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Original Research Article

Retrospective Evaluation of Risk Factors, Microbiological Profile, and Outcomes in Neonatal Sepsis

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Conflict of interest: Nil

Abstract:

Background: Neonatal sepsis is still an important cause of neonatal morbidity and mortality, especially among premature infants.

Aim: To assess the risk factors, microbiological profile, antimicrobial susceptibility, and clinical outcomes of neonatal sepsis.

Methodology: A retrospective study of observational nature was performed on 120 babies suffering from suspected or proven sepsis in Narayan Medical College and Hospital, Sasaram, Bihar, India. Clinical information, findings of blood culture, antibiogram and other laboratory reports were recorded and evaluated to analyze the clinical and microbial profile of neonatal sepsis.

Results: Major risk factors for infection include low birth weight (58.3%) and premature infants (45%). In addition, positive blood cultures occurred in 43.3%, where Klebsiella pneumoniae is the main causative organism in 28.8%. The mortality rate was 13.3% compared to 80.0% who responded positively. Independent predictors of mortality included hemodynamic instability (AOR=4.58).

Conclusion: Early identification of high-risk neonates, microbiological diagnosis, and culture-guided antimicrobial therapy are essential for improving neonatal sepsis outcomes.

Keywords: Neonatal sepsis; Risk factors; Blood culture; Antimicrobial susceptibility; Klebsiella pneumoniae; Neonatal mortality.

Introduction

Neonatal sepsis continues to be one of the significant clinical problems that occur in the first 28 days after delivery and account for many cases of morbidity and mortality among neonates, especially in developing countries [1]. It is defined as the presence of systemic signs of infection in the neonate, caused by pathogens such as bacteria and fungi and that can lead to serious problems if not diagnosed and treated in a timely manner [2]. Neonatal susceptibility to sepsis is attributed to various maternal, perinatal, and neonatal determinants, including premature birth, low birth weight, prolonged rupture of membranes, maternal infection, birth asphyxia, and exposure to invasive interventions [3]. Besides, the heterogeneity in the pathogens involved and the development of microbial resistance make the choice of effective empirical therapy even more difficult [4]. Hence, it is important to know about the risk factors, microbial flora, and treatment outcomes in order to be able to diagnose and treat sepsis successfully [5].

Background of the Study: Sepsis in newborns is still a considerable cause of morbidity and mortality in the first month after birth, especially in preterm and low birth weight newborns [6]. Infections in the mother, prolonged membrane rupture, perinatal asphyxia, interventions, and poor immune response make newborns more vulnerable to infections [7]. Causative pathogens and antimicrobial resistance patterns vary from setting to setting, but an increasing trend of antimicrobial resistance is making empirical therapy difficult [8]. Hence, knowing the local risk factors, microorganisms, and clinical outcomes is very important in diagnosing and treating sepsis in neonates [9]. This study was carried out with the objective of assessing these variables and determining the factors associated with unfavourable outcomes in neonatal sepsis [10].

Risk Factors and Clinical Outcomes of Neonatal Sepsis: Maternal, perinatal, and neonatal risk factors exist that contribute to neonatal sepsis through increasing the likelihood of becoming systemically infected [11]. Prematurity and low birth weight are key risk factors as the neonate will not be fully developed in terms of immunity and physiological functioning, thus making him/her

more susceptible to infection [12]. Other risk factors include prolonged rupture of membranes, maternal infection, asphyxia at delivery, resuscitation of the baby immediately after birth, and invasive procedures in intensive care [13]. Clinical outcomes depend on how advanced the infection is, the degree of the neonate's vulnerability, the pathogen, and how quickly the baby receives treatment [14]. Even though an early diagnosis and the proper antimicrobial drugs can bring about good clinical outcome, there might still be such serious outcomes as respiratory failure, hemodynamic instability, need for prolonged hospitalization, complications affecting multiple organs and even death [15].

Research Objectives

The objectives of the study are:

- To assess the maternal, perinatal, and neonatal risk factors associated with neonatal sepsis among neonates admitted during the study period.
- To determine the microbiological profile of neonatal sepsis and evaluate the antimicrobial susceptibility patterns of the isolated pathogens.
- To evaluate the clinical outcomes of neonates with sepsis, including recovery, requirement for supportive care, referral, and in-hospital mortality.
- To determine the association of selected maternal, perinatal, neonatal, and microbiological factors with in-hospital mortality and identify independent predictors of mortality among neonates with sepsis.

Methodology

This current research study aimed at assessing the clinical and epidemiological features of neonatal sepsis. The study specifically focused on the risk factors associated with sepsis, the microbial profile, and antimicrobial susceptibility profile, as well as the outcomes of the neonates. A retrospective study design was applied in reviewing the data obtained from the hospitals within one year of time period.

Study Design: This study was done in the form of a hospital-based retrospective observational study. The clinical and laboratory reports of neonates who fulfilled the inclusion criteria in the study period were reviewed retrospectively. There was no intervention or alteration of the treatment process carried out in the study since the information was collected from existing clinical and laboratory reports.

Study Area: The experiment was conducted in the Department of Pediatrics at Narayan Medical College and Hospital, Sasaram, Bihar, India

Study Duration: The study covered a period of one year from January 2020 to December 2020.

Study Participants: The study subjects were neonates between 0-28 days of age who had been admitted to the NICU within the study period and had been clinically identified/diagnosed with neonatal sepsis. Information on the variables of interest was obtained from the medical records available.

Inclusion and Exclusion Criteria

Inclusion Criteria

Neonates were included if they:

- were aged 0–28 days at the time of admission;
- had clinical features suggestive of neonatal sepsis and had undergone evaluation for sepsis;
- had complete or sufficiently documented clinical and laboratory records required for analysis;
- had undergone blood culture testing as part of the diagnostic evaluation for suspected sepsis; and
- had documented hospital outcomes, including discharge, referral, discharge against medical advice, or death.

Exclusion Criteria

Neonates were excluded if they:

- had incomplete medical records that prevented assessment of the principal study variables;
- had major congenital anomalies or chromosomal abnormalities likely to independently influence survival and clinical outcomes;
- had been admitted only for observation without clinical suspicion or evidence of sepsis;
- had missing microbiological or outcome-related information essential for the study analysis; or
- had duplicate admission records pertaining to the same episode of neonatal sepsis.

Sample Size: Since the research design was retrospective in nature, total enumeration method was used to obtain samples. Inclusion criteria were applied to all the neonate's medical records during the study year to select all those neonates meeting the set criteria. Thus, the number of samples obtained depended on the number of neonatal sepsis cases available after evaluation of hospital records.

Procedure: Following the necessary approvals, the records of neonates who were admitted in the study period were obtained from NICU admission registers, case records, laboratory registers and

microbiology records. Cases meeting the inclusion and exclusion criteria were identified. Structured data abstraction tool was used for the data collection in a retrospective manner.

Neonate demographic variables like age, sex, weight, gestational age, mode and place of delivery, admission status were documented. Maternal and perinatal factors like prematurity, low birth weight, prolonged rupture of membranes, maternal fever or suspicion of peripartum infection, birth asphyxia, resuscitation, any invasive procedures etc were collected whenever possible.

Sepsis among neonates was classified as early onset sepsis or late onset sepsis depending on the time of presentation as mentioned in the medical record. Clinical presentations which were suggestive of sepsis such as feeding problems, lethargy, unstable temperature, difficulty breathing, apnea, changes in activity, distended abdomen and hemodynamic changes were recorded if available.

The laboratory data obtained in clinical investigations were reviewed. Blood culture reports were analyzed for culture positivity and organisms isolated. Isolated organisms were classified as Gram positive bacteria, Gram negative bacteria or fungi wherever applicable. The antibiotic susceptibility data obtained from microbiology laboratory were reviewed for the susceptibility pattern of the organism isolated.

Therapeutic information including the use of empirical antibiotics and any modifications to the treatment based on culture and susceptibility results were obtained from the medical records. Duration of hospital stay, requirement of intensive care, discharge, discharge against advice, referral and in hospital death were some of the important outcomes considered in this study. Relationships between the maternal, perinatal, neonatal and microbiological factors and neonatal outcomes were evaluated subsequently.

The extracted data were entered into a structured database. The data were checked for accuracy, duplicates and consistencies before statistical analysis. Identifiers of patients were not included in the database to maintain the confidentiality of the records.

Statistical Analysis: The collected data was entered in Microsoft Excel and then analyzed through IBM SPSS Statistics software. For categorical variables such as gender, category of gestational age, category of birth weight, type of sepsis, risk factors, culture positivity, isolation of microorganisms, and neonatal outcomes, frequencies and percentages were used for data summarization. Mean and standard deviation were used for data summarization if the continuous variable is normally distributed, while median and interquartile range were used for skewed continuous variables.

Chi-square test or Fisher's Exact Test, depending on the appropriateness of application, was employed in order to find out association between categorical risk factors and outcomes like culture positivity and mortality. Independent samples t-test or other non-parametric tests were utilized in order to compare the continuous variable between different groups. Risk factors found in univariate analysis to be significantly associated with any adverse neonatal outcome were selected for multivariate logistic regression analysis in order to determine the independent predictors of adverse neonatal outcomes. Adjusted odds ratios with 95% confidence intervals were calculated. P value < 0.05 was considered statistically significant.

Results

The total number of neonates meeting the inclusion criteria was 120. The results were analyzed with regard to demographics, clinical parameters, maternal and neonatal risk factors, nature of sepsis, microbiology, antibiogram, treatment features, and outcome. The associations between specific risk factors and mortality rates were investigated to determine which risk factors contribute to poor outcome.

Table 1: Demographic and Clinical Characteristics of the Study Participants (N = 120)

Characteristics	Frequency (n)	Percentage (%)
Sex		
Male	68	56.7
Female	52	43.3
Gestational age		
Preterm (<37 weeks)	54	45.0
Term (≥37 weeks)	66	55.0
Birth weight		
<1500 g	24	20.0
1500–2499 g	46	38.3
≥2500 g	50	41.7
Mode of delivery		
Vaginal delivery	71	59.2

Caesarean section	49	40.8
Place of delivery		
Inborn	74	61.7
Outborn	46	38.3

Among the 120 neonates, 68 (56.7%) were male and 52 (43.3%) were female. Preterm neonates accounted for 45.0% of the study population, while 58.3% had a birth weight below 2500 g. Vaginal delivery was documented in 59.2% of cases, and 61.7% of the neonates were born within the study institution.

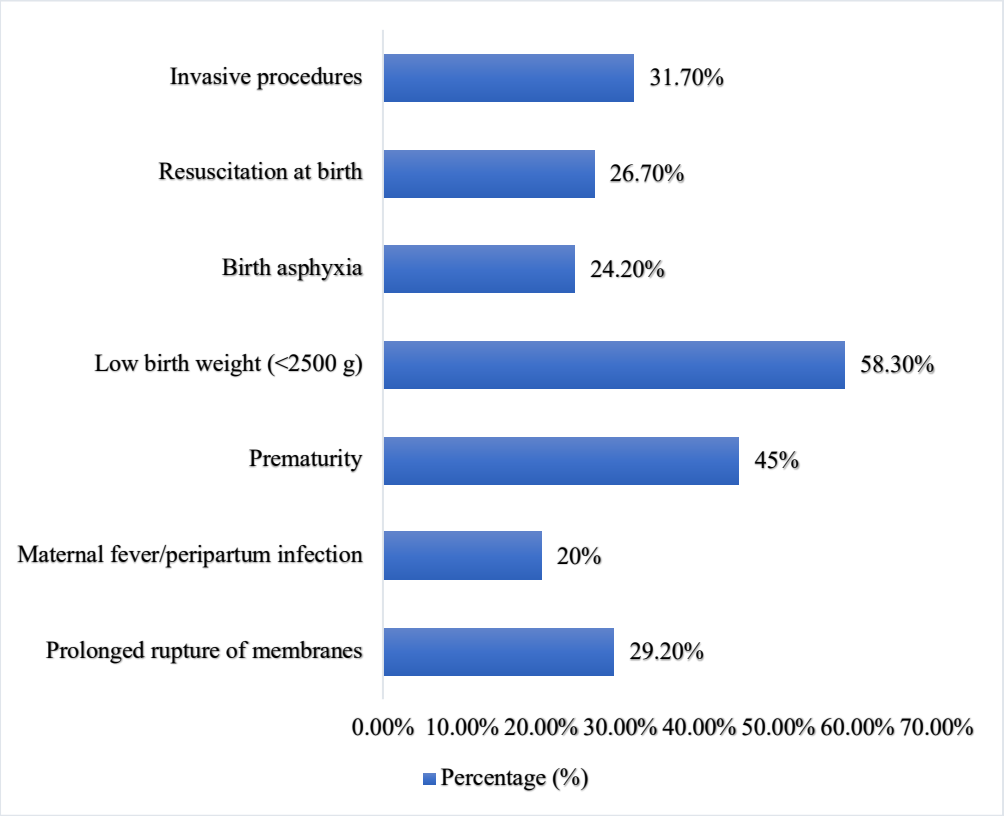

Figure 1: Distribution of Maternal and Perinatal Risk Factors (N = 120)

Among the most common risk factors is low birth weight, found in 70 babies (58.3%), then comes prematurity in 54 babies (45.0%). Invasive procedures occurred among 31.7% of babies, and prolonged rupture of membranes occurred in 29.2% of babies. Maternal fever and/or peripartum infection was present in 20.0% of babies.

Table 2: Distribution of Neonates According to Type of Sepsis (N = 120)		
Type of Sepsis	**Frequency (n)**	**Percentage (%)**
Early-onset sepsis	72	60.0
Late-onset sepsis	48	40.0
Total	**120**	**100.0**

Early-onset sepsis was more common than late-onset sepsis, accounting for 72 (60.0%) cases. Late-onset sepsis was identified in 48 (40.0%) neonates.

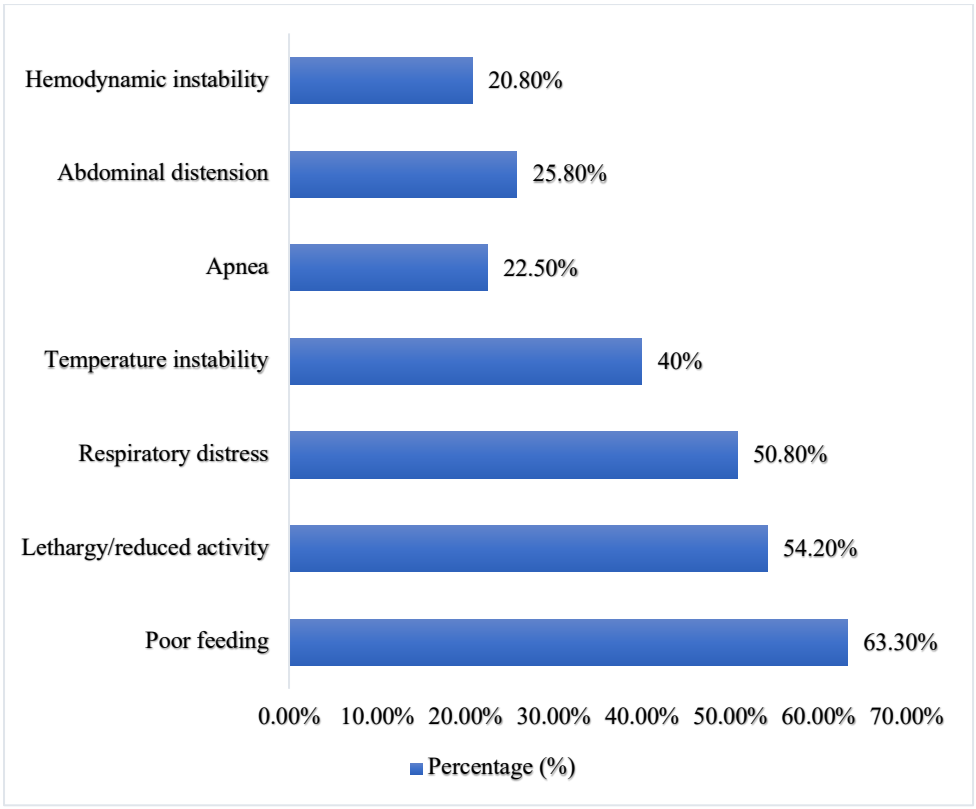

Figure 2: Clinical Manifestations Among Neonates with Sepsis (N = 120)

Poor feeding was the commonest presenting sign which was reported in 63.3% of babies. Other commonly reported symptoms included lethargy or decreased activity in 54.2% of babies, respiratory distress in 50.8% of babies, and temperature instability in 40.0%. About one fifth of babies had hemodynamic instability.

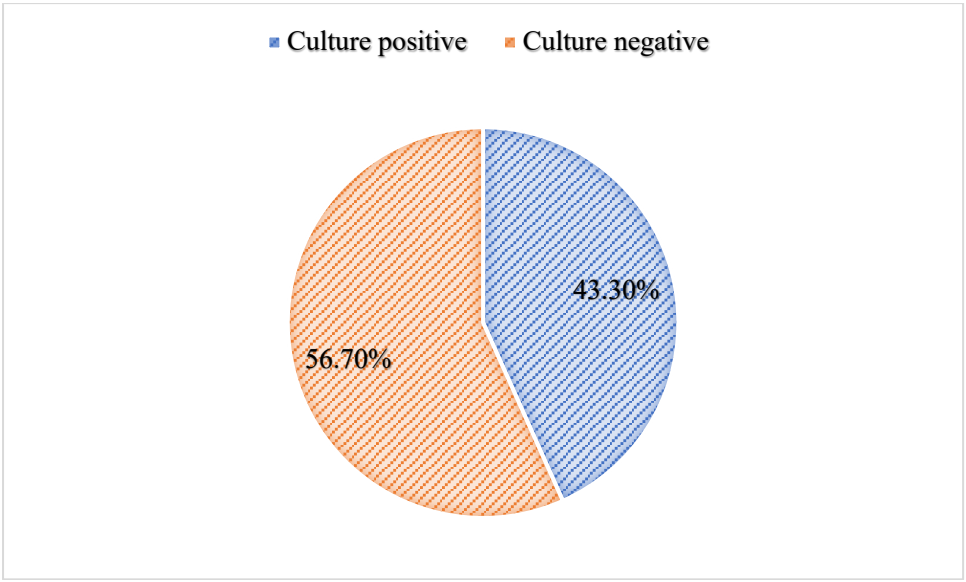

Figure 3: Blood Culture Findings Among the Study Participants (N = 120)

Positive blood cultures were obtained in 52 (43.3%) neonates, while 68 (56.7%) did not show any growth of bacteria or fungi in blood cultures. Therefore, microbiologically proven sepsis was more than two-fifths of the total subjects.

Table 3: Microbiological Profile of Culture-Positive Neonatal Sepsis (n = 52)		
Microorganism Isolated	Frequency (n)	Percentage (%)
Klebsiella pneumoniae	15	28.8
Escherichia coli	10	19.2
Acinetobacter spp.	7	13.5
Pseudomonas aeruginosa	4	7.7
Staphylococcus aureus	8	15.4
Coagulase-negative Staphylococcus	5	9.6
Enterococcus spp.	2	3.8
Candida spp.	1	1.9
Total	**52**	**100.0**

The majority of positive cultures contained gram-negative bacteria. The commonest organism was Klebsiella pneumonia, which formed 28.8% of the isolated organisms, then E. coli (19.2%), S. aureus (15.4%) and Acinetobacter (13.5%). One infant had fungal infection caused by Candida species.

Table 4: Antimicrobial Susceptibility Pattern of Major Bacterial Isolates		
Antimicrobial Agent	**Gram-Negative Isolates Sensitive n (%)**	**Gram-Positive Isolates Sensitive n (%)**
Ampicillin	6 (16.7)	8 (53.3)
Gentamicin	15 (41.7)	10 (66.7)
Amikacin	24 (66.7)	11 (73.3)
Cefotaxime	12 (33.3)	9 (60.0)
Piperacillin–tazobactam	25 (69.4)	11 (73.3)
Meropenem	31 (86.1)	13 (86.7)
Ciprofloxacin	20 (55.6)	9 (60.0)
Vancomycin	—	15 (100.0)
Linezolid	—	15 (100.0)

The antimicrobial susceptibility pattern indicated the presence of low susceptibility of Gram negative organisms to ampicillin and cefotaxime. High susceptibility was seen with respect to meropenem (86.1%), piperacillin/tazobactam (69.4%) and amikacin (66.7%). Susceptibility of all the major Gram-positive isolates studied for antimicrobial.

Table 5: Treatment and Clinical Outcomes of Neonates with Sepsis (N = 120)		
Treatment/Outcome Variable	**Frequency (n)**	**Percentage (%)**
Modification of empirical antibiotics after culture/clinical assessment	47	39.2
Required respiratory support	43	35.8
Required vasoactive support	21	17.5
Final outcome		
Discharged after improvement	96	80.0
Referred	5	4.2
Discharged against medical advice	3	2.5
Death	16	13.3
Total	**120**	**100.0**

Majority of neonates, 96(80.0%), responded favorably to treatment and were discharged. There were 16 neonatal deaths giving the total case fatality rate as 13.3%. Thirty-five-point eight percent of neonates needed respiratory support whereas 17.5% needed vasoactive support.

Table 6: Association of Selected Risk Factors with In-Hospital Mortality (N = 120)				
Risk Factor	**Death n/N (%)**	**Survival n/N (%)**	**χ^2**	**p-value**
Prematurity	12/54 (22.2)	42/54 (77.8)	7.84	0.005
Low birth weight (<2500 g)	14/70 (20.0)	56/70 (80.0)	6.59	0.010
Birth asphyxia	9/29 (31.0)	20/29 (69.0)	9.27	0.002
Culture-positive sepsis	11/52 (21.2)	41/52 (78.8)	5.17	0.023
Respiratory distress	13/61 (21.3)	48/61 (78.7)	7.26	0.007
Hemodynamic instability	10/25 (40.0)	15/25 (60.0)	20.31	<0.001

Premature birth, low birth weight, birth asphyxia, sepsis, respiratory distress, and hemodynamic instability were statistically significantly correlated with in-hospital mortality ($p<0.05$). Highest mortality rate was recorded for infants with hemodynamic instability, where 40.0% of such patients died while being hospitalized.

Table 7: Multivariable Logistic Regression Analysis of Predictors of In-Hospital Mortality

Predictor	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Prematurity	2.68	1.08–6.64	0.033
Low birth weight (<2500 g)	2.41	1.01–5.76	0.048
Birth asphyxia	3.19	1.29–7.88	0.012
Culture-positive sepsis	2.36	1.02–5.47	0.045
Respiratory distress	2.71	1.10–6.69	0.030
Hemodynamic instability	4.58	1.76–11.91	0.002

Multivariable logistic regression analysis showed that some clinical predictors were found to be significantly associated with mortality even after adjusting for other variables in the study. Hemodynamic instability proved to be the highest predictor of mortality (AOR = 4.58; 95% CI: 1.76–11.91; p = 0.002) while birth asphyxia came second (AOR = 3.19; 95% CI: 1.29–7.88; p = 0.012). There was a 2.7-fold increase in mortality with respiratory distress and prematurity. Other significant independent predictors included low birth weight and culture-positive sepsis. In summary, it appeared that there were various risk factors that influenced the outcome of neonatal sepsis.

Discussion

The present study identified Low birth weight (58.3%) and prematurity (45.0%) were identified as the major risk factors for sepsis among neonates, followed by invasive procedures (31.7%), prolonged rupture of membranes (29.2%), and birth asphyxia (24.2%). Early-onset sepsis accounted for 60.0% of all cases. The results obtained were in line with those of Jajoo et al. (2015) [16] who stressed the significance of the perinatal risk factors of early-onset neonatal sepsis and Adhikari et al. (2014) [17] who described the relation between maternal and neonatal risk factors and neonatal sepsis. Thus, neonates born prematurely and with a low birth weight appear to be at high risk of developing sepsis.

Positivity of blood culture was found in 43.3% of cases; Gram-negative bacteria accounted for the majority of isolates. Klebsiella pneumoniae (28.8%) turned out to be the predominant isolate, followed by Escherichia coli (19.2%), Staphylococcus aureus (15.4%), and Acinetobacter spp. (13.5%). Generally, the microbiological pattern obtained appeared similar to that obtained by Bhat et al. (2011) [18] and Aundhakar et al. (2015) [19]. The Gram-negative isolates proved relatively resistant to ampicillin and cefotaxime treatment but relatively sensitive to meropenem, piperacillin-tazobactam, and amikacin. These findings demonstrate the need for antimicrobial surveillance and culture-guided therapy.

Generally, 80.0% of neonates recovered and were discharged from the hospital; the in-hospital mortality rate was 13.3%. Prematurity, low birth weight, birth asphyxia, culture-positive sepsis, respiratory distress, and hemodynamic instability were associated with higher mortality. Hemodynamic instability was identified as the only independent predictor of death (AOR = 4.58). The results of this study corresponded to those of Pammi et al. (2014) [20] who have found increased mortality risk associated with bloodstream infection among NICU patients.

Conclusion

The present study concluded that neonatal sepsis still continued to be a significant cause of mortality and morbidity in the population of premature and low birth weight babies. The factors that stood out as significant risks were low birth weight and prematurity, and the majority of cases of sepsis were found to have early onset sepsis. The causative agents that caused infection included gram negative organisms; Klebsiella pneumoniae was the most common organism isolated from positive cultures and resistance to common antibiotics like ampicillin and cefotaxime was observed. Most of the babies recovered and were discharged, but in-hospital mortality rate was as high as 13.3%. Factors that were significantly associated with in-hospital mortality were prematurity, low birth weight, birth asphyxia, positive culture for sepsis, respiratory distress, and hemodynamic instability. The strongest predictor of mortality was hemodynamic instability.

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