) female neonates; however, this difference was also not statistically significant (p=0.127). Analysis by weight showed a comparable frequency of meningitis in neonates weighing less than 5 kg, 14 (23.73%) out of 59, and those weighing 5 kg or more, 15 (24.59%) out of 61, with p = 0.684. In contrast, prematurity showed a strong association with Bacterial Meningitis: 20 out of 38 (52.63%) premature neonates developed meningitis compared to only 9 (10.98%) out of 82 term neonates (p<0.001).

Regarding breastfeeding status, significantly lower rates of meningitis were observed among breastfed neonates 10 (15.15%) out of 66 compared to those who were not breastfed 19 (35.19%) out of 54, with a p-value of 0.007, indicating a statistically significant protective effect of breastfeeding. (Table II)

Table-II: Stratification of Bacterial Meningitis by Demographic and Clinical variables (n=120)

Variable	Category	Total Patients	Patients with Meningitis	P-value
Age Group (days)	**<14**	69	17 (24.64%)	0.883
	15–28	51	12 (23.53%)	
Gender	**Male**	72	13 (18.06%)	0.127
	Female	48	16 (33.33%)	
Weight (kg)	**<5 kg**	59	14 (23.73%)	0.684
	=5 kg	61	15 (24.59%)	
Prematurity	**Premature**	38	20 (52.63%)	<0.001
	Term	82	9 (10.98%)	
Breastfeeding	**Yes**	66	10 (15.15%)	0.007
	No	54	19 (35.19%)	

Discussion

Neonatal septicemia is the most common cause of mortality and morbidity in neonates throughout the world, including developed countries where there is the availability of good hygienic measures and advanced neonatal intensive care. A neonate with sepsis is at risk of meningitis. Meningitis in neonates

is defined as infection of the CNS and meninges in the 1st 28 days of life. Regarding the incidence of Neonatal Meningitis in sepsis, most of the studies done in developed countries have a lack of data from developing countries, where mortality and morbidity are high. In some studies, it is reported [11–14] that the incidence of bacterial meningitis throughout the world is 0.8 to 6.1/1000.

A multi-center survey was done in Hebei Province, China,[15] showed that the incidence of meningitis is 0.5/1000 in neonates. Out of all the causes of neonatal mortality, the most common is bacterial meningitis. Mortality of meningitis in the last 5 years is 9.1% and neurological complications occur at a rate of 5.9% in terms of studies in China.[16] The investigations for diagnosis of neonatal septicemia include complete blood count, C-reactive protein, gastric and tracheal aspirate, blood culture, urine culture, and, most importantly, CSF complete examination and culture to detect meningitis. The treatment for neonatal sepsis includes broad-spectrum antibiotics like ampicillin and aminoglycosides. The antibiotic should be narrowed once the causative organism is identified on culture. Treatment of uncomplicated meningitis due to group B streptococcus is given for 14 days, and meningitis due to gram negative organism is treated for 21 days or 14 days after obtaining a negative culture.

Most of the neonates with meningitis have negative blood cultures. This discordance between results of blood and CSF culture emphasize the need for culture of CSF in neonatal sepsis. Escherichia coli, coagulase-negative staphylococcus, and streptococcus are the 3 most common pathogenic bacteria, while in the developed countries, the most common organisms are group B streptococci and Listeria, according to a Chinese domestic study.[15] Current study was conducted to determine the frequency of bacterial meningitis in neonates presenting with sepsis. The mean age of neonates was 15.18±4.96 days. Out of the 120 patients, 79 (65.83%) were male and 41 (34.17%) were female, with a male-to-female ratio of 1.9:1. In this study, it was found that the frequency of bacterial meningitis was 29 (24.17%) in neonates presenting with sepsis. According to one study by Khurshid A et al, in their study on 73 neonates with sepsis, meningitis was seen in 20 (27.4%) of the cases.[10] Out of the 120 patients, 79 (65.83%) were male and 41 (34.17%) were female. There is a slight predominance of male neonates suffering from sepsis and meningitis, but not by infections in utero according to some historical data. Later on, studies failed to confirm this association among male infants.[9,11,12] Risk factors are the same for the development of neonatal meningitis and sepsis. The immature immune system of the neonate and decreased maternal antibodies all contribute to increased risk of sepsis in both preterm and term infants. Most of the maternal antibodies do not cross the placenta before 32 weeks of gestation, which is why neonates born extremely preterm are at the highest risk for infections. The majority of IgG is acquired by the fetus during the last 4 weeks of pregnancy,[17] as this study shows neonatal meningitis is slightly more common in preterm neonates (52.63%). Early start of breastfeeding is thought to be protective against infections due to transfer of antibodies (immunoglobulin A).[18] Out of 66 breastfed neonates, 10 (15.15%) had meningitis, and out of 54 who were not on breastfeeding, 19 (35.19%) had meningitis, showing that breastfeeding is protective against infection.

Conclusion

The study found a high frequency of Bacterial Meningitis among neonates presenting with sepsis, highlighting the critical need for routine cerebrospinal fluid evaluation in septic neonates. Prematurity was identified as a significant risk factor, while breastfeeding showed a protective effect, underscoring the importance of targeted preventive strategies and early intervention to reduce morbidity and mortality.

Authors Contribution: SC: Conception of work, Acquisition and Analysis of data and Drafting. **SK & HMU:** Acquisition and Analysis of data, Interpretation of data and revising. **JA & UM:** Design of work, Acquisition and Analysis of data and revising. **MT:** Interpretation of data and revising.
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Conflict of Interest: No conflict of interest among authors.

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