

Original Article



Incidence of Sepsis and Its Determinants among Neonates Admitted in Level III Neonatal Unit - A Prospective Observational Study

Lavanya Eswaran¹ , Vetriselvi Prabakaran^{2*} , Adhisivam Bethou³¹College of Nursing, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry, India²Department of Paediatric Nursing, College of Nursing, Jawaharlal Institute of Post Graduate Medical Education and Research (JIPMER), Puducherry, India³Department of Neonatology, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India**Article Info****Article History:**

Received: February 27, 2022

Accepted: April 26, 2022

e-Published: September 12, 2022

Keywords:

Sepsis, Neonates, Level III neonatal unit, Incidence, Risk factor

***Corresponding Author:**Vetriselvi Prabakaran,
Email: vetriselvijipmer1967@gmail.com**Abstract****Introduction:** Neonates are prone for sepsis due to their immature immune system. Sepsis is preventable if we aware of the maternal and neonatal risk factors. This study aimed to identify the incidence of sepsis and its risk factors.**Methods:** A prospective observational study was carried out among 288 neonates in level III Neonatal unit. Convenience sampling technique was used to enroll the neonates who met the inclusion criteria. Data pertaining to neonatal and maternal demographic and clinical characteristics, incidence of sepsis, risk factors of sepsis were collected by direct observation and from medical record. Data regarding number of skin pricks for blood sample and intravenous cannulation and number of handling of the baby were collected from Tally counters. Data were analysed using chi square test, t-test and logistic regression with SPSS software version 25.**Results:** The incidence of sepsis was 34.7% in level III neonatal unit. Culture positive sepsis constituted 7.3%, urinary tract infection 0.3%, meningitis 7 % and probable sepsis 26.4%. Neonatal factors like extreme preterm, extreme low birth weight, gestational age, birth weight, duration of stay in level III neonatal unit, number of handling, number of skin pricks, duration of intravenous line, duration of tube feeds, mechanical ventilation and maternal premature rupture of membrane were associated with neonatal sepsis significantly.**Conclusion:** Incidence of neonatal sepsis can be minimized by concentrating on modifiable risk factors and implementing the protocol of minimum handling and minimal skin pricks for the neonates.**Introduction**

Globally sepsis is still one of the major causes of morbidity and mortality in neonates in spite of recent advances in health care units.¹ Neonatal sepsis is the third most common cause of deaths among neonates accounting for 225000 deaths globally every year.² According to the global sepsis alliance, occurrence of neonatal infection is about 40 times higher and death rates are 2 times higher in developing countries than in developed countries. Neonate sepsis makes a major public health burden of developing countries.³ The prevalence of neonatal sepsis is about 1 to 10 per 1000 births in developed countries.⁴ In a systemic review assessing the global burden of sepsis among neonates and children, it was reported that mortality due to sepsis can reach 20% of affected cases.⁵ Neonatal sepsis is a syndrome characterized by systemic signs and symptoms of infection in the first month of life.⁶ It is a syndrome with systemic signs of circulatory compromise caused due to invasion of the blood stream

with bacteria.⁷ The major causative organisms of neonatal sepsis were gram negative bacteria such as *Klebsiella*, *Enterobacter*, *Acinetobacter* and gram positive bacteria like methicillin resistant *Staphylococcus aureus*.⁸ The diversity of organisms causing sepsis varies from region to another and changes overtime even in the same place.^{9,10} Newborns are prone to get sepsis due to immaturity of their immune system and exposure to various risk factors during their perinatal period.¹¹ Neonatal deaths occurs due to infections like sepsis, meningitis and pneumonia.¹² Early diagnosis and treatment of neonatal sepsis was a great challenge faced by physician in level III neonatal unit.¹³ Diagnosis and management of neonatal sepsis is challenging due to nonspecific clinical feature and variable laboratory parameters.^{14,15} Delay in identification and treatment of neonatal sepsis are among the main contributors to the high neonatal mortality.¹⁶ On the other hand the survivors of neonatal sepsis are vulnerable to short and long term neuro developmental morbidity.¹⁷

In spite of advancing health care system the admission of neonates to the Neonatal Unit with infection had been increased. Thus identifying the risk factors of neonatal sepsis is very important for formulating the infection prevention control policy in Neonatal Unit. Even though, the risk factors for early as well as late neonatal sepsis were documented in literature, these factors are centre specific. Hence, we can expect the difference in strength of association between the risk factors and the incidence of neonatal sepsis. Factors responsible for late neonatal sepsis may be depend on the man power and disposables availability in Neonatal Unit whereas in early onset sepsis it may be influenced by the delivery room practices. Hence, to identify the incidence and the risk factors associated with neonatal sepsis are required to find out our own strategy for prevention of neonatal sepsis.¹⁸

Only few studies have been conducted to identify the incidence of sepsis among neonates. Mersha et al conducted a study among 275 neonates in a Neonatal Unit in Ethiopia and reported that 33.8% had sepsis.³ Shehab El-Din et al reported that among 344 neonates 44.2% had sepsis.¹² so far studies conducted to identify the incidence of sepsis among neonates in Neonatal Unit included neonates in level 1, 2, and 3 of Neonatal Unit. Only in this study the incidence was identified in level III neonatal unit alone where neonates receive critical care.

Medhat et al revealed that sepsis had significant association with neonatal risk factors like prematurity, and birth weight.¹⁹

In this study in addition to common neonatal risk factors number of skin pricks, number of handling and duration of level III neonatal unit stay of neonates were also monitored.

Since nurses involved in planning nursing care for neonates knowledge on incidence of neonatal sepsis and the risk factors will aid them in formulating infection prevention strategies in neonatal unit.

Materials and Methods

A prospective observational study was adopted to identify the incidence and determinants of sepsis among neonates. This study was conducted in level III neonatal unit of a tertiary care hospital during December 2020 to April 2021. Based on prevalence of sepsis among neonates in level III neonatal unit as 25% at 5% absolute precision and 95% confidence level 288 neonates were enrolled in the study. Neonates admitted in level III neonatal unit and whose parent gave willingness to participate in the study were included in the study. Neonates with major congenital anomalies were excluded from the study. Everyday neonates who met the inclusion criteria were selected through convenience sampling method. Informed consent was obtained from parents.

Data regarding demographic and clinical characteristics of neonates and mothers were collected by interview with mother and from medical record. Neonates were observed

daily and data regarding sepsis was collected. Data regarding number of skin pricks and number of handling of the neonates were measured using commercially available Tally counters. Data regarding number of skin pricks for blood sample collection and intravenous cannulation were measured by blue colour tally counter attached with one side of the cradle of all the neonates and it was pressed by health care personnel after each skin prick. Similarly a red colour tally counter was attached with the other side of the cradle and health care personnel were asked to press the tally counter after each handling of the neonate. It took 45 minutes for each neonate to collect all the data.

Data collection instrument had four sections. The first section included data regarding clinical and demographic characteristics of the neonates. It comprised of gender, gestational age, birth weight, term or preterm, intra uterine growth retardation history of asphyxia, meconium aspiration, respiratory distress syndrome, resuscitation at birth, Jaundice, hypoglycemia, and hypoxic ischemic encephalopathy and also data pertaining nutrition like duration of total parental nutrition, intravenous fluid, tube feed, whether human milk fortifier used, whether donor milk from human milk bank used. It also included data regarding respiratory support like duration of mechanical ventilation and non-invasive ventilation. It also had date regarding duration of level III neonatal unit stay and whether the neonate was on urinary catheter.

Second section had data on maternal clinical characteristics. It comprised of place of delivery, mode of delivery and history of chorioamnionitis, premature rupture membrane for more than 18 hours, urinary tract infection and fever (temperature more than 100.4°F). Third section dealt with data pertaining to sepsis like culture positive sepsis, probable sepsis, central line-associated bloodstream infection (CLABSI), and ventilator associated pneumonia (VAP), urinary tract infection (UTI), septic arthritis, meningitis and surgical site infection.

Culture positive sepsis was evidenced by 2 positive blood cultures one positive blood culture plus a positive C-reactive protein (CRP). Probable sepsis was confirmed with clinical features and positive sepsis screen. CLABSI was laboratory confirmed blood stream infection not related to an infection at other sites and develops within 48 hours of a central line placement.

VAP was elicited by Centers for Disease Control and Prevention (CDC) as an alternate criterion for diagnosis of VAP among infant age ≤ 1 year, radiographic criteria like new or progressive infiltrate and persistent infiltrate, consolidation, cavitation and pneumatoceles. Clinical criteria like worsening gas exchange, temperature instability, Leukopenia, (< 4000 WBC/mm³) or leukocytosis ($> 15,000$ WBC/mm³) left shift (> 10 % band forms) new onset of purulent sputum or change in character of sputum or increased respiratory secretions or increased suctioning requirements, apnea, tachypnea, nasal flaring with retraction of chest wall or nasal flaring

with grunting, wheezing rales or rhonchi, cough and bradycardia (<100 beats/minute) or tachycardia (>170 beats/minute).

UTI was confirmed by positive urine culture (1 or 2 species) with at least 10^5 bacteria/mL with or without clinical symptoms. Septic arthritis was evidenced by inflammation of the synovial membrane with purulent effusion into the joint capsule. Meningitis was confirmed by cerebrospinal fluid examination. Surgical site infection was evidenced by any purulent discharge, or abscess or cellulitis at the surgical site during the month after the surgery.

Fourth section dealt with data regarding number of skin pricks experienced by the neonate and number of times the neonates were handled during their stay in Neonatal Unit. Data were collected with the help of tally counters (blue & red) attached to the cradles.

The study was approved by institute scientific advisory committee (JIP/ CON/ NRMC/M.SC/2019/PN/3) and ethics committee (JIP/CON/IEC/M.SC/2019/PN/3). Informed written consent was obtained from parent of all neonates under study. Confidentiality of the data, right to withdraw from the study and anonymity of the subjects were explained prior. The content validity of the four sections of the tool was obtained from the experts of neonatology and nursing field. Reliability was examined by Cronbach's alpha. (Alpha – 0.6). Data were analyzed using SPSS version 25 (SPSS Inc., Chicago, Ill., USA). Both descriptive and inferential statistics were used for analysis of data. Descriptive statistics (Frequency, percentage, mean, standard deviation) were used to describe the clinical and demographic variables of study participants. Chi-square test was used to identify the association of neonatal sepsis with clinical variables. Logistic regression analysis was used to explore the determinants of neonatal sepsis.

Results

Most of the neonates were male and 43.8% were preterm. 25.3% had low birth weight and mean (SD) gestational age was 34.89 (4.16). About 44.4% had respiratory distress syndrome and 29.5% were on mechanical ventilation. Mean skin pricks and handling of the neonate were 4.94 (2.31) and 17.14 (10.79) respectively (Table 1). Most of the neonates were delivered by cesarean section in emergency operation theatre. About 7.6% mother had premature rupture of membrane for more than 18 hours. About 0.3% had chorioamnionitis and none had UTI or fever (Table 2).

Among 288 neonates, 34.7% had sepsis (Table 3). About 26.4% had probable sepsis and 7.3% had culture positive sepsis. UTI and meningitis constituted 0.3% and 0.7% respectively (Table 4). There was significant association between sepsis and neonatal categorical clinical characteristics like extreme prematurity, extreme low birth weight, total parenteral nutrition, on human milk fortifier, on mechanical ventilation and on non-invasive

Table 1. Clinical characteristics among neonates (N=288)

| Variable | N (%) |
|--|----------------|
| Gender | |
| Male | 165 (57.3) |
| Female | 121 (42) |
| Indeterminant | 2 (0.7) |
| Duration of tube feeds (days) ^a | 3.74 (4.79) |
| Duration of mechanical ventilation (days) ^a | 1.39 (3.58) |
| Number of skin pricks (during level III stay) ^a | 4.94 (2.31) |
| Duration of catheter (days) ^a | 0.01 (0.11) |
| Preterm | |
| Yes | 126 (43.8) |
| No | 162 (56.2) |
| Extreme preterm | |
| Yes | 24 (8.3) |
| No | 264 (91.7) |
| Low birth weight | |
| Yes | 73 (25.3) |
| No | 215 (74.7) |
| Very low birth weight | |
| Yes | 60 (20.8) |
| No | 228 (79.2) |
| Extreme low birth weight | |
| Yes | 34 (11.8) |
| No | 254 (88.2) |
| HIE | |
| Yes | 5 (1.7) |
| No | 283 (98.3) |
| Meconium aspiration | |
| Yes | 9 (3.1) |
| No | 279 (96.9) |
| Need of intravenous fluid | |
| Yes | 266 (92.4) |
| No | 22 (7.6) |
| Need of tube feeds | |
| Yes | 256 (88.9) |
| No | 32 (11.1) |
| Need of milk from human milk bank | |
| Yes | 2 (0.7) |
| No | 286 (99.3) |
| Need of non-invasive respiratory support | |
| Yes | 188 (65.3) |
| No | 100 (34.7) |
| Gestational age (wk) ^a | 34.89 (4.16) |
| Birth weight (g) ^a | 2097.4 (891.8) |
| Duration of intravenous line (days) ^a | 4.55 (5.46) |
| Duration of intravenous fluids (days) ^a | 2.68 (2.93) |
| Duration of TPN (days) ^a | 0.32 (1.29) |
| Duration of non-invasive ventilation (days) ^a | 2.03 (4.39) |
| Number of handling (during level III stay) ^a | 17.14 (10.79) |
| Duration of level III Neonatal Unit stay (days) ^a | 5.35 (7.13) |
| Respiratory distress syndrome | |
| Yes | 128 (44.4) |
| No | 160 (55.6) |
| Post resuscitation care in level III | |
| Yes | 32 (11.1) |
| No | 256 (88.9) |
| Neonatal jaundice | |
| Yes | 4 (1.4) |
| No | 284 (98.6) |

Table 1. Continued

| Variable | N (%) |
|--------------------------------|------------|
| Hypoglycemia | |
| Yes | 14 (4.9) |
| No | 274 (95.1) |
| IUGR | |
| Yes | 8 (2.8) |
| No | 280 (97.2) |
| Asphyxia | |
| Yes | 60 (20.8) |
| No | 228 (79.2) |
| Need of intravenous line | |
| Yes | 283 (98.3) |
| No | 5 (1.7) |
| Need of TPN | |
| Yes | 23 (8) |
| No | 265 (92) |
| Need of human milk fortifier | |
| Yes | 14 (4.9) |
| No | 274 (95.1) |
| Need of mechanical ventilation | |
| Yes | 85 (29.5) |
| No | 203 (70.5) |
| Requiring urinary catheter | |
| Yes | 1 (0.3) |
| No | 287 (99.7) |

IUGR: Intrauterine growth restriction, HIE: Hypoxic ischemic encephalopathy, TPN: Total parental nutrition, ^a Mean (SD) was reported.

Table 2. Maternal clinical characteristics (N=288)

| Maternal clinical characteristics | N (%) |
|-----------------------------------|------------|
| Maternal fever (BT > 100.4F) | |
| Yes | 0 (0) |
| No | 288 (100) |
| Maternal urinary tract infection | |
| Yes | 0 (0) |
| No | 288 (100) |
| PROM | |
| Yes | 22 (7.6) |
| No | 266 (92.4) |
| Maternal chorioamnionitis | |
| Yes | 1 (0.3) |
| No | 287 (99.7) |
| Mode of delivery | |
| SVD | 118 (41) |
| Instrumental | 17 (5.9) |
| Caesarean section | 153 (53.1) |
| Delivered in this hospital | |
| Yes | 281 (97.6) |
| No | 7 (2.4) |
| Place of delivery | |
| Septic labour room | 55 (19.1) |
| Clean labour room | 79 (27.4) |
| Elective operation theatre | 2 (0.7) |
| Emergency operation theatre | 151 (52.4) |
| Casualty | 1 (0.3) |

PROM: Premature rupture of membrane duration (if > 18 hours), SVD: Spontaneous vaginal delivery.

Table 3. Incidence of sepsis among neonates (N=288)

| Incidence of neonatal sepsis | N (%) |
|------------------------------|------------|
| Neonatal sepsis | |
| Yes | 100 (34.7) |
| No | 188 (65.3) |

Table 4. Distribution of sepsis among neonates (N=288)

| Neonatal sepsis | N (%) |
|-------------------------|------------|
| Probable sepsis | |
| Yes | 76 (26.4) |
| No | 212 (73.6) |
| Culture positive sepsis | |
| Yes | 21 (7.3) |
| No | 267 (92.7) |
| CLABSI | |
| Yes | 0 (0) |
| No | 288 (100) |
| VAP | |
| Yes | 0 (0) |
| No | 288 (100) |
| UTI | |
| Yes | 1 (0.3) |
| No | 287 (99.7) |
| Septic arthritis | |
| Yes | 0 (0) |
| No | 288 (100) |
| Meningitis | |
| Yes | 2 (0.7) |
| No | 286 (99.3) |
| Surgical site infection | |
| Yes | 0 (0) |
| No | 288 (100) |

CLABSI: Central line associated bloodstream infection, VAP: Ventilator associated pneumonia, UTI: Urinary tract infection.

respiratory support (Table 5).

There was significant association between sepsis and neonatal continuous clinical characteristics like gestational age, birth weight, and duration of intravenous line, intravenous fluid, total parenteral nutrition, tube feeds, mechanical ventilation, and stay in level III neonatal unit, number of skin pricks and number of handling of the neonate (Table 6). Among maternal risk factors there was significant association between sepsis and premature rupture of membrane (Table 7). Respiratory distress syndrome, premature rupture of membrane for more than 18 hours and number of skin pricks during level III neonatal unit stay were identified as significant determinants of sepsis among neonates (Table 8).

Table 1 illustrated that majority of the neonates were male and nearly half of them were preterm. Their mean gestational age and birth weight were 34 weeks and 2

Table 5. Association between sepsis and neonatal risk factors (categorical variables) among neonates (N=288)

| Variable | N (%) | | P value ^a |
|--------------------------------------|-----------------|------------|----------------------|
| | Neonatal sepsis | | |
| | Yes | No | |
| Gender | | | |
| Male | 61 (61) | 104 (55.3) | 0.41 |
| Female | 39 (39) | 82 (43.6) | |
| Indeterminant | 0 (0) | 2 (1.1) | |
| Preterm | | | |
| Yes | 45 (45) | 81 (43.1) | 0.75 |
| No | 55 (55) | 107 (56.9) | |
| Extreme preterm | | | |
| Yes | 14 (14) | 10 (5.3) | 0.01* |
| No | 86 (86) | 178 (94.7) | |
| Low birth weight | | | |
| Yes | 19 (19) | 54 (28.7) | 0.07 |
| No | 81 (81) | 134 (71.3) | |
| Very low birth weight | | | |
| Yes | 25 (25) | 35 (18.6) | 0.20 |
| No | 75 (75) | 153 (81.4) | |
| Extreme low birth weight | | | |
| Yes | 21 (21) | 13 (6.9) | 0.001* |
| No | 79 (79) | 175 (93.1) | |
| Respiratory distress syndrome | | | |
| Yes | 42 (42) | 86 (45.7) | 0.54 |
| No | 58 (58) | 102 (54.3) | |
| Post resuscitation care in level III | | | |
| Yes | 9 (9) | 23 (12.2) | 0.40 |
| No | 91 (91) | 165 (87.8) | |
| Neonatal jaundice | | | |
| Yes | 0 (0) | 4 (2.1) | 0.14 |
| No | 100 (100) | 184 (97.9) | |
| Hypoglycemia | | | |
| Yes | 3 (3) | 11 (5.9) | 0.28 |
| No | 97 (97) | 177 (94.1) | |
| Intrauterine growth restriction | | | |
| Yes | 5 (5) | 3 (1.6) | 0.09 |
| No | 95 (95) | 185 (98.4) | |
| Hypoxic ischemic encephalopathy | | | |
| Yes | 0 (0) | 5 (2.7) | 0.10 |
| No | 100 (100) | 183 (97.3) | |
| Asphyxia | | | |
| Yes | 25 (25) | 35 (18.6) | 0.20 |
| No | 75 (75) | 153 (81.4) | |
| Meconium aspiration | | | |
| Yes | 4 (4) | 5 (2.7) | 0.53 |
| No | 96 (96) | 183 (97.3) | |
| Need of intravenous line | | | |
| Yes | 100 (100) | 183 (97.3) | 0.10 |
| No | 0 (0) | 5 (2.7) | |
| Need of intravenous fluid | | | |
| Yes | 95 (95) | 171 (91) | 0.21 |
| No | 5 (5) | 17 (9) | |
| Need of TPN | | | |
| Yes | 13 (13) | 10 (5.3) | 0.02* |
| No | 87 (87) | 178 (94.7) | |
| Need of tube feeds | | | |
| Yes | 91 (91) | 165 (87.8) | 0.40 |
| No | 9 (9) | 23 (12) | |

Table 5. Continued

| Variable | N (%) | | P value ^a |
|--|-----------------|------------|----------------------|
| | Neonatal sepsis | | |
| | Yes | No | |
| Need of human milk fortifier | | | |
| Yes | 12 (12) | 2 (1.1) | 0.001* |
| No | 88 (88) | 186 (98.9) | |
| Need of milk from human milk bank | | | |
| Yes | 2 (2) | 0 (0) | 0.05 |
| No | 98 (98) | 188 (100) | |
| Need of mechanical ventilation | | | |
| Yes | 51 (51) | 34 (18.1) | 0.001* |
| No | 49 (49) | 154 (81.9) | |
| Need of non-invasive respiratory support | | | |
| Yes | 57 (57) | 131 (69.7) | 0.03* |
| No | 43 (43) | 57 (30.3) | |
| Need of urinary catheter | | | |
| Yes | 100 (100) | 187 (99.5) | 0.46 |
| No | 0 (0) | 1 (0.5) | |

TPN: Total parental nutrition, ^aChi- square test; * Statistically significant.

Kg respectively. Preterm neonates were 43.8% and 8.3% were extreme preterm. Low birth weight and very low birth weight babies were 25.3% and 20.8% respectively. About 44.4% had Respiratory Distress Syndrome (RDS) and 20.8% had asphyxia. About 29.5% had mechanical ventilation.

Table 2 Illustrated that majority of the neonates were delivered by caesarean section in emergency operation theatre, 7.6% mother had premature rupture of membrane and 8.3% had chorioamnionitis.

Table 3 Illustrated that among 288 neonates 34.7% had sepsis.

Table 4 illustrated that 26.4% neonates probable sepsis and 7.3% had culture positive sepsis. UTI and meningitis constituted 0.3% and 0.7% respectively.

Table 5 Illustrated that there was significant association between sepsis and neonatal categorical clinical characteristics like extreme prematurity, extreme low birth weight, parenteral nutrition, on human milk fortifier, on mechanical ventilation and on non-invasive respiratory support.

Table 6 Illustrated that there was significant association between sepsis and neonatal continuous clinical characteristics like gestational age, birth weight, duration of intravenous line, intravenous fluid, total parenteral nutrition, tube feeds, mechanical ventilation, duration of stay in level III neonatal unit, number of skin pricks and number of handling of the neonate.

Table 7 Illustrated that there was significant association between sepsis and premature rupture of membrane.

Table 8 Illustrated that respiratory distress syndrome, premature rupture of membrane and number of skin pricks were the risk factors associated with sepsis in neonates.

Table 6. Association between sepsis and neonatal risk factors (continuous variables) (N=288)

| Variable | Mean (SD) | | P value ^a |
|--|----------------|----------------|----------------------|
| | Sepsis | Non sepsis | |
| Birth weight (g) | 1857.3 (913.7) | 2225.2 (855.3) | 0.001* |
| Duration of intravenous line (days) | 6.75 (5.70) | 3.38 (4.96) | 0.001* |
| Duration of intravenous fluids (days) | 3.97 (3.89) | 1.99 (1.96) | 0.001* |
| Duration of TPN (days) | 0.55 (1.69) | 0.19 (1.00) | 0.02* |
| Duration of tube feeds | 5.62 (5.54) | 2.73 (4.01) | 0.001* |
| Duration of mechanical ventilation (days) | 3.16 (5.38) | 0.45 (1.31) | 0.001* |
| Duration of noninvasive ventilation (days) | 2.35 (3.32) | 1.86 (4.87) | 0.36 |
| Number of skin pricks | 6.12 (2.63) | 4.31 (1.84) | 0.001* |
| Number of handling | 22.77 (12.24) | 14.14 (8.57) | 0.001* |
| Duration of catheter (days) | 0 (0) | 0.01 (0.11) | 0.46 |
| Duration of level III stay (days) | 8.37 (8.72) | 3.75 (5.52) | 0.001* |

^aIndependent t-test; *Statistically significant.

Table 7. Association between sepsis and maternal risk factor (N=288)

| Variable | Neonatal sepsis N (%) | | P value ^a |
|----------------------------------|--------------------------|------------|----------------------|
| | Yes | No | |
| Maternal fever (T > 100.4F) | | | constant |
| Yes | 0 (0) | 0 (0) | |
| No | 100 (100) | 188 (100) | |
| Maternal urinary tract infection | | | constant |
| Yes | 0 (0) | 0 (0) | |
| No | 100 (100) | 188 (100) | |
| PROM duration (if > 18 hours) | | | 0.01* |
| Yes | 13 (13) | 9 (4.8) | |
| No | 87 (87) | 179 (85.2) | |
| Maternal chorioamnionitis | | | 0.17 |
| Yes | 1 (1) | 0 (0) | |
| No | 99 (99) | 188 (100) | |
| Mode of delivery | | | 0.81 |
| SVD | 43 (43) | 75 (39.9) | |
| Instrumental | 5 (5) | 12 (6.4) | |
| Caesarean section | 52 (52) | 101 (53.7) | |
| Delivered in this institute | | | 0.56 |
| Yes | 97 (97) | 184 (97.9) | |
| No | 3 (3) | 4 (2.1) | |
| Place of delivery | | | 0.05 |
| Septic labour room | 24 (24) | 31 (16.5) | |
| Clean labour room | 22 (22) | 57 (30.3) | |
| Elective operation theatre | 2 (2) | 0 (0) | |
| Emergency operation theatre | 51 (51) | 100 (53.2) | |
| Casualty | 1 (1) | 0 (0) | |

^aChi-square test; *Statistically significant.

Discussion

This prospective observational study included 288 neonates. The incidence of sepsis was 34.7%. Similarly a cross sectional study conducted by Mersha et al in Southern hospital, Ethiopia among 275 neonates during April to June 2018 in Neonatal Unit revealed that 33.8% had sepsis.³ In consistent with this a prospective study conducted by Chakravarthi and Veera Kumar in Ganni Subba Lakshmi medical college and hospital, Rajamundry among 200 neonates showed that 14.5% had sepsis.¹⁸ A retrospective cross sectional study by Medhat et al in South Sinai, Egypt from 2010 to 2014 among 1023 neonates reported 8.6% of sepsis.¹⁹ Furthermore Jajoo et al's prospective study done

in India among 174 neonates showed the incidence of sepsis as 18/1000 live birth.²⁰ Similarly Kayom et al did a cohort study in urban Uganda from March to May 2012 among 325 neonates and identified the incidence of sepsis as 11%.²¹ Similarly a cross sectional study carried out by Ansari et al in Nepal from January 2012 to December 2013 among 918 neonates showed 12.6% sepsis.²² In consistent with this a prospective analytical study by Shehab et al in Egypt from March 2011 to August 2012 among 344 neonates revealed that the incidence of sepsis was 44.2%.¹² In addition to this Woldu et al performed a prospective cross sectional study in Ethiopia among 306 neonates and revealed that the incidence of sepsis was 77/1000 live births.²³

The incidence of sepsis in current study was 34.7%. In consistent with this studies by Mersha et al and Shehab et al also showed the incidence has 33.8% and 44.2% respectively.^{3,12} This consistency could be due to similarity in total sample size in these studies. In contrast to this a study by Mustefa et al showed only 14.5% of sepsis.⁸ This inconsistency could be due to small sample size.

Among 34.7% of sepsis 7.3% was constituted by culture positive sepsis and 26.4% by probable sepsis. Similarly a study by Jajoo et al revealed that 18% had culture positive sepsis and 57% had sepsis screen positive.²⁰

In current study there was no significant association between sepsis and gender of the neonate. In contrary to this a study by Medhat et al showed significant association with gender.¹⁹ Similarly prematurity also showed no significant association in this study but contrary to this a study by Jabiri et al conducted in Tanzania among 220 neonates revealed significant association and studies by Medhat et al, Alemu et al and also Chakravarthi & Veera Kumar showed significant association.^{18,19,24,25} In addition to this a retrospective study by Alam et al in Pakistan from 2007 to 2011 among 564 neonates also showed significant association ($P < 0.001$).⁴

There was no significant association between sepsis and low birth weight. In contrary to this studies by Chakravarthi & Veera Kumar and Medhat et al showed significant association.^{18,19} Post resuscitation showed no significant

Table 8. To identify the risk factors associated with sepsis in neonates (N=288)

| Variables | Odds ratio | SE | P value ^a | 95% CI | |
|---|------------|------|----------------------|--------|-------|
| | | | | Lower | Upper |
| Gender | 1.92 | 0.78 | 0.10 | 0.86 | 4.29 |
| Preterm (<37 wk) | 2.68 | 2.21 | 0.23 | 0.53 | 13.57 |
| Extreme preterm (<28 wk) | 1.36 | 1.78 | 0.81 | 0.10 | 17.59 |
| Low birth weight | 0.19 | 0.18 | 0.08 | 0.03 | 1.27 |
| Very low birth weight | 0.32 | 0.41 | 0.38 | 0.02 | 4.05 |
| Extreme low birth weight | 0.50 | 0.88 | 0.69 | 0.01 | 15.66 |
| Respiratory distress syndrome | 2.87 | 1.43 | 0.03 * | 1.07 | 7.66 |
| Post resuscitation care in level III | 2.10 | 1.63 | 0.33 | 0.46 | 9.61 |
| Hypoglycemia | 4.91 | 5.47 | 0.15 | 0.55 | 43.54 |
| Intrauterine growth restriction | 2.67 | 3.04 | 0.38 | 0.28 | 24.83 |
| Gestational age | 0.88 | 0.11 | 0.34 | 0.67 | 1.14 |
| Birth weight (g) | 1.00 | 0.00 | 0.06 | 0.99 | 1.00 |
| Asphyxia | 1.23 | 0.63 | 0.67 | 0.45 | 3.36 |
| Meconium aspiration | 0.10 | 0.12 | 0.06 | 0.00 | 1.15 |
| Duration of IV line (days) | 0.92 | 0.09 | 0.44 | 0.75 | 1.13 |
| Need of IV fluid | 1.29 | 1.14 | 0.77 | 0.22 | 7.33 |
| Duration of IV fluids (days) | 0.93 | 0.11 | 0.58 | 0.74 | 1.18 |
| Need of total parental nutrition | 0.30 | 0.35 | 0.31 | 0.03 | 3.01 |
| Duration of total parental nutrition (days) | 1.13 | 0.32 | 0.64 | 0.65 | 1.98 |
| Need of tube feeds | 1.26 | 0.61 | 0.63 | 0.48 | 3.29 |
| Duration of tube feeds (days) | 1.02 | 0.11 | 0.82 | 0.82 | 1.27 |
| Need of human milk fortifier | 3.28 | 4.08 | 0.34 | 0.28 | 37.56 |
| Need of mechanical ventilation | 3.04 | 2.34 | 0.14 | 0.67 | 13.79 |
| Duration of mechanical ventilation (days) | 0.70 | 0.13 | 0.07 | 0.47 | 1.03 |
| Duration of noninvasive ventilation (days) | 0.99 | 0.08 | 0.97 | 0.84 | 1.18 |
| Number of skin pricks (during level III stay) | 0.76 | 0.08 | 0.02* | 0.61 | 0.96 |
| Number of handling | 0.96 | 0.03 | 0.37 | 0.90 | 1.03 |
| Duration of level III stay (days) | 1.05 | 0.06 | 0.44 | 0.92 | 1.19 |
| PROM > 18 hours | 5.65 | 4.42 | 0.02* | 1.21 | 26.18 |
| Mode of delivery | 0.86 | 0.48 | 0.80 | 0.29 | 2.57 |
| Born in this hospital | 0.38 | 0.31 | 0.24 | 0.07 | 1.90 |
| Place of delivery | 0.97 | 0.40 | 0.94 | 0.42 | 2.21 |

PROM: Premature rupture of membrane; SE: standard error; CI, confidence interval.

^a Logistic regression, *Statistically significant.

association with sepsis. In contrary to this a retrospective case control study by Adatara et al in Ghana from January to December 2017 among 900 neonates revealed significant association.²⁶ Similarly studies by Jabiri et al and Alemu et al also showed significant association.^{24,25} There was no association between sepsis and asphyxia. In contrary to this a cross sectional study by Getabelew et al conducted in Ethiopia among 244 neonates showed significant association.²⁷ Similarly Alemu et al and Ketema et al also showed significant association respectively.^{25,28}

Birth weight showed significant association with neonatal sepsis. In consistent with this a case control study by Ketema et al in southern Ethiopia among 335 neonates in Neonatal Unit also showed similar result.²⁸ Duration of level III neonatal unit stay revealed significant association with sepsis. congruently a cross sectional study conducted by Yismaw et al in Ethiopia among 423 neonates showed significant association.²⁹ Association between sepsis and maternal risk factors revealed that premature rupture of membrane showed significant association which is similar to the studies by Yismaw et al and Medhat et al.^{19,29} Similarly a retrospective study by Adatara et al also

showed significant association and studies by Alemu et al and Kayom et al also supported above result.^{21,25,26}

Maternal chorioamnionitis showed no significant association with neonatal sepsis. In contrary to the above result studies by Yismaw et al and Alam et al showed significant association.^{4,29} Mode of delivery also not had significant association with sepsis which is also contrary to the findings of the studies by Medhat et al and Woldu et al.^{19,23} Similarly place of delivery also had no significant association but in contrary to this study by Woldu et al as showed significant association.²³

Birrie et al in Woldia did a study on neonatal sepsis and stated that the prevalence was 79.4%.³⁰ Wilar and Lestari expressed that in neonatal sepsis the presence of tachypnea and sclerema were significant risk factors for mortality.³¹ It has to be mentioned that extreme caution should exercised in generalizing the findings of the study to other populations because the current study was conducted in one region only, moreover neonates in level III neonatal unit were only included in the study. Neonatal intensive care unit nurses play a major role in implementing infection prevention strategies in level III

Research Highlights

What is the current knowledge?

Due to increase in knowledge and practice of infection prevention strategies among health care professionals in critical care, the incidence of neonatal sepsis may be very less.

What is new here?

In this study number of skin pricks and number of handling of the neonate showed significant association with neonatal sepsis. These two modifiable risk factors may be reduced by individualized nursing care plan for each neonate and clubbing the procedures together. Similarly number of skin pricks can be reduced by allotting sufficient skilled persons in level III neonatal unit.

unit. By meticulous hand hygiene, by proper securing and maintenance of intravenous access, and by minimum handling of the neonate the incidence of sepsis may be reduced.

Conclusion

The findings of this study showed that among neonates in level III neonatal unit 34.7% had sepsis. Well-tailored identification of risks during labour and early triaging and managing can decrease the risk. This study adds one more piece of evidence that infection prevention strategies need to be strengthened in level III neonatal unit.

Acknowledgments

The authors would like to express their gratitude to all the neonates who were participated in the study.

Authors' Contributions

VP, LE, AB: Conception and design; VP, LE, AB: Analysis and Interpretation of the data; VP, LE, AB: Drafting of the article; VP, AB: Critical revision of the article for important intellectual content; VP, LE, AB: Final approval of the article.

Funding

The authors have declared that there was no funding.

Data Accessibility

The datasets are available from the corresponding author on reasonable request.

Ethical Issues

The current study is a part of MSc thesis approved by the ethics committee of JIPMER. The objectives of the study were explained to the parents and all of them signed written informed consent forms. Parents were also assured about the confidentiality of the data.

Conflict of Interests

The authors declare no conflict of interest in this study.

References

1. Wu JH, Chen CY, Tsao PN, Hsieh WS, Chou HC. Neonatal sepsis: a 6-year analysis in a neonatal care unit in Taiwan. *Pediatr Neonatol*. 2009; 50 (3): 88-95. doi: [10.1016/s1875-9572\(09\)60042-5](https://doi.org/10.1016/s1875-9572(09)60042-5)
2. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017; 390 (10100): 1151-210. doi: [10.1016/s0140-6736\(17\)32152-9](https://doi.org/10.1016/s0140-6736(17)32152-9)
3. Mersha A, Worku T, Shibiru S, Bante A, Molla A, Seifu G, et al. Neonatal sepsis and associated factors among newborns in hospitals of Wolaita Sodo Town, Southern Ethiopia. *Res Rep Neonatol*. 2019; 9: 1-8. doi: [10.2147/rrn.s193074](https://doi.org/10.2147/rrn.s193074)
4. Alam MM, Saleem AF, Shaikh AS, Munir O, Qadir M. Neonatal sepsis following prolonged rupture of membranes in a tertiary care hospital in Karachi, Pakistan. *J Infect Dev Ctries*. 2014; 8 (1): 67-73. doi: [10.3855/jidc.3136](https://doi.org/10.3855/jidc.3136)
5. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. *Lancet Respir Med*. 2018; 6 (3): 223-30. doi: [10.1016/s2213-2600\(18\)30063-8](https://doi.org/10.1016/s2213-2600(18)30063-8)
6. Chaurasia S, Sivanandan S, Agarwal R, Ellis S, Sharland M, Sankar MJ. Neonatal sepsis in South Asia: huge burden and spiralling antimicrobial resistance. *BMJ*. 2019; 364: k5314. doi: [10.1136/bmj.k5314](https://doi.org/10.1136/bmj.k5314)
7. Edmond K, Zaidi A. New approaches to preventing, diagnosing, and treating neonatal sepsis. *PLoS Med*. 2010; 7 (3): e1000213. doi: [10.1371/journal.pmed.1000213](https://doi.org/10.1371/journal.pmed.1000213)
8. Mustefa A, Abera A, Aseffa A, Abathun T, Degefa N, Tadesse H, et al. Prevalence of neonatal sepsis and associated factors amongst neonates admitted in Arbaminch General Hospital, Arbaminch, Southern Ethiopia, 2019. *J Pediatr Neonatal Care*. 2020; 10 (1): 1-7. doi: [10.15406/jpnc.2020.10.00404](https://doi.org/10.15406/jpnc.2020.10.00404)
9. Shrestha S, Adhikari N, Rai BK, Shreepaili A. Antibiotic resistance pattern of bacterial isolates in neonatal care unit. *JNMA J Nepal Med Assoc*. 2010; 50 (180): 277-81.
10. Ghotaslou R, Ghorashi Z, Nahaei MR. Klebsiella pneumoniae in neonatal sepsis: a 3-year-study in the pediatric hospital of Tabriz, Iran. *Jpn J Infect Dis*. 2007; 60 (2-3): 126-8.
11. Almudeer AH, Alibrahim MA, Gosadi IM. Epidemiology and risk factors associated with early onset neonatal sepsis in the south of KSA. *J Taibah Univ Med Sci*. 2020; 15 (6): 509-14. doi: [10.1016/j.jtumed.2020.08.009](https://doi.org/10.1016/j.jtumed.2020.08.009)
12. Shehab El-Din EM, El-Sokkary MM, Bassiouny MR, Hassan R. Epidemiology of neonatal sepsis and implicated pathogens: a study from Egypt. *Biomed Res Int*. 2015; 2015: 509484. doi: [10.1155/2015/509484](https://doi.org/10.1155/2015/509484)
13. Iyer CR, Naveen G, Suma HR, Kumarguru BN, Sweta K, Janakiraman. Clinical profile and outcome of neonates with suspected sepsis from a rural medical college hospital of South India. *Int J Contemp Pediatr*. 2018; 5 (1): 55-60. doi: [10.18203/2349-3291.ijcp20175146](https://doi.org/10.18203/2349-3291.ijcp20175146)
14. Shaw CK, Shaw P, Malla T, Malla KK. The clinical spectrum and outcome of neonatal sepsis in a neonatal intensive care unit at a tertiary care hospital in western Nepal: January 2000 to December 2005-a retrospective study. *East J Med*. 2012; 17 (3): 119-25.
15. Garg D, Agrawal N. Aetiology and presentation of neonatal septicaemia at tertiary care hospital of southern Rajasthan. *Int J Med Sci Educ*. 2014; 1 (1): 12-20.
16. Gebremedhin D, Berhe H, Gebrekirstos K. Risk factors for neonatal sepsis in public hospitals of Mekelle city, North Ethiopia, 2015: unmatched case control study. *PLoS One*. 2016; 11 (5): e0154798. doi: [10.1371/journal.pone.0154798](https://doi.org/10.1371/journal.pone.0154798)
17. Ferreira RC, Mello RR, Silva KS. Neonatal sepsis as a risk factor for neurodevelopmental changes in preterm infants with very low birth weight. *J Pediatr (Rio J)*. 2014; 90 (3): 293-9. doi: [10.1016/j.jped.2013.09.006](https://doi.org/10.1016/j.jped.2013.09.006)
18. Chakravarthi GK, Veera Kumar S. Incidence of neonatal sepsis

- in relation to prolonged rupture of membranes (PROM) > 18 hours and associated risk factors for early onset neonatal sepsis (EONS). *Int J Pediatr Res.* 2019; 6 (9): 444-53. doi: [10.17511/ijpr.2019.i09.02](https://doi.org/10.17511/ijpr.2019.i09.02)
19. Medhat H, Khashana A, El Kalioby M. Incidence of neonatal infection in South Sinai, Egypt. *Int J Infect.* 2017; 4 (1): e36615. doi: [10.17795/iji-36615](https://doi.org/10.17795/iji-36615)
 20. Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. To study the incidence and risk factors of early onset neonatal sepsis in an out born neonatal intensive care unit of India. *J Clin Neonatol.* 2015; 4 (2): 91-5. doi: [10.4103/2249-4847.154106](https://doi.org/10.4103/2249-4847.154106)
 21. Kayom VO, Mugalu J, Kakuru A, Kiguli S, Karamagi C. Burden and factors associated with clinical neonatal sepsis in urban Uganda: a community cohort study. *BMC Pediatr.* 2018; 18 (1): 355. doi: [10.1186/s12887-018-1323-4](https://doi.org/10.1186/s12887-018-1323-4)
 22. Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Chapagain ML. Neonatal septicemia in Nepal: early-onset versus late-onset. *Int J Pediatr.* 2015; 2015: 379806. doi: [10.1155/2015/379806](https://doi.org/10.1155/2015/379806)
 23. Woldu MA, Guta MB, Lenjisa JL, Tegegne GT, Tesafye G, Dinsa H. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia. *Int J Contemp Pediatr.* 2017; 1 (3): 135-41. doi: [10.5455/2349-3291.ijcp20141102](https://doi.org/10.5455/2349-3291.ijcp20141102)
 24. Jabiri A, Wella HL, Semiono A, Saria A, Protas J. Prevalence and factors associated with neonatal sepsis among neonates in Temeke and Mwananyamala Hospitals in Dar es Salaam, Tanzania. *Tanzan J Health Res.* 2016; 18 (4): 10-23. doi: [10.4314/thrb.v18i4.4](https://doi.org/10.4314/thrb.v18i4.4)
 25. Alemu M, Ayana M, Abiy H, Minuye B, Alebachew W, Endalamaw A. Determinants of neonatal sepsis among neonates in the northwest part of Ethiopia: case-control study. *Ital J Pediatr.* 2019; 45 (1): 150. doi: [10.1186/s13052-019-0739-2](https://doi.org/10.1186/s13052-019-0739-2)
 26. Adatara P, Afaya A, Salia SM, Afaya RA, Konlan KD, Agyabeng-Fandoh E, et al. Risk factors associated with neonatal sepsis: a case study at a specialist hospital in Ghana. *ScientificWorldJournal.* 2019; 2019: 9369051. doi: [10.1155/2019/9369051](https://doi.org/10.1155/2019/9369051)
 27. Getabelew A, Aman M, Fantaye E, Yeheyis T. Prevalence of neonatal sepsis and associated factors among neonates in neonatal intensive care unit at selected governmental hospitals in Shashemene town, Oromia regional state, Ethiopia, 2017. *Int J Pediatr.* 2018; 2018: 7801272. doi: [10.1155/2018/7801272](https://doi.org/10.1155/2018/7801272)
 28. Ketema E, Mamo M, Miskir D, Hussen S, Boti N. Determinants of neonatal sepsis among neonates admitted in a neonatal intensive care unit at Jinka General Hospital, Southern Ethiopia. *Int J Nurs Midwifery.* 2019; 11 (3): 18-24. doi: [10.5897/ijnm2018.0335](https://doi.org/10.5897/ijnm2018.0335)
 29. Yismaw AE, Abebil TY, Biweta MA, Araya BM. Proportion of neonatal sepsis and determinant factors among neonates admitted in University of Gondar comprehensive specialized hospital neonatal Intensive care unit Northwest Ethiopia 2017. *BMC Res Notes.* 2019; 12 (1): 542. doi: [10.1186/s13104-019-4587-3](https://doi.org/10.1186/s13104-019-4587-3)
 30. Birrie E, Sisay E, Tibebu NS, Tefera BD, Zeleke M, Tefera Z. Neonatal sepsis and associated factors among newborns in Woldia and Dessie comprehensive specialized hospitals, North-East Ethiopia, 2021. *Infect Drug Resist.* 2022; 15: 4169-79. doi: [10.2147/idr.s374835](https://doi.org/10.2147/idr.s374835)
 31. Wilar R, Lestari H. Risk factors and clinical outcomes of neonatal sepsis in Manado tertiary referral hospital: a single-center study. *Open Access Maced J Med Sci.* 2022; 10 (B): 93-8. doi: [10.3889/oamjms.2022.7993](https://doi.org/10.3889/oamjms.2022.7993)