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Research Article

# Predictors of mortality in neonatal sepsis in a resource-limited setting

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## Abstract

**Introduction:** Sepsis remains a major cause of death in neonatal period. Although significant advances in diagnosis, therapeutic and prevention strategies have been noted, sepsis remains a common concern in clinical practice especially in low-resource countries. The aim of this study was to determine the predictors of mortality in neonatal sepsis in Lubumbashi city (Democratic Republic of Congo).

**Methods:** The records of newborns with sepsis managed in Neonatal Intensive Care Units in two University Hospitals between November 2019 and October 2020 were studied. Binary and multiple logistic regressions have been used to observe the association between independent variables and dependent variable.

**Results:** A total of 162 cases of neonatal sepsis were reviewed. The mortality rate of neonatal sepsis was 21% of babies admitted. Very low birth weight (< 1500 grams) and primiparity were significantly associated with mortality in neonatal sepsis (AOR = 12.66; 95% CI 2.40 to 66.86; $p$ = 0.003 and AOR = 3.35; 95% CI 1.31 to 8.59; $p$ = 0.012, respectively).

**Conclusion:** The mortality rate of neonatal sepsis was 21%. Very low birth weight and primiparity were significantly associated with mortality in neonatal sepsis.

**More Information**

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**Keywords:** Neonatal sepsis; Risk factors; Mortality; Lubumbashi



## Introduction

Neonatal sepsis (NS) is a systemic infection that occurs in newborns under 28 days of life. It is a condition of bacterial, viral or fungal origin which is accompanied by a range of clinical manifestations [1,2]. The newborns exposed to these pathogens during the perinatal period are sensitive to invasive infections because of their relatively weakened immune system [3]. The incidence of NS varies from 1 to 170 per 1,000 live births [4.5]. In Lubumbashi (in the Democratic Republic of the Congo [DRC]), it was 31.39% [6].

NS remains a major cause of death in this population, although significant advances in diagnosis, therapeutic and prevention strategies [2]. In 2019, the World Health Organization (WHO) estimated that 2.4 (2.3 - 2.7) million newborns died within 28 days of birth [7]. The main causes of these neonatal deaths were infections (35%), premature births (28%), intrapartum complications (24%) and asphyxia (23%). In developing countries, each year, sepsis is the most common cause of neonatal mortality and is probably responsible for 30 to 50% of the total neonatal deaths [8.9]. Nyenga, et al. [10], in a recent study conducted in Lubumbashi (in the DRC), reported that sepsis was responsible for 21% neonatal deaths.

The purpose of our study was to identify the factors associated with NS mortality in Lubumbashi, DRC.

## Methodology

We conducted an analytical cross-sectional study in

Neonatal Intensive Care Units in two University Hospitals in Lubumbashi (University Clinics and Sendwe Hospital) in the Haut-Katanga Province in the November 2019 to October 2020. We included all the newborn admitted NS in neonatal intensive care units of these tertiary care hospitals. The recruitment of the subjects was exhaustive and consecutive to the oral consent of their mother. The sample size was 162.

NS is a clinical syndrome with or without a bacteremia occurring during the first month of life. In this study, sepsis has been diagnosed on the basis of clinical symptoms by applying the criteria of the WHO [11,12]. This clinical diagnosis was supplemented by the iterative dosage of the C-reactive protein at a significant threshold ≥ 20 mg/L from the 24th hour after suspicion of the infection.

NS was classified in early onset sepsis (EONS) if it occurred at the beginning of 72 hours of life and late onset sepsis (LONS) if it occurred after 72 hours of life. The results have been defined as the condition of the patient at the exit and grouped by living and deceased. The variables studied were related to: maternal sociodemographic characteristics (age, parity, marital status, level of education, occupation) and neonatal characteristics (gestational age, birth weight, sex, delivery routes, admission mode, type of sepsis, concept of medical assistance and presence of antecedent of infectious risk).

Data were analyzed using the Stata software (version 15.0). Variables have been categorized and summarized in percentages. A bivariate analysis was performed followed by a multivariate analysis to reduce the effect of confounding factors. Adjusted odds ratios (AOR) with Confidence intervals of 95% (95% CI) were used to measure the degree of association between the variables. A *p* - value of 0.05 was considered statistically significant.

Ethical authorization was obtained from the Medical Ethics Committee of the University of Lubumbashi (Approval No. UNILU/CEM/038/2019). The privacy of the respondent and the confidentiality of the information has been ensured throughout the study procedure.

## Results

We found that most cases of NS occurred in male newborns (51.85%), those born at term (68.52%), those born with low weight (52.46%), and those born spontaneously by vaginal route (71.6%).

Of the 162 newborns with NS, most cases (93.21%) were EONS. Most patients (82.72%) had at least one infectious risk factor; the main maternal risk factors identified were genito-urinary tract infections (42.59%), premature membrane rupture (32.10%), meconium-stained amniotic fluid (25.31%) and prolonged labor (20.37%).

The mortality rate was 21%. In a bivariate analysis, NS-related mortality was significantly correlated with: primiparity (OR = 2.56 [1.17-5.59]; $p$ = 0.016), admission mode (OR = 2.50 [1.16-5.41]; $p$ = 0.017), gestational age < 37 weeks (OR = 3.80 [1.73-8.34]; $p$ = 0.0005), birth weight < 1500 grams (OR = 12.59 [4.27-37.10]; $p$ < 0.0001), and non-medical assistance at birth (OR = 2.49 [1.08-5.74]; $p$ = 0.029) (Tables 1 and 2). Further analysis by multivariate logistic regression showed that primiparity (adjusted OR = 3.35 [1.31-8.59]; $p$ = 0.012) and birth weight < 1500 grams (adjusted OR = 12.66 [2.40-66.86]; $p$ = 0.003) were significantly associated with NS-related mortality (Table 3).

## Discussion

The neonatal mortality rate is a reliable criterion for assessing the overall progress of perinatal care in a

**Table 1:** Unadjusted association between neonatal sepsis related mortality and socio-demographic characteristics of mothers.

| Variable | Neonatal sepsis | | | | | Crude OR [95% CI] | *p* - value |
|---|---|---|---|---|---|---|---|
| | Total (N = 162) | Non survivor (*n* = 34) | | Survivor (*n* = 128) | | | |
| Maternal age | | | | | | | |
| < 20 years | 28 | 9 | 32.14% | 19 | 67.86% | 1.67 [0.67-4.18] | 0.272 |
| 20-34 years | 104 | 23 | 22.12% | 81 | 77.88% | Reference | |
| ≥35 years | 30 | 2 | 6.67% | 28 | 93.33% | 0.25 [0.03-1.14] | 0.065 |
| Parity | | | | | | | |
| Primiparous | 49 | 16 | 32.65% | 33 | 67.35% | 2.56 [1.17-5.59] | 0.016 |
| Multiparous | 113 | 18 | 15.93% | 95 | 84.07% | Reference | |
| Marital status | | | | | | | |
| Single | 15 | 5 | 33.33% | 10 | 66.67% | 2.03 [0.64-6.41] | 0.218 |
| Married | 147 | 29 | 19.73% | 118 | 80.27% | Reference | |
| Education level | | | | | | | |
| Primary | 20 | 5 | 25.00% | 15 | 75.00% | 1.51 [0.45-5.05] | 0.497 |
| Secondary | 81 | 18 | 22.22% | 63 | 77.78% | 1.30 [0.56-3.00] | 0.539 |
| Higher/University | 61 | 11 | 18.03% | 50 | 81.97% | Reference | |
| Profession | | | | | | | |
| Student | 3 | 2 | 66.67% | 1 | 33.33% | 14.67 [0.61-526.05] | 0.056 |
| Functionary | 21 | 4 | 19.05% | 17 | 80.95% | 2.01 [0.30-15.48] | 0.434 |
| Liberal | 29 | 3 | 10.34% | 26 | 89.66% | Reference | |
| Housewife | 109 | 25 | 22.94% | 84 | 77.06% | 2.56 [0.69-14.33] | 0.194 |

N: Number; OR: Odds Ratio; 95% CI: Confidence Interval at 95%.

**Table 2:** Unadjusted association between neonatal sepsis related mortality and neonatal characteristics.

| Variable | Neonatal sepsis | | | | | Crude OR [95% CI] | *p* - value |
|---|---|---|---|---|---|---|---|
| | Total (N = 162) | Non survivor (*n* = 34) | | Survivor (*n* = 128) | | | |
| Type of sepsis | | | | | | | |
| EONS | 151 | 32 | 21.19% | 119 | 78.81% | 1.21 [0.23-12.04] | 1.000 |
| LONS | 11 | 2 | 18.18% | 9 | 81.82% | Reference | |
| Transfer from another hospital | | | | | | | |
| Yes | 62 | 19 | 30.65% | 43 | 69.35% | 2.50 [1.16-5.41] | 0.017 |
| No | 100 | 15 | 15.00% | 85 | 85.00% | Reference | |
| Gestational age | | | | | | | |
| < 37 weeks | 51 | 19 | 37.25% | 32 | 62.75% | 3.80 [1.73-8.34] | 0.0005 |
| ≥ 37 weeks | 111 | 15 | 13.51% | 96 | 86.49% | Reference | |
| Sex | | | | | | | |
| Female | 78 | 19 | 24.36% | 59 | 75.64% | Reference | |
| Male | 84 | 15 | 17.86% | 69 | 82.14% | 1.48 [0.69-3.17] | 0.310 |
| Birth weight | | | | | | | |
| < 1500 grams | 24 | 15 | 62.50% | 9 | 37.50% | 12.59 [4.27-37.10] | <0.00001 |
| 1500-2499 grams | 61 | 10 | 16.39% | 51 | 83.61% | 1.48 [0.56-3.91] | 0.426 |
| ≥ 2500 grams | 77 | 9 | 11.69% | 68 | 88.31% | Reference | |
| Delivery mode | | | | | | | |
| Obstructed vaginal delivery | 4 | 1 | 25.00% | 3 | 75.00% | 0.96 [0.10-9.54] | 1.000 |
| Caesarean section | 42 | 3 | 7.14% | 39 | 92.86% | 0.22 [0.06-0.77] | 0.013 |
| Eutocical delivery | 116 | 30 | 25.86% | 86 | 74.14% | Reference | |
| Medical assistance at birth | | | | | | | |
| No | 35 | 12 | 34.29% | 23 | 65.71% | 2.49 [1.08-5.74] | 0.029 |
| Yes | 127 | 22 | 17.32% | 105 | 82.68% | Reference | |
| Infectious risk | | | | | | | |
| Yes | 134 | 29 | 21.64% | 105 | 78.36% | 1.27 [0.44-3.63] | 0.655 |
| No | 28 | 5 | 17.86% | 23 | 82.14% | Reference | |

N: Number; OR: Odds Ratio; 95% CI: Confidence Interval at 95%; EONS: Early Onset Sepsis; LONS: Late Onset Sepsis.

**Table 3:** Multiple logistic regression of risk factors for neonatal sepsis related mortality in newborns in Lubumbashi.

| Variable | Adjusted OR | St. Error | t-value | p - value | [95% Confidence Interval] | |
|---|---|---|---|---|---|---|
| Medical assistance at birth | | | | | | |
| Yes | 2.09 | 1.13 | 1.36 | 0.174 | 0.72 | 6.04 |
| No | Ref. | | | | | |
| Delivery mode | | | | | | |
| Obstructed vaginal delivery | 2.36 | 3.02 | 0.67 | 0.503 | 0.19 | 29.05 |
| Cesarean section | 0.57 | 0.41 | -0.78 | 0.434 | 0.14 | 2.30 |
| Eutocical delivery | Ref. | | | | | |
| Gestationnel age | | | | | | |
| < 37 weeks | 0.99 | 0.66 | -0.01 | 0.992 | 0.27 | 3.62 |
| ≥ 37 weeks | Ref. | | | | | |
| Birth weight | | | | | | |
| < 1500 grams | **12.66** | 10.75 | 2.99 | **0.003** | 2.40 | 66.86 |
| 1500-2499 grams | 1.82 | 1.14 | 0.96 | 0.339 | 0.53 | 6.19 |
| ≥ 2500 grams | Ref. | | | | | |
| Parity | | | | | | |
| Primiparous | **3.35** | 1.61 | 2.52 | **0.012** | 1.31 | 8.59 |
| Multiparous | Ref. | | | | | |
| Transfer from another hospital | | | | | | |
| Yes | 2.31 | 1.19 | 1.62 | 0.106 | 0.84 | 6.35 |
| No | Ref. | | | | | |

community. Knowledge of local or regional health problems is a prerequisite for an effective health care delivery system [13]. The mortality rate of NS varies between hospitals and between countries. This study reports a mortality rate of 21%. Comparable rates have been found in other studies conducted in India (16%) [14], Nigeria (19.3%) [15], South Africa (20.8%) [16] and Indonesia (28.3%) [17]. While high rates were reported in Nigeria (32.2%) [18], India (38.24%) [19], Mexico (43.9%) [20], and Iraq (44.2%) [13]. These differences in mortality rates between studies are attributable to many factors such as socio-economic factors, geographical factors, equipment levels and the effectiveness of each hospital's prophylactic and therapeutic approach [13]. NS may have subtle, diverse and non-specific symptoms and signs, often leading to delayed diagnosis and treatment leading to high morbidity and mortality [21].

We found that primiparity was a risk factor for neonatal death in the case of sepsis. Munan, et al. [22] reported that perinatal death was higher in primipares than in multipares and noted that the need for neonatal intensive care was significantly recorded in primiparous newborns. According to these authors, this would be due to high rates of intrapartal complications (prolonged or obstructed labour, dystocies, caesarean sections, fetal distress, poor Apgar scores) in primipares [22]. The same finding was reported by Kaur and Kaur, [23]. Although these authors did not take an interest in NS, it is logical that this finding is also applicable in the case of NS. This combination of primiparity-related morbid events could compromise the life-threatening prognosis of the newborn with sepsis. Primiparous newborn is therefore considered to be at risk and gestation as the postnatal period should be given special care [24]. Trotman, et al. [25] found an association between early childhood and death in neonates with sepsis. Similarly, young age may be considered a characteristic of primiparous mothers in our contexts where the prevalence of teenage motherhood is high [26]. In our series, we found a high death rate among mothers under 20 years of age (32.1%) although this association with maternal age was not statistically significant. Lack of experience with lower-risk behavior during pregnancy would also be an important factor.

This study showed that low birth weight (< 1500 grams) was a risk factor for death in neonates with sepsis. A similar finding has been reported in many previous studies in different countries [13,14,19,20]. Infectious disease morbidity and mortality are known to be high in low-birth-weight infants [27]. This is explained either by an inherent immune deficiency or because these newborns require prolonged hospitalization that increases the risk of nosocomial infection. Infection is therefore added to all the complications that already darken the life-threatening prognosis of low-birth-weight infants. Transplacental maternal antibodies are mainly involved in humoral and cellular immunity, so premature neonates are less likely to receive as many immunoglobulins as neonates born at term [25]. Indeed, although prematurity in general is not a statistically related factor to NS-related mortality in our series, we nonetheless noted a high mortality rate in premature neonates (37.3%).

The results of this study should be interpreted with certain limitations. First, because of the cross-sectional nature of the study. Secondary to the fact that the study is conducted with newborns admitted to urban reference hospitals, the results may not be generalizable to the general population.

## Conclusion

This study identified primiparity and very low birth weight as independent risk factors for mortality in NS. Strategies to reduce morbidity and mortality in newborns with sepsis should include measures that will reduce the incidence of low birth weight or even premature birth. Primiparity will need to be given particular attention in programs to monitor mother-to-child infections and to manage the risk of sepsis-related complications.

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