Objective: The objective of this study was to determine the incidence of meningitis in neonates with late-onset sepsis (LOS) in the West India population.

Materials and Methods: This prospective observational study enrolled 208 neonates with signs and symptoms suggestive of sepsis with positive C-reactive protein at or more than 72 h of postnatal age. Results: Out of total 208 neonates with LOS, 12.5% neonates had meningitis. The incidence of LOS in preterm and low-birth-weight neonates were 73.6% and 72.1%, respectively. Most common presenting features in neonates with LOS with or without meningitis were respiratory distress (72.6%), followed by lethargy (68.8%) and refusal to feed (63%). Blood culture was positive in 53.8% neonates who had meningitis. Mortality in neonatal meningitis was 3.84%. Conclusion: This study demonstrated that a significant number of neonates with LOS have coexistent neonatal meningitis. Our study highlights the diagnostic utility of routine lumbar puncture in neonates with clinical features of sepsis.

Keywords: Incidence, late-onset sepsis, meningitis

INTRODUCTION

Neonatal sepsis is one of the most common causes of neonatal mortality.[1] Worldwide, neonatal mortality accounts for approximately 5 million deaths each year, 96% of which occurs in developing countries.[2,3] In developing countries, sepsis is responsible for approximately 30%–50% of the total neonatal deaths.[2] According to the data from the National Neonatal-Perinatal Database (NNPD), incidence of neonatal sepsis is 30/1000 live births.[4]

Neonatal sepsis is mainly categorized as early-onset sepsis and late-onset sepsis (LOS). LOS presents after 72 h of age with septicemia, pneumonia, or meningitis.[1] Neonatal meningitis is a serious consequence of LOS with a mortality of 33%–48% in developing countries.[2] NNPD reported the incidence of meningitis 3/1000 live births.[1] Incidence of LOS-associated meningitis ranges from 3% to 30%.[5-7] Studies in the UK have found that the incidence of meningitis varies from 1.3% to 3.5% in neonates with LOS.[5] Kaul et al. reported 22.5% incidence of meningitis in neonates with suspected clinical sepsis in a tertiary care referral neonatal unit in North India.[9] Two other studies from North India[9] and Central India[10] reported approximately 17% incidence of meningitis in neonates with LOS. However, there is a paucity of data from West India. Hence, this study was planned to evaluate the incidence of meningitis in LOS.

Objective

The main objective of this study was to estimate the incidence of meningitis in LOS at a tertiary care center in the West Indian population.

MATERIALS AND METHODS

This descriptive observational study was conducted at a tertiary level neonatal intensive care unit (NICU) of Surya Children’s Hospital, Santacruz West, Mumbai, West India. Ethical Committee of the Institute approved the study protocol. Neonates, who were born in our Department of Neonatology, Surya Children’s Medicare Pvt. Ltd., Mumbai, Maharashtra, India

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hospital or transferred to the NICU from January 2015 to December 2016 and presented with signs and symptoms suggestive of sepsis with positive C-reactive protein (CRP) at or more than 72 h of postnatal age, were enrolled in the study.

Signs and symptoms of sepsis were defined as the following: lethargy, reduced feeding ability, no spontaneous movement, temperature >38°C, hypothermia, cyanosis, abdominal distension, increased prefeed aspirates in preterm/low birth weight (LBW), purpuric lesions, umbilical sepsis, presence of excessive crying, high-pitched cry, bulging fontanelle and/or occurrence of or history of convulsions, grunting, flaring, retraction, tachypnea (respiratory rate >60/min), apnea lasting more than 20 s, tachycardia (heart rate [HR] >160/min) or bradycardia (HR <100/min), or capillary refill time >3 s. CRP >10 mg/L was considered positive as per our unit protocol. Quantitative CRP estimation was performed by using turbidimetric immunoassay method. Neonates with neural tube defects, such as spina bifida (meningocele, meningomyelocele, and lipomeningocele), anencephaly, and very sick neonates even after initial stabilization, were excluded from the study.

Neonates with positive CRP were undergone following investigations: blood culture, urine culture, and cerebrospinal fluid (CSF) routine microscopic examination and culture. Other blood investigations and neuroimaging as and when required. Meningitis was defined according to the National Neonatology Forum guidelines 2010.[11] Meningitis was labeled in a neonate whose CSF findings satisfied all the following criteria: (1) CSF glucose less than the plasma glucose (sample to be taken before lumbar puncture) by ≥50%; (2) CSF white cell count >10/cu mm; (3) CSF protein >80 mg/dl, and (4) with/without CSF culture positive. Baseline characteristics of the study population were recorded in predesigned pro forma.

**Study outcomes**

1. To determine the incidence of meningitis in neonates with LOS
2. The outcome of meningitis.

**Statistical methods**

Descriptive statistics were used to describe the baseline outcome variables. Mean (±standard deviation) and median (interquartile range) were used to analyze normally distributed and nonparametric data. Categorical variables were reported as a percentage. Fisher’s exact test was used to compare categorical data. The Chi-square test was used for assessing the relationship between the two proportions. \( P < 0.05 \) was considered as statistically significant. PASW Statistics for Windows, Version 18.0. (SPSS Inc., Chicago, USA) was used for analysis.

**RESULTS**

A total of 2039 neonates were admitted during the study for various indications. Out of these 2039 neonates, 225 neonates were presented with LOS. A total of 208 neonates were eligible for the study after exclusion. The demographic profile of neonates with LOS is summarized in Table 1. Out of total 208 neonates with LOS, 12.5% \((n=26)\) of neonates had meningitis. The incidence of LOS in preterm and LBW neonates was 73.6% and 72.1%, respectively. Correlation of meningitis with demographic factors is summarized in Table 2, which was not statistically significant.

The most common presenting features in neonates with LOS with or without meningitis were respiratory distress (72.6%), followed by lethargy (68.8%) and refusal to feed (63%) [Table 3]. Overall blood culture was positive in 26% of neonates who presented with LOS. The incidence of blood culture positive rate was significantly higher in neonates who had meningitis (53.8%) as compared to no meningitis (22%) [Table 4]. The most common organisms isolated in blood culture and CSF culture were *Acinetobacter baumannii*, followed by *Klebsiella*.
pneumoniae] [Tables 5 and 6]. Overall mortality in neonates with LOS was 3.36% \((n = 7/208)\). Mortality was not statistically significant in between meningitis and no meningitis group [Table 7].

**DISCUSSION**

This study revealed incidence of neonatal meningitis in LOS was 12.5%, which was almost similar to other Indian observational studies such as Bhagat *et al.* [16%] and Mehta [17%]. Similar observational studies from Kenya, Brazil, and Asia reported the incidence of meningitis in neonates with LOS was 17.9%, 17%, and 17.2%, respectively. However, Kaul *et al.* reported a higher incidence of meningitis (22.5%) compared to our study. The minor difference in the incidence can be attributed to the various epidemiological and geographical factors in community-acquired infection in late-onset variety of sepsis.

There was no gender prediction for meningitis in our study similar to other observational studies. Kaul *et al.* reported male predominance in neonates who had meningitis. Incidence of LOS in preterm and LBW neonates was 73.6% and 72.1% in our study, respectively. Out of neonates having meningitis, 73% and 76.9% were preterm and LBW, respectively. Similarly, other observational studies reported a high incidence of LOS and meningitis in preterm and LBW neonates. Major presenting sign and symptoms of LOS with or without meningitis were respiratory distress, lethargy, and refusal to feed in our study. Similar observation was reported by Hoque *et al.*, Karthikeyan *et al.*, and Bhagat *et al.*

Blood culture was positive in 53.8% cases of meningitis in our study. Bhagat *et al.* and Mehta [18] reported 42.6% and 49.6% positive blood culture in neonates with meningitis, respectively. The most common organism recovered from culture was *Acinetobacter* followed by *Klebsiella* in the present study. Mehta and Bhagat *et al.* reported *Klebsiella* and methicillin-resistant *Staphylococcus aureus* most common isolate, respectively, in blood culture. The overall mortality in neonatal meningitis was 3.84% which was comparatively less as reported by other studies such as Mehta [20.6%], Tiskumara *et al.* [20%), Kaul *et al.* (26.1%) and Bhagat *et al.* (17.6%). This low mortality in our study can be attributed to continuous efforts to improve intensive care facilities.

The strength of the study includes adequate sample size and strict study protocol. Limitation of our study includes not evaluating the effect of exclusive breast milk feeding on the prognosis of neonates with LOS. Despite this, the present study provides important data on the incidence of neonatal meningitis in the Western Indian population. Moreover, there is an urgent need for...
studies looking at simple and sustainable interventions to reduce the burden of neonatal infection such as adequate implementation of simple infection control methods, exclusive breastfeeding, restriction of antibiotic use, increasing trend toward noninvasive ventilation, and rationalization of admissions to and discharges from neonatal units.

**Conclusion**

This study demonstrated that a significant number of neonates with LOS have coexistent neonatal meningitis. A vigilant attitude toward the presence of postnatal risk factors associated with an increased risk of mortality in cases of suspected sepsis can be helpful for early treatment initiation. Through the current study, we would like to recommend that a blood culture should be performed in all cases of suspected sepsis before starting antibiotics. In addition, our study highlights the diagnostic utility of routine lumbar puncture in neonates with clinical features of sepsis.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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