BACKGROUND
Neonatal septicemia is one of the important causes of neonatal mortality worldwide. Early diagnosis of neonatal septicemia is the cornerstone for the successful management and favorable outcome. It is a challenge because of non-specific symptoms and signs of neonatal sepsis. There are many risk factors associated with neonatal sepsis, in EOS source of infection is usually from the maternal genital tract and in LOS it is either nosocomial or community acquired. The primary objective of the study is to find out the different risk factors of septicemia in newborns.

METHODS
Cross sectional study conducted in a tertiary care hospital and total of 120 newborns between 0 to 28 days with clinical suspicion of septicemia were included in the study. The detailed maternal and neonatal risk factors were studied in relation to EOS and LOS.

RESULTS
Out of total 120 cases (male 65%), the number of pre-terms with sepsis were 55%. The number of Low Birth Weight (<2500 gms) cases were 73% and Normal Birth Weight (≥ 2500 gms) cases were 27%. Majority cases were from VLBW 34% followed by LBW 24% and ELBW 15%. Among the different risk factors, multiple PV examinations (45%), inadequate ANC (40%), Prolonged labour (37%), PROM (23%), birth asphyxia (32%), birth asphyxia requiring resuscitation (22%) and difficult delivery with application of forceps and vacuum were associated with 16% of the cases of neonatal sepsis. Blood culture was positive in 47% cases with Staphylococcus aureus being most commonly found followed by E.coli. And Culture was positive more in LOS than EOS. Mortality was observed in 35% cases.

CONCLUSIONS
Low Birth Weight is the single most predominant risk factor for neonatal septicemia followed by prematurity with a male predominance. So early diagnosis and early institution of antibiotics probably improve the outcome.

KEYWORDS
Neonatal sepsis, prematurity, low birth weight, early onset sepsis, C-reactive protein


BACKGROUND
Neonatal septicaemia is one of the important causes of neonatal mortality worldwide. Nearly, 0.75 million newborns died in India in 2013, being highest in the world.¹ The NMR in 2013 is 28 per 1000 live births.² This neonatal mortality rate accounts for about 70% of total infant deaths and more than half of under-five deaths.³,⁴ Neonatal sepsis can be early onset (EOS), when the newborn presents within 72 hours of life and late onset sepsis (LOS) if presents after 72 hrs of life. Newborns with EOS usually present with respiratory distress or pneumonia and the source of infection is usually from the maternal genital tract. The source of infection in LOS is either nosocomial or community acquired and usually present with sepsicaemia, pneumonia or meningitis.⁴

There are many risk factors associated with neonatal sepsis as premature rupture of membranes (PROM), meconium stained amniotic fluid (MSAF), foul smelling amniotic fluid, prematurity, low birth weight, prolonged labour, maternal fever within last two weeks of delivery, more than three vaginal examinations and low Apgar score at birth.³,⁴

Early diagnosis of neonatal septicemia is the cornerstone for the successful management and favourable outcome. It is a challenge because of non-specific symptoms and signs of neonatal sepsis. Blood culture, which is the gold standard for diagnosis takes minimum of 48 hrs to 72 hrs and moreover it is positive in only about 40 to 60% of cases. Neonatal septicemia is frequently a devastating disease with involvement of multi organ system and majority of survivors having significant neurological sequelae as a consequence of central nervous system involvement. Hence keeping in mind the devastating nature of neonatal...
septicaemia, the present study was conducted prospectively to assess the risk factors during pregnancy period, perinatal period and neonatal period, along with assessment of haematological lab parameters to suspect and diagnose neonatal septicaemia as early as possible.

With this background the present study was planned with the primary objective to find out the risk factors of septicaemia in newborns.

**METHODS**

**Study Design and Setting**

This cross sectional study was undertaken in the S.N.C.U. (Special Newborn Care Unit) of the Department of Pediatrics M.K.C.G. Medical College, Berhampur, Odisha, from October 2014 to August 2016.

**Sampling Technique**

Convenience sampling technique was used to recruit the study participants and all newborns aged between 0 to 28 days admitted to SNCU with clinical suspicion of septicaemia were selected for the study. The newborn babies with congenital malformations, birth injury and syndromic babies were excluded from the study.

**Case Definition**

For the present study Neonatal Septicaemia was diagnosed as per the recommendations of National Neonatology Forum (NNF) – Clinical Practice Guidelines- 2010.5

**Culture Negative Sepsis**

Neonates having clinical picture of sepsis with any one of the following. i). Maternal fever or foul smelling liquor or prolonged rupture of membranes (>18 hrs) or gastric aspirate > 5 polymorphs / HPF. ii) Rapid sepsis screen (any two of the following) a) TLC < 5000 / mm³ b) Immature to total neutrophil ratio > 0.2 c) CRP > 10 mg/ Ltr d) Micro ESR > 10 mm/ 1st hour. iii. Clinical picture of NEC iv. Radiological evidence of Pneumonia.

**Culture Positive Sepsis**

Neonates having clinical picture of sepsis (meningitis or pneumonia or septicaemia) with presence of either of the following. i) Isolation of pathogen from blood or CSF or urine or abscess. ii) Pathological evidence of sepsis on autopsy.

**Sample Size**

Assuming a prevalence rate of 8% from available literature,4 the sample size was calculated to be 113 at a confidence level of 95%, two tailed and a precision of 5% using n Masters Software. Finally 120 patients were included in the study.

**Data Collection**

Data was collected in a predesigned case record form. Sepsis was suspected clinically in the newborn babies, who presented with features as poor feeding, decreased activity than before, lethargy, abdominal distension, vomiting, loose stools, fever, hypothermia, jaundice, uprolling of eyes, seizures, difficulty in respiration, apnea and cyanosis. The detailed history of mother including the antenatal and perinatal events were taken. Information was collected regarding the antenatal check-ups, fetus within last two weeks of delivery and UTI. The place of delivery, mode of delivery, attending personnel, duration of labour, duration of rupture of membrane, condition of liquor, number of PV examinations during labour and mode of resuscitation were recorded in detail. The detailed neonatal history and thorough physical examination findings were recorded for inborn and outborn babies separately. The low birth weight and very low birth weight babies were also included to their risk profile for sepsis. The babies presenting within 72 hrs of life with features of sepsis were included as EOS (Early Onset Sepsis) and other babies after 72 hrs of life were taken as LOS (Late Onset Sepsis). The relevant investigations like Hb%, TLC, TPC, ANC, I: T Ratio, RBS were done from heel prick. Micro ESR was done in pre-heparinised capillary tube and the value of more than 15mm was taken as significant. CRP estimation was done in all the cases by Latex Agglutination test and the value of over 6mg/ltr was considered positive. Blood culture was done in all the babies with aseptic measures before starting any antibiotics. Blood is inoculated into Brain Heart infusion and subsequently subcultures were made on both Blood agar and MacConkey agar after 24hrs and 48hrs. Organisms were isolated by Kirby Baur’s disc diffusion method and antibiotic sensitivity done according to standard guidelines (CLSI-2006). CSF examination and culture, urine examination and culture were done as per the institutional policy. Pus was collected for Gram’s stain and culture from the abscess sites. Gastric aspirate cytology was done in all cases of early onset sepsis and the babies presenting with Pneumonia. Radiological examinations were done in the needful cases.

**Ethical Approval**

This study had been approved by the institutional ethics committee.

**Statistical Analysis**

Graphpad Prism was used to analyse the data. Discrete variables were expressed as percentage and continuous variables were expressed as mean ± SD. Z test for proportions was used to find out the statistical significance between the dependant variables and neonatal sepsis. A p value of ≤0.05 was taken to be statistically significant.

**RESULTS**

In this prospective study one hundred and twenty neonates suffering from septicaemia were included. The number of pre-terms (<37 wks) with sepsis were 67 cases (55%). The total number of Low Birth Weight (LBW < 2500 gms) cases were 88 (73%) and Normal Birth Weight (NBW ≥ 2500 gms) cases were 32 (27%). Majority cases were from VLBW (1000-1499 gms) comprising 41 cases followed by LBW (1500-2499gms) 29 cases and ELBW (<1000 gms) 18 cases. The demographic details of the study participants are...
presented in Table 1. It was observed that difficult delivery with application of forceps and vacuum was associated with 16% of the cases of neonatal sepsis (Table 2). Among all perinatal risk factors for neonatal sepsis, LBW and prematurity were most common and found in 73% and 56% of cases respectively (Table 3). The haematological assessment of the cases is presented in Table 4. Blood culture was positive in 56 cases (47%) of neonatal sepsicaemia. The type of organism isolated is presented in Table 5 with the most common organism being found was Staphylococcus aureus in 24 (43%) cases followed by E.coli in 11 (20%) and Klebsiella in 8 (14%) cases. Blood culture was positive more in LOS than EOS (31% vs 16%). Urine culture was positive in 1 case of the 16 cases showing growth of E.coli. CSF culture and sensitivity was done in the suspected cases of meningitis and revealed positive in 5 cases (S.aureus 3, E.coli 1). Gastric aspirate cytology showing >5 WBC/mm³ was found in 18 cases. Out of total EOS cases culture positivity was found in 19 cases (33%) and LOS cases with culture positivity in 37 cases (59%). Mortality was seen in most of the ELBW cases (14 cases) followed by VLBW (19 cases). Pre-term babies being high risk had mortality in 34 cases. It was observed more predominantly in EOS babies and also in male babies (28 cases).

<table>
<thead>
<tr>
<th>Sepsis Screen Parameter</th>
<th>No. of Cases (N=120)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC &lt;5000/mm³</td>
<td>34</td>
<td>28</td>
</tr>
<tr>
<td>5000–1500</td>
<td>39</td>
<td>33</td>
</tr>
<tr>
<td>&gt;15000</td>
<td>47</td>
<td>39</td>
</tr>
<tr>
<td>ANC &lt;500</td>
<td>33</td>
<td>28</td>
</tr>
<tr>
<td>500–1500</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>I:T ratio ≥0.2</td>
<td>53</td>
<td>44</td>
</tr>
<tr>
<td>TP C &lt;1.5 lakhs/mm³</td>
<td>49</td>
<td>41</td>
</tr>
<tr>
<td>CRP &gt;6 mg/L</td>
<td>92</td>
<td>73</td>
</tr>
<tr>
<td>Micro ESR &gt;15 mm in 1 hr</td>
<td>93</td>
<td>78</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Out of total 120 cases, it was observed that 15% were ELBW, 34% were VLBW, 24% were LBW, 27% were NBW. Thus showing total low birth weight (73%) is a very important risk factor for neonatal sepsicaemia. Similar observations were made by Ogunlesi et al and Buch et al who had reported neonatal sepsis of 57.5% and 80.8% in low birth weight (LBW) babies respectively.7,8 Septicaemia is more common in LBW babies due to low cellular immunity and low levels of immunoglobulin, mainly IgG. Similarly, Shah et al have reported increased sepsis in LBW babies (56%) than normal weight babies (44%).9 Sepsis was common in preterm babies (<37wks) and found to be 56% in our study, similar observations were made by Antoniette et al and Buch et al.8,10 This may be because, several phagocytic functions are impaired including chemotaxis, phagocytosis, bacterial killing. There is low opsonic activity of the serum in preterms, due to low levels as well as reduced activity of complement factors and deficiency of antibodies.11 It was observed that male were predisposed with a male to female ratio of 1.8:1. Similar observations were made by many studies who had observed an almost two fold higher incidence of infection in males than in females suggesting the possibility of sex linked factor.8,10,12,13 It was found that Pre-term babies had more EOS (54% vs 46%) which could
be due to maternal risk factors like chorioamnionitis. More premature and ELBW babies are at risk due to their inadequate immunity, poor metabolic homeostasis, more use of incubators, warmers, bag and mask ventilation and intubation which makes them more vulnerable for sepsis and rapid deterioration. Among cases of neonatal septicaemia there were more hospital delivery cases 84% as compared to less home delivery 16%. This may be due to introduction of ambitious Government programmes namely Janani Suraksha Yojana (JSY), creation of cadre of ASHA (Accredited Social Health Activist) by National Health Mission. Maternal and neonatal benefit schemes improved the hospital delivery more than home deliveries. In the present study 69% were Normal Vaginal Delivery. Significant risk factors observed were multiple PV examinations (45%), inadequate ANC (40%), Prolonged labour (37%), PROM (23%), birth asphyxia (32%) and birth asphyxia requiring resuscitation (22%). One North Indian study showed perinatal asphyxia in 37.5% cases and premature rupture of membranes (PROM) in 28.9% cases. Leucopenia (<5000/mm³) was seen in 28% cases with a sensitivity of 23% and specificity of 69% and I:T ratio of >0.2 was found in 44% of cases with a sensitivity of 45% and specificity of 55%, many studies showed wide range of results of white cell counts and ratios, with sensitivity and specificity ranging from 17% to 90% and 31% to 100% respectively. Thrombocytopenia was seen in 41% cases. CRP positivity seen in 77% cases with a sensitivity of 71.4% and specificity of 28%. Positive predictive value and negative predictive value of CRP was 46.5% and 52.9% respectively. Previous studies reported, widely differing sensitivities and specificities of CRP ranging from 29 to 100% and from 6 to 100% respectively. Serial measurements after 24 and 48 hours of the onset of illness considerably improve the sensitivity and specificity of CRP. Limitation of our study is that we did not do quantitative estimation and serial measurement of CRP. Culture positive sepsis with blood culture positivity was seen in 47% cases. Similar results were found in many of the previous studies. Most common organism being Staphylococcus aureus in 43% followed by E.coli in 20% and Klebsiella in 14% in our study, similar results with S.aureus being predominant organism were found in many studies. However other studies showed Klebsiella pneumoniae to be the most predominant organism.

**CONCLUSIONS**

Low Birth Weight is the single most predominant risk factor for neonatal septicaemia followed by prematurity with a male predominance. Late onset septicaemia (LOS) is more common than early onset septicaemia (EOS). Neonatal septicaemia has an overall mortality rate of 35%. So early diagnosis and early institution of antibiotics probably improve the outcome.

**REFERENCES**


parameters as predictors of early onset neonatal sepsis.


