Clinico-Bacteriological Study of Sepsis in VLBW Neonates in Tertiary Care NICU in Central India: A Descriptive Observational Study

ABSTRACT

Introduction: Low birth weight (LBW) is one of the most serious challenges in Maternal and Child Health in developing countries. Neonatal sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries. Given the high prevalence of Very Low Birth Weight (VLBW) neonates and the increasing incidence of sepsis in this population, there is a need to study the clinical and bacteriological profile of sepsis.

Aim: To study the clinico-bacteriological profile of neonatal sepsis in VLBW neonates (Birth weight <1500 gm) in a tertiary care NICU in central India.

Materials and Methods: The descriptive observational study was conducted among VLBW neonates with clinically suspected sepsis admitted to the NICU of Indira Gandhi Government Medical College and Mayo Hospital in Nagpur, Maharashtra, India, from November 2019 to October 2021. All 160 VLBW neonates with clinically suspected sepsis and positive sepsis screen consisting of four parameters {Absolute Neutrophil Count (ANC), Total Leucocyte Count (TLC), Immature/Total Neutrophil Ratio (I/T Ratio), C-Reactive Protein (CRP)+} and whose mothers provided informed consent were included in the study within 24 hours of admission. Details such as demographic data, maternal risk factors and type of delivery, clinical signs of sepsis presentation, any Central Nervous System (CNS) signs, day of onset of sepsis, sepsis screen parameters (CRP, TLC, ANC, I/T Ratio), blood culture, and Cerebro-spinal Fluid (CSF) examination findings were studied. Continuous variables were evaluated using the student t-test, and categorical variables were evaluated using the chi-square test.

Results: There were 96 (60%) males and 64 (40%) females. In the sepsis screen parameters, the majority of the neonates were CRP positive 148 (92.3%) followed by TLC positive among 119 (74.38%) neonates. Lethargy was the most common clinical presentation among 147 (91.88%) neonates followed by difficulty in feeding among 121 (75.63%) neonates. Blood culture was positive among 61 (38.13%) neonates, and Escherichia coli was the most common organism isolated among 21 (34.43%) neonates.

Conclusion: The most common clinical presentation of neonatal sepsis was lethargy followed by difficulty in feeding. In the present study, the most common organism isolated was E.coli.

INTRODUCTION

Low birth weight (LBW) is one of the most serious challenges in Maternal and Child Health in developing countries. The lower the birth weight, the lower the survival chances [1]. The World Health Organisation (WHO) defines LBW as birth weight less than 2500 gm [2] and Very Low Birth Weight (VLBW) as birth weight less than 1500 gm. The WHO estimates that globally about 25 million LBW babies are born each year, constituting 17 percent of all live births, with nearly 95 percent of them in developing countries [2]. In India, VLBW babies constitute 4% to 7% of live births [3]. The World Health Organisation estimates that of the four million neonatal deaths worldwide each year, over 35% are due to infection in the neonatal period; this translates to approximately two deaths per minute [2].

Neonatal mortality from sepsis has remained around 20% for nearly three decades [4]. Neonatal sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries [5]. In India, according to the national neonatal perinatal database, the incidence of neonatal sepsis was 30 per thousand live births, and it was found to be one of the commonest causes of neonatal mortality, contributing to 19% of all neonatal deaths [6]. Studies have already proven that there is an increased risk of sepsis in VLBW neonates. It is well established that the incidence of sepsis is inversely proportional to birth weight and Gestational Age (GA) [7]. There is a decreased risk of Early Onset Neonatal Sepsis (EONS) in infants who are Small for Gestational Age (SGA) but at higher risk for Late Onset Neonatal Sepsis (LONS) than their appropriately grown GA-matched peers [8]. EONS is typically caused by colonisers of the maternal genito-urinary tract, leading to contamination of the amniotic fluid, placenta, cervix, or vaginal canal [9]. The principal causes of early neonatal sepsis are bacteria such as Streptococcus such as S. pneumoniae, group D Streptococci, α-haemolytic Streptococci, L. monocytogenes, E. faecalis, E. faecium, Staphylococci, and H. influenzae type B [9]. Late-onset sepsis is predominantly caused by Staphylococci species and E. coli and is frequently related to LBW of infants.

The use of intravascular catheters, endotracheal intubation, assisted ventilation, surgery, contact with the hand of colonised personnel, and contact with contaminated equipment are the main risk factors for the LONS [10]. The problem of neonatal sepsis is also complicated by its changing bacteriological profile. Several studies have documented that the sepsis fatality rate is highest for gram-negative and fungal infections [11-13]. Thus, a rational protocol for sepsis management must be based on continuously updated knowledge of the prevalent organisms causing neonatal sepsis. In view of the high prevalence (18%) of VLBW neonates in our institute and the increasing incidence of sepsis in them, the present study was undertaken to determine the clinical and bacteriological profile of sepsis in VLBW neonates admitted in the NICU in a tertiary care hospital in Central India.

Keywords: Blood culture, Lethargy, Sepsis screen, Very low birth weight

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MATERIALS AND METHODS

The present descriptive observational study was conducted in the NICU of Indira Gandhi Government Medical College and Mayo Hospital, Nagpur, Maharashtra, India, from November 2019 to October 2021 after obtaining approval from the Institutional Ethics Committee (approval no. 589-90/2019). Written informed consent was obtained from all the parents.

Inclusion criteria: All VLBW (<1500 gm) neonates with clinically suspected sepsis and a positive sepsis screen admitted to the NICU of the study hospital were included in the study.

Exclusion criteria: All VLBW neonates with clinically suspected sepsis but a negative sepsis screen, and neonates whose parents did not give consent, were excluded from the study.

A sepsis screen was considered positive if more than or equal to two points for the parameters were present as shown in [Table/Fig-1] [14]. If the onset of symptoms is within 72 hours of life, they are classified as EONS, and if the onset of symptoms is after 72 hours of life, they are classified as LONS [14,15].

### Points

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute Neutrophil Count (ANC) &lt;1750/mm³</td>
<td>1</td>
</tr>
<tr>
<td>Total white blood cell count (TLC) &lt;7500/mm³ or &gt;40,000/mm³</td>
<td>1 point</td>
</tr>
<tr>
<td>Immature/Total Neutrophil ratio (I/T) more than or equal to 0.20</td>
<td>1 point</td>
</tr>
<tr>
<td>Immature/total neutrophil ratio more than or equal to 0.40</td>
<td>2 points</td>
</tr>
<tr>
<td>C-Reactive protein (CRP) + (more than or equal to 1 mg/dL)</td>
<td>1 point</td>
</tr>
<tr>
<td>CRP + (more than or equal to 5 mg/dL)</td>
<td>2 points</td>
</tr>
</tbody>
</table>

A total of 188 neonates with clinically suspected sepsis were admitted to the tertiary care NICU in central India during the study period. Among these 188 neonates, only 160 neonates whose sepsis screen was positive were included in the study.

Procedure

After obtaining written informed consent from the parents, cases were enrolled in the study within 24 hours of admission. Basic information of each neonate such as name, age, sex, date of admission, registration number, address, and contact details were obtained. Mothers of enrolled cases were interviewed about antenatal history, obstetric history, and any history of high-risk pregnancy. Detailed natal history of enrolled cases was collected, including mode of delivery, birth weight, whether the baby cried immediately after birth, and details of any required resuscitation. The GA was assessed using the New Ballard Score [12]. GA <37 weeks indicated preterm neonates, and ≥37 weeks indicated full-term neonates [12].

Presenting clinical features of the enrolled babies such as decreased acceptance of feed, lethargy, fever or hypothermia, bleeding manifestations, convulsions, fast breathing, abdominal distension, vomiting, etc., were noted. Anthropometric classification was used to categorise neonates into SGA/AGA/IUGR. A neonate with a birth weight for GA less than the 10th percentile for GA was considered SGA/IUGR [12]. A thorough physical examination of each neonate, including general examination, systemic examination, and head-to-toe examination, was conducted. Laboratory investigations such as CBC, CRP, and CSF culture (in suspected meningitis cases) were performed. Blood culture was conducted using Trypticase soy broth incubated overnight, followed by repeated sub-cultures for five days to study the bacteriological profile. Radiological investigations such as X-ray were performed in suspected cases of necrotizing enterocolitis and respiratory distress/apnea, as shown in [Table/Fig-2a,b,3].

STATISTICAL ANALYSIS

The collected data was then entered into Microsoft excel and analysed using the Statistical Package for the Social Sciences (SPSS) version 10.0. Categorical variables were presented as frequency and percentage.

RESULTS

This study was conducted among 160 VLBW neonates with clinically suspected sepsis who tested positive on the sepsis screen and were admitted to the tertiary care NICU in central India. In the present study, the majority, 96 (60%) of the neonates, were males, and 64 (40%) were females. About 97 (60.63%) neonates were delivered via normal vaginal delivery, while 63 (39.37%) were delivered through LSCS. Preterm birth was present in 141 (88.12%) neonates, and 116 (72.5%) neonates had a birth weight of 1201-1500 gm. LONS was present in 84 (52.5%) neonates, while EONS was present in 76 (47.5%) neonates [Table/Fig-4].

Among the maternal risk factors, maternal anaemia was the most common risk factor, present in 99 (62%) cases, followed by PIH in 26 (16.25%) cases. Among the neonatal risk factors, prematurity was present in 107 (66.88%) cases, and birth asphyxia was present in 08 (5%) cases as shown in [Table/Fig-5].
Characteristics | Frequency (N=160) | Percentage |
--- | --- | --- |
Gender | | |
Male | 96 | 60.0 |
Female | 64 | 40.0 |
Residence | | |
Rural | 99 | 61.87 |
Urban | 61 | 38.12 |
Type of delivery | | |
Normal vaginal delivery | 97 | 60.63 |
LSCS | 63 | 39.37 |
Cried immediately after birth | 152 | 95.0 |
 Didn’t cry immediately after birth | 08 | 5.0 |
Gestational Age (GA) | | |
Pre-term (<37 weeks) | 141 | 88.12 |
Full-term (≥37 weeks) | 19 | 11.87 |
Birthweight (gm) | | |
1000-1200 | 44 | 27.5 |
1201-1500 | 116 | 72.5 |
Appropriateness of Gestational Age (GA) | | |
SGA | 78 | 48.75 |
AGA | 82 | 51.25 |
Age of onset of sepsis | | |
EOS | 76 | 47.5 |
LOS | 84 | 52.5 |

Risk factors | Number (n) | Percentage |
--- | --- | --- |
Maternal risk factors | (N=160) | Percentage |
Maternal anaemia | 99 | 62 |
PIH* | 26 | 16.25 |
Abruptio placenta | 7 | 4.38 |
Cardiovascular disease in mother | 3 | 1.88 |
Fetal illness in mother during pregnancy | 18 | 11.25 |
Foul smelling liquor | 25 | 15.63 |
Meconium-stained liquor | 21 | 13.13 |
Prolong rupture of membranes (>18 hrs) | 21 | 13.13 |
More than 3 P/V* examinations | 25 | 15.63 |
Prolonged and difficult delivery with instrumentation | 10 | 6.25 |
Neonatal risk factors | | |
Birth asphyxia | 8 | 5 |
Prematurity | 107 | 66.88 |

In the present study, CRP was positive in the majority, 148 (92.3%) of the neonates, followed by TLC being positive in 119 (74.38%) neonates [Table/Fig-6].

Most of the neonates, 147 (91.88%), presented with a complaint of lethargy, followed by feeding intolerance among 121 (75.63%) neonates. The cardiovascular system and coagulation system were also involved, showing clinical manifestations like mottling and gastrointestinal bleeding in 54 (33.75%) and 50 (31.25%) neonates, respectively [Table/Fig-7].

Blood culture was positive in 61 (38.12%) neonates. *E.coli* was the most common organism, present in 21 (34.43%) neonates,
followed by Klebsiella in 13 (21.31%) neonates. In the present study, Acinetobacter was the least common organism. Non-fermenters including Burkholderia and Legionella were cultured in 3 (4.91%) and 5 (8.20%) cases, respectively [Table/Fig-8].

<table>
<thead>
<tr>
<th>Isolated organisms</th>
<th>Frequency (N=61)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>21</td>
<td>34.43</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>13</td>
<td>21.31</td>
</tr>
<tr>
<td>Non-fermenters Burkholderia</td>
<td>3</td>
<td>4.91</td>
</tr>
<tr>
<td>Non fermenter Legionella</td>
<td>5</td>
<td>8.20</td>
</tr>
<tr>
<td>Candida</td>
<td>07</td>
<td>11.4</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>06</td>
<td>9.84</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>05</td>
<td>8.19</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>01</td>
<td>1.64</td>
</tr>
</tbody>
</table>

DISCUSSION
The present study was conducted among 160 VLBW neonates with a positive sepsis screen who were admitted to a NICU in a tertiary care hospital in Central India to study the clinico-bacteriological profile of neonatal sepsis. Among them, 60% were males and 40% were females, which is comparable to the study by Tallur SS et al., and Kuruvilla KA et al., which also showed a higher incidence of sepsis in males (63.63%) and (68.3%) respectively. Conversely, a higher incidence of sepsis in females (53.9%) was noted by Hornik CP [14, 16, 17]. The majority (87.13%) of the babies in the present study group belonged to the preterm group. Similar to this study findings, a higher incidence of sepsis in premature babies has also been noted by Jatsho J et al., and Ahmed NU et al., [18,19].

In this study, 60.63% of the babies were born through vaginal delivery, and 39.37% were delivered by LSCS. This was also observed in a study conducted by Kuruvilla KA et al., where 73.3% were born through vaginal delivery and 26.7% were born through LSCS [16]. Prematurity/LBW was the most common risk factor, present in 66.88% of all cases, which is comparable to that of Germe JW et al., [78%] [20]. Tallur SS et al., and Roy I et al., also reported a high incidence of prematurity/LBW in their series [14, 21]. EOS was present among 47.5% of neonates, and LOS was present among 52.5% of neonates in this study. In a study by Varsha et al., the incidence of EOS was 74.6%, and LOS was 25.3% [22].

Lethargy and Respiratory distress were the two most common presenting features in our study and were present in >90% of cases. Ahmed NU et al., also reported a high incidence of respiratory distress (46.7%) in their study [19]. Conversely, in a study done by Hornik CP [17], feeding difficulty (92.3%) was the most common presentation. In the present study, Blood culture was positive in only 38.13% of cases. In studies by Roy I et al., and Tallur SS et al., blood culture positivity was 47.5% and 64.8%, respectively [14, 21].

In this study group of 61 cases of neonatal sepsis, E.coli (13.13%) was the most common organism isolated in both the EONS and LONS groups. E.coli was reported as the most common pathogen (23.5%) of neonates by Kuruvilla KA et al., in their study [16]. While Tallur SS et al., found it to be the least common cause of neonatal sepsis (2.93%) in their study [14]. We did not find any cases of Group B Streptococcus (GBS) sepsis in our study, which was also the case in the study by Tallur SS et al., [14]. This is in sharp contrast to the trend in western developed countries where it is a major agent of early-onset neonatal septicemia [18].

Limitation(s)
Since the study was a single-centered observational study, the findings cannot be generalised to other study settings.

CONCLUSION(S)
The most common clinical presentation was lethargy, followed by feeding difficulty, and E.coli was the most common organism isolated among neonates with sepsis. Considering the common risk factors for sepsis such as prematurity, maternal anemia, and PIH, and common clinical features like lethargy, tachypnea, refusal to feed, and delayed CRT were present in the overwhelming majority of cases, it is suggested that a scoring system which takes into consideration risk factors, clinical features, and sepsis screen should be formulated. This would be a more reliable tool for the early presumptive diagnosis of sepsis.

REFERENCES

