MS No: PJMDS/OA/010/2024

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 hospital Larkana.

Methodology: A cross-sectional study was carried out in the Paediatrics Department of Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU), Larkana from January 2022 to July 2022. In this study, lumbar puncture under aseptic measures was done and sent for CSF analysis in microbiology and biochemistry lab for cytology, protein, and glucose to assess the outcome variable i.e. bacterial meningitis. All the data was evaluated and interpreted using SPSS version 26.0.

Results: A total of 250 participants diagnosed with neonatal sepsis were included. The mean age was 16.48 days with an age range of 7 to 27 days. Males were 58.4% and females were 41.6%. Meningitis was noted in 16% of patients.

Conclusion: In conclusion, the significant occurrence of bacterial meningitis in neonates with late-onset sepsis highlights the need for routine screening and prompt treatment. Early lumbar punctures and standardized protocols for diagnosis and management should be prioritized to improve outcomes in this vulnerable population.

Keywords: Bacterial meningitis, Neonates, Prevalence, Sepsis

INTRODUCTION

Meningitis poses substantial risks, especially for infants. Several causes can trigger meningitis, with viruses and bacteria being chief among them. Roughly a quarter of cases have unknown origins[1]. Bacterial meningitis in newborns, occurring within the first 28 days of life with proof of bacteria in the cerebrospinal fluid, is an inflammation of the protective membranes surrounding the brain and spinal cord[2]. Incidence varies between 0.25 and 1 case per 1000 live births and impacts 25% of infants with bacteria in the bloodstream[3]. Regrettably, approximately 10% of affected babies die and 20-50% of survivors live with seizures, hearing or vision problems, cognitive difficulties, and motor impairments[4]. Prenatal factors risking neonatal bacterial meningitis include premature rupture of membranes, vaginal infections in the mother, untreated bladder bacteria, preterm birth, low birth weight, and lack of oxygen during delivery. Bacterial meningitis is commonly the complication arising from neonatal sepsis[5].

Sepsis is responsible for around 30 to 50 percent of total neonatal deaths in developing nations such as India and Pakistan, according to various reports[6]. Early and late onset sepsis have been documented as occurring either before or after 48 hours of age, 72 hours of age, or 96 hours of age[7]. Late Onset Sepsis (LOS) was characterized as an infection arising after 7 days of age up until 28 days of age with two or more clinical signs of sepsis like reluctance to feed, letharginess, unstable temperature, axillary temperature below 36°C or above 38°C, feeding intolerance, apnea, respiratory distress, capillary filling time exceeding 3 seconds on the forehead or sternum, vomiting, diarrhea, abdominal distension, rapid rise in serum bilirubin over 15mg% in the absence of a blood group incompatibility, petechiae or bleeding diathesis, mottling, bulging fontanelle and convulsions and so on were present [8]. Laboratory markers of complete blood count and C-reactive protein level were deemed abnormal if - total white blood cell count under 5000/ cm or over 25000/cm, absolute neutrophil count below 1500/ cm, immature total neutrophil ratio over 0.2 and peripheral blood film showed nucleated red blood cells with the presence of toxic granules and bands and thrombocytopenia (platelet count under 1500000/cm[9]. Any newborn with bacterial sepsis is also at risk for meningitis. As such, the incidence of meningitis in neonatal sepsis has varied from 0.3-3% in various studies, but late onset septicemia has been reported to be fairly associated with meningitis; with percentages ranging from 3 to 30%[10]. In cases of LOS, a lumbar puncture should be performed on all infants prior to starting antibiotics.

Studies have shown that the incidence of meningitis in newborns with late-onset sepsis (LOS) varies significantly, ranging from 1.3% to 3.5%[11,12]. In one study, Kaul V et al. reported an unusually high prevalence of 22.5% of meningitis in neonates with suspected clinical sepsis at a major tertiary care neonatal center in Northern India[13]. Additionally, two other studies from Northern[14] and Central India[15] documented meningitis frequencies of approximately 17% in infants with LOS.

However, localized information from Pakistan remains scarce[16]. The initial signs of bacterial meningitis in newborns and late sepsis lack distinguishing characteristics, complicating distinctions across a diverse population[17]. This could induce delays in diagnosis which subsequently affect the outcomes and survival rates of patients[18]. Research found the mortality rate in neonates with meningitis in suspected late-onset sepsis was a devastating 45.5%[19]. Considering these backgrounds, we require identifying the frequencies and risk factors of bacterial meningitis in late-onset neonatal sepsis at tertiary medical centers.

METHODOLOGY

This cross-sectional study was conducted by the Pediatrics Department of Shaheed Mohtarma Benazir Bhutto Medical University (SMBBMU) in Larkana over a six-month period from January to July 2022. A total of 250 children were included in the

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Submitted: *June 03, 2024*
Revised: *August 19, 2024*
Accepted: *September 02, 2024*

study, selected using a non-probability consecutive sampling technique. Participants were enrolled sequentially as they presented or became available during the study. The sample size was determined using the W.H.O. sample size calculator, based on a 22.5% frequency of bacterial meningitis in neonates with late-onset sepsis, with a margin of error of 6.1% and a 95% confidence level.

The study included neonates aged 7 to 27 days from both genders who presented with late-onset sepsis. To maintain the accuracy of clinical findings, infants who had received antibiotics prior to enrollment were excluded to avoid interference with cerebrospinal fluid (CSF) results. Additionally, infants with low birth weight (<1000 grams) were excluded due to their higher risk of complications that could confound the results. Infants on total parenteral nutrition were also excluded, as this intervention can alter CSF composition and inflammatory response, potentially skewing the outcomes. Infants with dysmorphic features were not included due to potential confounding from underlying genetic or developmental conditions.

Eligible participants were identified upon visiting the Pediatrics department, and those meeting the inclusion criteria were enrolled after obtaining informed consent from their parents. Ethical approval was secured from the ethical review committee, and strict confidentiality was maintained throughout the study.

Demographic data, including age, gestational age, weight, and gender, were recorded on a pre-designed proforma. A lumbar puncture was performed under aseptic conditions at the lumbar region between the L3 and L4 vertebrae to collect CSF samples. The diagnosis of acute bacterial meningitis was confirmed if the CSF examination revealed all of the following: leukocyte count > 10/mm³, predominance of neutrophils, CSF protein level > 45 mg/dl, and a CSF glucose level < 2/3rd of the corresponding blood glucose level. These CSF samples were analysed in the microbiology and biochemistry laboratories for cytology, protein, and glucose levels to assess the primary outcome variable, which was the presence of bacterial meningitis.

Data analysis was conducted using SPSS version 26.0. Descriptive statistics was calculated to summarize the data. The Chi-square test was applied to assess the statistical significance, with a 5% level of significance ($p < 0.05$) considered as the threshold for determining significant associations.

RESULTS

The study encompassed 250 participants diagnosed with neonatal sepsis, and their demographic and clinical characteristics were examined. The gender distribution revealed 58.4% males and 41.6% females. Gestational age varied, with 54.4% classified as preterm and 45.6% as term. The mean age was 16.48 days, with 42.4% falling within the 7-14 days category. Weight distribution showed 88.0% with a weight of 1.6-3.0 kg. Laboratory parameters, including platelets, WBC, leukocyte count, CRP level, protein level, and glucose level, were measured, providing valuable insights. Clinical features observed in neonates with sepsis included seizures (88.8%), fever (53.2%), abdomen distension (14.0%), lethargy (68.0%), shock (22.0%), convulsions (14.4%), temperature instability (34.8%), respiratory distress (71.2%), and reluctance to feed (25.0%). These findings contribute to a comprehensive understanding of the characteristics associated with neonatal sepsis in the studied population as shown in Table I.

The data reveals the distribution of different bacterial species, with 15 occurrences of Klebsiella, 19 occurrences of E. coli, 8 occurrences of Pseudomonas, 19 occurrences of Acinetobacter, and 14 occurrences of Enterobacter (Figure 1).

In the bacterial meningitis cohort, 18 out of 40 patients (45.0%) demonstrated blood culture positivity, compared to 67 out of 210 patients (31.9%) in the non-meningitis cohort. Conversely, blood culture negativity was observed in 22 patients (55.0%) within the meningitis group and 143 patients (68.1%) in the non-meningitis group. The association between blood culture positivity and bacterial meningitis yielded a 95% confidence interval of 0.878 to 3.472, with a p-value of 0.109 as shown in Table II.

The discharge rate was 80.0% for meningitis and 77.1% for non-meningitis, with no significant difference (p=0.691). Eight cases in the meningitis group (20.0%) and 48 cases in the non-meningitis group (22.9%) resulted in death. The duration of hospital stays was 20.7±8.5 days for meningitis and 19.3±9.7 days for non-meningitis, with no significant difference (p=0.402). Additionally, the duration of antibiotic treatment showed no significant difference between the two groups (p=0.803) as documented in Table III.

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

Variable	**n (%)**
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)
LABORATORY PARAMETERS (Mean ± SD)	
Platelets	146612 ± 63512.8
White Blood Cells	12376 ± 4120.9
Leukocyte	22801.1 ± 8563.6
C-Reactive Protein	5.8 ± 1.3
Protein Level	128.9 ± 42.9
Glucose Level	34.1 ± 13.7

Presenting features in neonates with sepsis with or without meningitis	
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 1: Microorganisms isolated in the study group.

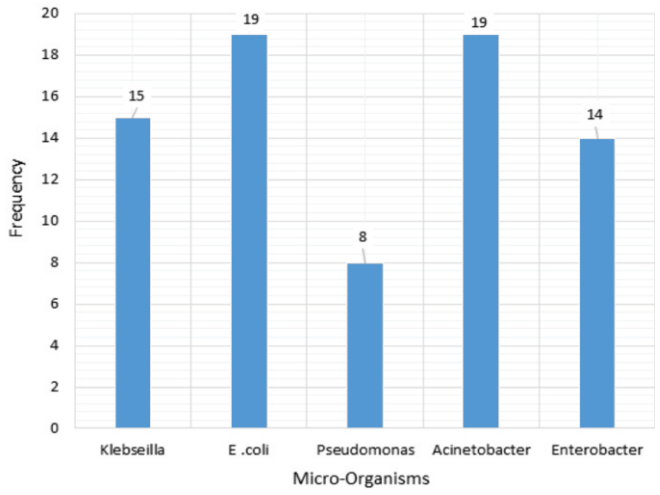

Table II: Showing Blood culture positivity in bacterial meningitis and non-meningitis patient (n=250)

Blood Culture	Bacterial Meningitis			P-Value
	Meningitis (n=40)	**Non-Meningitis** (n=210)	**95% C. I**	
Positive	18 (45.0%)	67 (31.9%)	(0.878----3.472)	0.109
Negative	22 (55.0%)	143 (68.1%)		

Table III: In-Hospital Outcome of bacterial meningitis and non-meningitis patient (n=250)

Outcome	Bacterial Meningitis			P-Value
	Meningitis (n=40)	**Non-Meningitis** (n=210)	**95% C. I**	
Discharge	32 (80.0%)	162 (77.1%)	(0.512----2.743)	0.691
Died	8 (20.0%)	48 (22.9%)		
Hospital Stays (days)	20.7 ± 8.5	19.3 ± 9.7	(18.42----20.80)	0.402
Duration of antibiotic treatment (days)	9.7 ± 2.3	9.8 ± 2.3	(9.54----10.13)	0.803

DISCUSSION

Bacterial meningitis in infants presenting with late-onset bloodstream infections is a grave medical circumstance marked by inflammation of the protective layers enveloping the mind and spinal cord brought on by bacterial invasion. Infants are newborns who are under 28 days old, and late-onset bloodstream infections generally surface after the initial week of life. This circumstance is an acute and potentially deadly complication that necessitates instant medical attention.

Neonatal bacterial meningitis is a rare but potentially devastating condition that can have profound consequences on a baby's health and development. It often presents as a secondary infection in infants who are already suffering from sepsis, a systemic infection that can affect various organs in the body. Late-onset sepsis refers to infections that occur after the first few days of life and are usually associated with hospitalization or healthcare exposure.

The clinical presentation of neonatal bacterial meningitis in the context of late-onset sepsis can be subtle and nonspecific, making it challenging to diagnose promptly. Infants may exhibit symptoms such as fever, poor feeding, irritability, lethargy, vomiting, and abnormal movements. The condition can progress rapidly, leading to severe neurological complications, including seizures, developmental delays, hearing loss, and even death if not managed promptly.

Neonatal sepsis is a complex clinical syndrome characterized by indicators and manifestations of infection with or without

accompanying bacteremia in the primary month of life. It can encompass diverse systemic infections of the newborn like meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections. There is no consensus on how exactly to separate neonatal sepsis and meningitis in times after birth. Earlier and late onset sepsis has been documented as arising before or following 72 hours of age or potentially 96 hours of age[21]. The initial week of life is often reported as early onset sepsis with a subgroup of infections that blossom during the primary 24 hours of life called extraordinarily early onset infections[22]. Later onset infections occur during the second to fourth weeks of life while infections from day 28-30 to day 120-180 are called remarkably late onset infections.

In this study, bacterial meningitis was noted in 16% of neonates. In another study, meningitis was reported in children with late-onset sepsis to be 16%[13]. A study by Saleem S, et al stated the frequency of bacterial meningitis in neonates with late onset of sepsis as 39.5%[23].

Given the serious nature of this condition, early recognition and intervention are crucial. Timely administration of antibiotics and supportive care are essential to improve the chances of a positive outcome. This often involves a combination of diagnostic tests such as lumbar punctures to analyze cerebrospinal fluid, blood cultures, and imaging studies to confirm the diagnosis and guide treatment.

The study's sample size and single-site focus may limit generalizability and fail to capture all risk factors for bacterial meningitis in neonates with LOS. Non-probability sampling and reliance on conventional diagnostic methods might introduce bias and underdiagnosis.

Future studies should expand to multiple centers and larger samples, develop better diagnostic tools, and explore long-term outcomes and preventive strategies to reduce the incidence of neonatal bacterial meningitis.

CONCLUSION

In conclusion, the significant occurrence of bacterial meningitis in neonates with late-onset sepsis highlights the need for routine screening and prompt treatment. Early lumbar punctures and standardized protocols for diagnosis and management should be prioritized to improve outcomes in this vulnerable population.

Conflict of Interest: Authors declare that there is no conflict of interest.

Authors' Contributions: The successful completion of the research was the result of the collaborative efforts of all authors. **Altaf T;** conceived the study, led the design, and prepared the manuscript, playing a key role in the project. **Bhojwani SL;** supervised the study and contributed to manuscript revision. **Rahman A;** handled patient recruitment and data collection. **Lal S;** assisted with data analysis. Each author played a crucial role in the study's success.

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How to cite: Altaf T, Bhojwani SL, Rahman A, Lal S. Frequency of Meningitis in Neonatal Late Onset Sepsis. Pak J Med Dent Sci. 2024;1(1):21-25