

Neonatal Sepsis and Associated Risk Factors among Newborns in Gbagada General Hospital, Massey Street Children Hospital, and Lagos Island Maternity Hospital, Lagos State

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Abstract Introduction: Neonatal sepsis is a systemic illness that affects neonates under the age of 28 days. It is one of the primary causes of neonatal mortality in both developed and developing countries. The main aim of this study was to assess the risk factors associated with neonatal sepsis among newborns at Massey Street Children's Hospital, Lagos Island Maternity Hospital, and Gbagada General Hospital in Lagos State. **Materials and methods:** A case-control study design was employed on 200 neonates in Massey Street Children's Hospital, Lagos Island Maternity Hospital, and Gbagada General Hospital. Data were collected using a pre-tested standardized questionnaire. Data were entered using the Statistical Package for Social Sciences Version (SPSS). Bivariate and multivariate analyses were done by using binary logistic regression and used to determine the risk factors. **Results:** A total of 200 neonates were recruited, 82 (41%) had sepsis. The risk factors associated with neonatal sepsis were bottle feeding (AOR= 1.58(0.31, 8.05), Skin/local infection [AOR=1.6(0.36, 6.87), Prolonged rupture of the membrane [AOR = 1.48; (0.57, 3.88) and Previous history of neonatal admission [AOR = 16.91(2.08, 381.76] were the independent predictors of neonatal sepsis. **Conclusion:** This study indicates that the proportion of neonatal sepsis is high. Prolonged rupture of the membrane, Previous history of neonatal admission, Skin/local infection, and bottle feeding were identified as risk factors for neonatal sepsis.

Keywords: Neonatal sepsis, Risk factors, Neonates, Neonatal intensive care unit, Hospitals, Case-Control

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1. Introduction

Neonatal sepsis, a life-threatening dysregulated, inflammatory response to bloodstream infections in infants and a key challenge to neonatal medicine [1,2], is a leading cause of almost all morbidity and mortality globally in children younger than 5 years. Despite recent advances in neonatal care, there has been limited progress in mortality reduction. Neonatal sepsis can be categorized as Early-onset sepsis (EOS) and late-onset sepsis (LOS) [3]. Early onset neonatal sepsis (EOS) is defined as an infection appearing in the first 72 h after the child's birth, as opposed to late-onset neonatal sepsis (LOS) occurring more than or equal to 72 h after the child's birth [4], with different experts using 72 hours or 7 days as the cutoff [5]. The source of infection for EOS is highly associated with the organisms carried in the maternal genital tract, leading to vertical transmission, while LOS is typically caused by

either nosocomial (hospital-acquired) or community-acquired sources [3].

Neonatal sepsis is one of the major health problems throughout the world. Every year, an estimated 30 million newborns acquire an infection, and 1-2 million die from neonatal sepsis [6]. While the World Health Organization (WHO) declared neonatal sepsis a global concern and the burden of neonatal infectious diseases a major challenge [7], an estimated 2.5 million neonatal deaths occur each year, representing 47% of all deaths in children younger than 5 years globally [8]. The incidence of EOS with positive blood cultures in the United States is estimated to be 0.77 to 1 per 1000 live births [9,31]. Approximately 7% to 13% of all neonates are treated for sepsis, and only 3% to 8% are considered culture-positive [10]. In contrast, the incidence mortality rate of neonatal sepsis in Nigeria is an average of 38.2 infant deaths per 1,000 live births [11]. Despite advances in diagnosis and treatment, neonatal sepsis is now the primary cause of neonatal mortality, and it is attributed to sociodemographic, maternal, and

neonatal factors [12]. Numerous risk factors for neonatal sepsis should be considered in the diagnostic approach, given the challenges and prolonged nature of sepsis diagnosis. Although [10] indicated that group B streptococcus status, presence of chorioamnionitis, infant prematurity, or prolonged rupture of membranes as maternal factors, and [13] indicated pre-existing maternal infection, protracted rupture of membranes, perinatal hypoxia, and Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score as risk factors for neonatal sepsis, understanding the risk factors for neonatal sepsis may help with the illness's early detection and treatment [14]. Consequently, it is critical to look at the risk factors for neonatal sepsis to institute policies that will enhance the care given to newborns and, in particular, lower the risk of exposure of neonates to infections able to cause sepsis. Policymakers and other relevant entities will benefit from the study's findings as they develop the essential health professional training program, which will help them become better informed about the issue and recognize common risk factors. This may aid in overcoming the difficulties associated with early sepsis diagnosis and treatment. Early identification of the risk factors for neonatal sepsis would enable early clinical diagnosis and treatment, aiming to reduce morbidity and mortality. This study aimed to assess the risk factors of neonatal sepsis in two specialist hospitals and a General Hospital in Lagos, Nigeria.

2. Methods and Materials

2.1 Study Area, Design, and Period

A facility-based unmatched case-control study was conducted in three Lagos State-based hospitals, namely Island Maternity, Massey Street Children's Hospital, and Gbagada General Hospital, between 6th June 2023 and 22nd February 2024. All newborns ≤ 28 days of life were involved in the study.

2.1.1. Study Population

All neonates, both with and without sepsis, who met the inclusion criteria during the study period and received treatment at Island Maternity, Massey Street Children's Hospital, and Gbagada General Hospital, following the same guidelines for the diagnosis of neonatal sepsis, were included. Cases were neonates admitted to the Neonatal Intensive Care Unit (NICU) with sepsis and aged less than or equal to 28 days at these hospitals. Controls were neonates who did not fulfill the criteria for sepsis and who were admitted to the pediatric ward or NICU of the hospitals.

2.1.2. Inclusion Criteria

Neonates with consecutive clinical signs and symptoms of sepsis were admitted into the neonatal unit, or neonates who developed signs and symptoms in the post-natal ward.

2.1.3. Exclusion Criteria

Neonates with congenital malformations and inborn

errors of metabolism were excluded from the study.

2.2. Operational Definitions

Neonatal sepsis: neonates with sepsis within 0–28 days of life

Early-onset neonatal sepsis: neonates with sepsis within 0–3 days of life

Late-onset neonatal sepsis: neonates with sepsis within 4–28 days of life

Premature infant: a live-born infant delivered before 37 weeks of pregnancy (based on the Ballard score or from the first day of the last menstrual period)

Low birth weight: a neonate whose birth weight is less than 2,500 g

Prolonged rupture of the membrane (PROM): the time from membrane rupture to the onset of delivery is more than 18h.

2.3. Data Collection

Socio-demographic data of the study participants and associated risk factors for neonatal sepsis were collected using a structured questionnaire. The questionnaire was checked for its completeness and validity before the collection of data. Convenience sampling was used to select neonates who met the inclusion criteria. A standardized questionnaire was used to obtain information about neonatal characteristics (age, sex, birthweight, Apgar score, fever, skin infection, and mode of delivery). In addition, obstetrics information, including parity, gestational age at delivery, and premature rupture of the membrane (PROM), were collected.

2.4. Data Processing and Analysis

Data from the questionnaire were entered into a computer using SPSS Version 20, followed by data cleaning and generation of frequency distribution tables. Logistic regression analysis was done to assess the strength of association between dependent (neonatal sepsis) and independent variables (age, sex, birth weight, Apgar score, gestational age at delivery, and premature rupture of membrane). Both the Odds Ratio (OR) and the Adjusted Odds Ratio (AOR) with a 95% confidence interval (CI) were computed to test the strength of association, and a p -value ≤ 0.05 was considered significant.

2.5. Ethical Consideration

Ethical clearances were obtained from Babcock University Research and Ethics Committee and the Research and Ethical Committees in the three Lagos State Hospitals involved. The study proposal gained approval from each specifically selected hospital through official administrative channels. This study only utilized hospital clinical records. The name of the parents/caretakers of the study neonates were not included in the data entry and analysis. All identifying data was anonymized. Mothers with their index neonates were selected for the study, and their written consents were obtained.

3. Results

3.1 Maternal Characteristics

A total of 200 neonates (82 cases and 118 controls) were included. Nearly half (65%) of the cases, were aged less than 72hrs (<72hrs). The majority of the neonates were male (61%). Of all the newborns, 106 (53.27%) were born by spontaneous vaginal delivery and 169 (84.92%) were delivered at the medical facility. The percentage of responders from cases and controls who had a history of urinary tract infection during the index pregnancy was 9 (9.57%) and 10 (9.52%), respectively. Concerning intrapartum fever, a history of fever during labor was reported by 16 (17.02%) respondents from the case group and 17 (16.19%) respondents from the control group. More than three-quarters of respondents from case group 17 (18.09%) and 28 (26.67%) respondents from the control group had a history of prolonged rupture of the membrane (Table 1).

Table 1. Maternal Characteristics Of Cases and Controls Attending Selected Lagos State Hospitals 2024

Variable	Case N (%)	Control N (%)	Total N (%)
Age of Neonate in Hours			
<72 h	57 (60.64)	73 (69.52)	130 (65.33)
>72 h	37 (39.36)	32 (30.48)	69 (34.67)
Sex			
Male	54 (57.45)	67 (63.81)	121 (60.8)
Female	40 (42.55)	38 (36.19)	78 (39.2)
Residence			
Urban	86 (91.49)	94 (89.52)	180 (90.45)
Rural	8 (8.51)	11 (10.48)	19 (9.55)
Place of delivery			
Health Facility	77 (81.91)	92 (87.62)	169 (84.92)
Home	11 (11.7)	11 (10.48)	22 (11.06)
Health Post	4 (4.26)	1 (0.95)	5 (2.51)
On Transport	2 (2.13)	1 (0.95)	3 (1.51)
Mode of delivery			
Spontaneous	52 (55.32)	54 (51.43)	106 (53.27)
Cesarean section	40 (42.55)	51 (48.57)	91 (45.73)
Instrumental	2 (2.13)	0 (0)	2 (1.01)
Prolonged rupture of membrane (>18-24 h)			
Yes	17 (18.09)	28 (26.67)	45 (22.61)
No	77 (81.91)	77 (73.33)	154 (77.39)
Prolonged labor (>24 h)			
Yes	8 (8.51)	27 (25.71)	35 (17.59)
No	86 (91.49)	78 (74.29)	168 (82.41)
Intrapartum fever			
Yes	16 (17.02)	17 (16.19)	33 (16.58)
No	78 (82.98)	88 (83.81)	166 (83.42)
UTI			
Yes	9 (9.57)	10 (9.52)	19 (9.55)
No	85 (90.43)	95 (90.48)	180 (90.45)
Treatment by health personnel			
Yes	6 (6.38)	8 (7.62)	14 (7.04)
No	88 (93.62)	97 (92.38)	185 (92.96)

3.2. Neonatal Characteristics

Forty-nine (46.67%) of controls and thirty-nine (41.49%) of cases were delivered with a gestational age of less than 37 weeks. Fifty-five (52.38%) of controls and fifty-two (55.37%) of cases were delivered between the gestational ages of 37 and 42 weeks. Regarding birth weight, twenty-three (24.47%) of cases and thirty-two (30.48%) controls were born with normal birth weights (1500-2500). The proportion of neonates who had an APGAR score > 7 at the fifth minute was higher in cases 68 (72.34%) than in controls 67 (63.81%). One (0.95%) control and seven (7.45%) cases of neonates had previously been admitted. Neonates with Skin/local infections were higher in 8 (8.51%) cases than in controls, 6 (5.71%) (Table 2)

Table 2. Neonatal Characteristics Of Cases and Controls Attending Selected Lagos State Hospitals 2024

Variable	Case N (%)	Control N (%)	Total N (%)
Gestational age			
37-42 weeks	52 (55.32)	55 (52.38)	107 (53.77)
< 37 weeks	39 (41.49)	49 (46.67)	88 (44.22)
> 42 weeks	3 (3.19)	1 (0.95)	4 (2.01)
Birth Weight			
>2500	55 (58.51)	47 (44.76)	102 (51.26)
1500-2500	23 (24.47)	32 (30.48)	55 (27.64)
<1500	16 (17.02)	26 (24.76)	42 (21.11)
APGAR score			
<7/5	26 (27.66)	38 (36.19)	64 (32.16)
>7/5	68 (72.34)	67 (63.81)	135 (67.84)
Previous history of neonatal admission			
Yes	7 (7.45)	1 (0.95)	8 (4.02)
No	87 (92.55)	104 (99.05)	191 (95.98)
Bottle feeding			
Yes	10 (10.64)	4 (3.81)	14 (7.04)
No	84 (89.36)	101 (96.19)	185 (92.96)
Skin/Local infection			
Yes	8 (8.51)	6 (5.71)	14 (7.04)
No	86 (91.49)	99 (94.29)	185 (92.96)
After how many days of delivery			
<3 Days	69 (73.4)	84 (80)	153 (76.88)
>3 Days	25 (26.6)	21 (20)	46 (23.12)

3.3. Factors Associated with Neonatal Sepsis

Cesarean section mode of delivery, UTI during pregnancy, maternal fever, birth weight, APGAR score less than 7 (<7) in the fifth minute, previous history of neonatal admission, skin infection, and bottle feeding were subjected to the final model (multivariate) analysis to adjust for possible confounders, and these variables had

p -value ≤ 0.25 in bivariable logistic regression analysis. In multivariable logistic regression analysis, maternal fever, urinary tract infection (UTI) during pregnancy, PROM, and previous history of neonatal admission showed a significant association with neonatal sepsis. Accordingly, the previous history of neonatal admission showed a significant association with the risk of neonatal sepsis. The odds of neonatal sepsis among neonates with a previous history of neonatal admission were 16.91 times higher than those among neonates who had no previous history of neonatal admission [AOR = 16.91 (2.08, 381.76)]. The odds of neonatal sepsis among mothers who gave birth after prolonged rupture of the membrane were 1.48 times higher than those among mothers who gave birth before prolonged rupture of the membrane [AOR =

1.48; (0.57, 3.88)]. Neonates born to mothers who had UTIs during the index pregnancy had 1.36 times higher odds of developing sepsis than those neonates who were born to mothers who did not have a UTI during the index pregnancy [AOR = 1.36 (0.14, 14.58)]. Maternal fever had a significant association with the risk of neonatal sepsis; neonates born to mothers who had a fever during labor had 1.3 times higher odds of developing sepsis than those neonates whose mothers did not have a fever during labor [AOR = 1.3(0.49, 3.4)]. Skin lesion/infection was significantly associated with the risk of neonatal sepsis. Specifically, neonates with skin/local infection were 1.6 times more likely to present neonatal sepsis than those without skin/local infection [AOR=1.6(0.36, 6.87)]. (Table 3).

Table 3. Multivariable Logistic Regression Analysis of Risk Factors of Neonatal Sepsis At Selected Lagos State Hospitals 2024

Variables	Case N (%)	Control N (%)	COR	AOR
Mode of delivery				
Spontaneous	47 (57.32)	59 (50.43)	1	1
CS	33 (40.24)	58 (49.57)	1.4 (0.79, 2.49)	1.22 (0.59, 2.53)
Instrumental	2 (2.44)			
Prolonged rupture of the membrane				
Yes	15 (18.29)	30 (25.64)	0.65 (0.32, 1.3)	1.48 (0.57, 3.88)
No	67 (81.71)	87 (74.36)	1	1
Prolonged labor greater than 24 h				
Yes	7 (8.54)	28 (23.93)	0.30 (0.12, 0.72) *	0.18 (0.05, 0.53) *
No	75 (91.46)	89 (76.07)	1	1
UTI During Pregnancy				
Yes	9 (10.98)	10 (8.55)	1.32 (0.51, 3.41)	1.36 (0.14, 14.58)
No	73 (89.02)	107 (91.45)	1	1
Intrapartum Fever				
Yes	15(18.29)	18(15.38)	1.23(0.58, 2.61)	1.3(0.49, 3.4)
No	67(81.71)	99(84.62)	1	1
Birth weight (g)				
>2500	48(58.54)	53(45.69)	1	1
1500-2500	18(21.95)	37(31.9)	1.86(0.94, 3.69)	1.27(0.47, 3.49)
<1500	16(19.51)	26(22.41)	1.47(0.71, 3.07)	1.53(0.81, 2.36)
Gestational Weeks				
37-42 weeks	43 (52.44)	64 (54.7)	1	1
<37 weeks	36 (43.9)	52 (44.44)	0.97 (0.55, 1.72)	1 (0.3, 3.37)
>42 weeks	3 (3.66)	1 (0.85)	0.22 (0.02, 2.22)	0.4 (0.02, 12.99)
APGAR score				
<7/5 minute	57 (69.51)	78 (66.67)	1.14 (0.62, 2.09)	0.98 (0.46, 2.1)
>7/5 minute	25 (30.49)	39 (33.33)	1	1
Previous history of neonatal admission				
Yes	7 (8.54)	1 (0.86)	10.73 (1.29, 89.01) *	16.91 (2.08, 381.76)
No	75 (91.46)	115 (99.14)	1	1
Bottle feeding				
Yes	9 (10.98)	5 (4.27)	2.84 (0.91, 8.79)	1.58 (0.31, 8.05)
No	73 (89.02)	112 (95.73)	1	1
Skin/local infection				
Yes	Yes 7 (8.54)	7 (6.03)	1.45 (0.49, 4.31)	1.6 (0.36, 6.87)
No	75(91.46)	109(93.97)	1	1

4. Discussion

To address the illness burden and particular issues related to it, the current study evaluated the risk factors for neonatal sepsis in mothers and newborns. The risk factors

for newborn sepsis were examined in this study. This study found that having a history of maternal PROM, having skin/local infection, having a previous history of neonatal admission, being a preterm neonate, having a history of UTIs in mothers, and receiving resuscitation at birth were all predictors of neonatal sepsis.

In this study, a history of urinary tract infection was found to be one of the risk factors contributing to neonatal sepsis during pregnancy. Neonates born to mothers who had UTIs during pregnancy had higher odds of developing sepsis than neonates born to mothers who did not have UTIs. The odds of developing sepsis increased by a ratio of 1.38. The result of this finding shows urinary tract infection is a risk factor for neonatal sepsis, and these findings are consistent with studies done by [15,16,17,18]. This finding supported the hypothesis that maternal UTIs are frequently linked to early-onset neonatal sepsis, particularly if untreated during the third trimester of pregnancy or labor, and that it may also be related to neonatal sepsis after the infectious agent colonizes the birth canal [19]. Prolonged rupture of the membrane significantly affected the development of neonatal sepsis. Neonates born to mothers who had prolonged rupture of the membrane for more than 18 h before delivery had about 1.48 times higher odds of developing sepsis than neonates born to their counterparts. This is comparable to the studies conducted by [17,20,21].

Intrapartum fever was one of the risk factors contributing to the development of neonatal sepsis. This study showed that neonates born to mothers who had a fever during labor had 1.3 times higher odds of developing sepsis than neonates born to mothers who did not have a fever during labor. Similar findings were observed in earlier studies conducted in different parts of the world, such as Ethiopia [30] and Pakistan [28]. This research also discovered a link between neonatal sepsis and previous history of neonatal admission. The previous history of neonatal admission in this study was defined as neonates admitted into the neonatal intensive care unit for one complication or the other including birth asphyxiation and neonatal resuscitation. The odds of developing neonatal sepsis among neonates who had a history of neonatal admission were more than 10 times higher as compared to neonates who had no history of neonatal admission.

Multivariate analysis indicated that neonates exposed to bottle feeding were 1.6 times more likely to develop sepsis than neonates not exposed to bottle feeding. This study is similar to reports done by [22,23,24]. Numerous bioactive chemicals in breast milk give newborns an inherent immune system. Limited exposure to breast milk is common in preterm newborns, and these factors increase the risk of infection. It is possible that the bottles used during the process of bottle feeding could be contaminated with infectious pathogens, thereby promoting pathogen entry into the bloodstream, resulting in neonatal sepsis. These findings highlighted the importance of ongoing health education about the dangers of bottle feeding.

Place of delivery has a significant association with neonatal sepsis [17], but in our study, it was not a significant factor. The possible reason could be the high proportion of hospital deliveries and no home deliveries. The mode of delivery signifies that neonates conceived via Cesarean section are 1.22 times more likely to develop neonatal sepsis than neonates conceived vaginally. This report is similar to studies done by [11,25,26,27]. This is in contrast to previous research which stated that neonates delivered vaginally were more likely to develop neonatal sepsis than those delivered through the Cesarean section. While it has been reported that babies delivered via

Cesarean section do not come into contact with fecal or vaginal bacteria, they frequently spend longer time in the hospital and start breastfeeding later than expected [32]. In this study, after the multivariate analysis, prematurity, Apgar score, and place of delivery were not significantly associated with neonatal sepsis. This is similar to studies done by [17,23]. In addition, those discrepancies may be study setting, study period differences, healthcare delivery systems, and awareness of the health professionals regarding the prevention strategy of sepsis.

Conclusion

According to this study, prolonged membrane rupture, intrapartum fever, maternal UTI/STI infection, Previous history of neonatal admission, and bottle feeding were the independent factors associated with neonatal sepsis. These results indicate the potential for routine neonatal evaluation to determine risk factors for neonatal sepsis. The study also found that most of the newborns had early-onset sepsis (<72hrs). Healthcare providers who work in the maternal and child health units at Massey Street Children Hospital, Lagos Island Maternity Hospital, and Gbagada General Hospital should educate mothers about risk factors during Antenatal care (ANC) follow-ups, such as prolonged rupture of the membrane, intrapartum fever, maternal UTI/STI infection, and bottle feeding, to screen and treat them early.

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