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Original Research Article

Prevalence and Pattern of Neonatal Sepsis in a Southwestern Nigerian Tertiary Institution

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Abstract: ***Background:*** Neonatal sepsis is a leading cause of morbidity and mortality among neonates in both developing and developed countries and the clinical manifestations are non-specific. Delayed identification and inappropriate treatment are key factors causing high neonatal mortality. This study aimed to report the prevalence and pattern of neonatal sepsis from a southwestern institution in Nigeria. ***Methods:*** The study was carried out on 174 neonates admitted with risk factors and features suggestive of sepsis into the Special Care Baby Unit (SCBU) of a Tertiary Hospital over a period of one year. The babies were evaluated clinically, and blood cultures were collected from all suspected cases prior to the initiation of antibiotic therapy. Data obtained were analyzed using SPSS version 25. Statistical significance was set at $p < 0.05$. ***Results:*** Neonatal sepsis was responsible for 25.2% of the 294 neonates that were admitted into the SCBU over the one-year period of study. Of the 174 neonates that were clinically diagnosed with sepsis, bacterial isolates were obtained from 74 (42.5%) while 100 (57.5%) had negative blood culture. *Staphylococcus aureus* was the most common isolated organism. Lack of ANC (41.4%) and premature ruptured of membranes (27.6%) were the prevailing maternal risk factors while Low birth weight (57.5%) and preterm delivery (66.1%) were the most common risk factors in the neonates. Fever (27.6%), and respiratory distress (48.3%) were the most common complaints among the studied neonates. There was a statistically significant correlation between sepsis and place of birth ($p < 0.05$). ***Conclusion:*** Neonatal sepsis remains an important threat to lives of newborns. Babies delivered in the facility (in-born) showed significant lower incidence of sepsis compared to those brought from outside the facility (out-born) where asepsis is questionable. It is paramount to advocate preventive measures for neonatal sepsis even right from antenatal periods to delivery.

Keywords: Neonatal sepsis, prevalence, Southwest Nigeria.

INTRODUCTION

Neonatal sepsis is a generalized infection of the neonate's blood with or without other symptoms during the first 28 days of life.[1] It is a common and important cause of morbidity and mortality throughout the world, most especially in developing countries where it accounts for 30% - 50% of neonatal deaths.[2–4] continues to be a common and significant healthcare burden, especially among Low birth weight (LBW) infants, even with advancement in neonatal care.[5]

Neonatal sepsis can be classified as early-onset neonatal sepsis (EOS), which occurs within 72 hours of life, or late-onset neonatal sepsis (LOS), which occurs after this 3-day period. [9.6,7] EOS is usually caused by organisms acquired from the mother's genital tract or the organism prevalent in the designated place of delivery within the hospital. LOS usually is due to organisms acquired from the environment as well as from the care-givers [10] Babies with sepsis can present asymptomatically or with non-specific symptoms. [2–6]They include fever or hypothermia, respiratory distress, cyanosis, apnea, poor feeding, diminished sucking reflex, lethargy or irritability, high-pitched cry, hypotonia, bulging fontanelle, poor perfusion, bleeding problems, petechiae, abdominal distension, hepatomegaly, guaiac-positive stools, unexplained jaundice or even a baby not just looking well. [8,9] Early diagnosis is important as the neonate may present with minimal or no signs even when the disease is advanced,

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and early initiation of antibiotic therapy helps to reduce neonatal mortality.[10,11]

The risk factors for neonatal sepsis can be from host factors which include prematurity, LBW, male gender, congenital anomalies, and perinatal asphyxia; maternal factors which include: prolonged rupture of fetal membranes, premature rupture of fetal membranes, chorioamnionitis, urinary tract infection (UTI), vaginal / cervical infections; and environmental factors which include: overcrowding, unhygienic place of delivery, poor hand hygiene, and prolonged hospitalization.[12–14]

The incidence, risk factors, pattern, antimicrobial sensitivities and mortality differ between the developed and developing countries. The prophylactic use of intrapartum antibiotics has drastically reduced the incidence of EOS with Group B streptococcal (GBS) infection. However, studies still regard GBS as the major cause of neonatal sepsis.[5,15,16] Similarly, *Escherichia coli* has been implicated in neonatal sepsis, especially in preterm newborns,[5] likewise, other pathogens including *Streptococcus viridans*, *Enterococci*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

The gold standard for diagnosing neonatal sepsis is still blood culture, which has been the convention.[17–20] However, pathogens in the blood are detectable in about 25% - 55% of cases, [1,3,4,7] because of the small amount of blood (inoculum) and maternal prenatal antibiotic use. Neonates, whether term or preterm, are highly vulnerable to bacterial infections.[5,8] Prompt diagnosis and administration of antimicrobial therapy are essential to reduce complications associated with sepsis-related organ failure.[8,21,22] However, sepsis response is complex, and not all patients with infections display related signs or symptoms.[8,21–23]

METHODOLOGY

Study Design

The study was a descriptive cross-sectional study carried out on the newborns admitted into the Special Care Baby Unit (SCBU) of the LAUTECH Teaching Hospital (LTH), Ogbomoso. The SCBU admits babies delivered in the hospital setting and outside the hospital into the in-born and out-born sections respectively.

Sample Size Determination

The total number of babies enrolled in the study was calculated by the formula [24]

$$n = \frac{z^2 pq}{d^2}$$

Since the estimated population size is less than 10,000, our minimum sample size, N_f, was derived by the formula given below:

$$N_f = \frac{n}{\left(1+\frac{(n)}{N}\right)}$$

Subjects were reviewed based on “clear and definite” infection symptoms, “probable or suspected” infection and babies “without any sign or symptom” of infection.

The total sample size is 148, and a further 10% was added to the calculated sample size for non-responders.

i.e., 148 + 14.8 = 162.8

Therefore, the minimum sample size was 163. However, the study involved a total of 174 subjects.

Procedure

All consecutive babies aged 0-28 days admitted to the SCBU of LTH, Ogbomoso with presumed or probable sepsis were recruited. Septicaemia was presumed when a newborn baby has specific risk factors for sepsis like prematurity, delivery outside the hospital, prolonged labour, prolonged rupture of membranes, maternal peri-partum pyrexia, and chorioamnionitis without clinical manifestation. Sepsis was probable in the presence of clinical features adjudged to be suggestive of sepsis, particularly fever or hypothermia, respiratory distress, jaundice, poor feeding, lethargy, poor cry, and unexplained poor perfusion. Prolonged rupture of membranes was defined as rupture of foetal membranes greater than 24 hours. Prolonged labour was defined as one lasting greater than12 hours in the active phase of labour or 24 hours in totality. A general examination of each baby to elicit physical signs like pallor, fever, jaundice, respiratory distress, and other features of sepsis was initially carried out.

Babies with features suggestive of congenital heart diseases and metabolic disorders such as hypothyroidism were excluded from the study as well as neonates without risk factors or features suggestive of septicaemia.

Information about the age at admission, weight at admission, sex, estimated gestational age (EGA) at delivery, place of birth, mode of delivery, and details of perinatal events like duration of labour, interval between rupture of foetal membranes and the delivery of baby, occurrence of maternal pyrexia during labour and primary diagnosis on admission, were obtained with the use of a pre-tested study proforma.

Maternal data obtained included age, parity, occupation, educational status, history of antenatal care, details of labour and delivery including the place of delivery, history of peri-partum fever, preterm labour, pre-labour rupture of foetal membranes, prolonged

rupture of membranes, duration of labour and the mode of delivery.

Babies delivered at the LTH, Ogbomoso were designated in-born babies while babies delivered outside LTH, Ogbomoso were designated out-born babies.

Blood Culture

After recruitment, 3mls of blood was taken from peripheral veins, under aseptic conditions, 1.5mls was added into each of the two BACTEC Peds Plus® (Becton Dickinson, New Jersey, USA) blood culture broth media, the bottles were labelled with the patient identification number and incubated for at least 8 hours at 37ºC. Samples were inoculated into three Agars: blood agar, chocolate agar and MacConkey agar. The agars were incubated for 18-24 hours at 37ºC. Colonies formed from bacterial growth then followed the line of streaking. The chocolate agars were incubated anaerobically in a candle jar, while the other two agars were incubated aerobically in the incubator. Gram staining was done for colonies grown on the agar plates to identify gram-positive or gram-negative organisms. This was followed by a biochemical test to determine the species of the bacteria's growth. Afterward, an antibiotic susceptibility test (AST) was done.

After blood sample collection, the neonates were commenced on empirical antibiotics according to the standard operating procedure of the hospital SCBU for sepsis prior to the availability of blood culture results.

The outcome of hospitalization was recorded as either discharge in good condition, discharge against medical advice or death.

Data Analysis

Data obtained was analyzed on the IBM SPSS version 25.0. Data was summarized using means, ranges, and standard deviations for normally distributed numerical data. Categorical data was summarized using frequencies and percentages. Data was presented using tables, figures, and charts as appropriate. Relevant associations were described in tables using Chi-square for categorical variables and Student t-test for continuous variables. T-test was used to compare the mean. P-values < 0.05 was statistically significant.

Ethical Approval

Ethical approval was obtained from the Research and Ethical Clearance Committee of LAUTECH Teaching Hospital, Ogbomoso (LTH/OGB/EC2021/263) before the commencement of the study. Written informed consent was obtained from the parents/ care-givers of the studied neonates.

RESULTS

A total 294 neonates were admitted during the study period into the SCBU. One hundred and seventy of these babies met the inclusion criteria and were studied. Of these, 74 had proven neonatal sepsis (confirmed by blood culture), therefore neonatal sepsis accounted for 25.2% of all admissions into the SCBU. Fifty-two (70.3%) of the babies with confirmed sepsis were out-born while 22 (29.7%) were in-born. Ninety-one (52.3%) of the subjects were females and 83 (47.7%) were males, female to male ratio 1.1:1.

The majority 115 (66.1%) of the studied neonates were preterm and seen within the age of 72 hours. The admission weights of the neonates ranged from 0.76 kg to 3.90 kg, with a mean weight of 2.28 kg (± 0.78), low birth weight accounted for 57.5% of the subjects.

The mean age of the mothers was 29.31 ± 5.66 years. Additional details are shown in Table I.

Table I: Admission Weight, gestational age, and age at admission

Birthweight	**Frequency**	**Percentage %**
ELBW	8	4.6
VLBW	20	11.5
LBW	72	41.4
Normal Weight	74	42.5
Macrosomic baby	0	0
	Frequency	**Percentage %**
Preterm	115	66.1
Term	59	33.9
Gestational Age		
< 28 weeks	8	4.6
28 – 31 weeks	12	6.9
32 – 36 weeks	95	54.6
37 – 41 weeks	59	33.9
Age at Admission	**Frequency**	**Percentage %**
< 72 hrs.	109	62.6
> 72 hrs.	65	37.4

ELBW: Extreme low birthweight, VLBW: Very low birthweight

The majority of the neonates 96 (55.2%) were delivered spontaneously, vaginally. Also, most of them were delivered at government-owned hospitals, while home delivery was the least common place of delivery (Table II).

Table II: Mode and Place of Delivery

Mode of Delivery	**Frequency**	**Percentage %**
Spontaneous Vaginal Delivery	96	55.2
Caesarean Section	78	44.8
Place of Delivery	**Frequency**	**Percentage %**
Home Delivery	2	1.1
Maternity Home	5	2.9
Private Hospital	61	35.1
Government Hospital	106	60.9

Fever 27.6% and respiratory distress 48.3% were the most common presenting complaints among studied neonates.

Table III: Clinical features of studied neonates

Variables	**Frequency**	**Percentage %**
Respiratory Distress	84	48.3
Fever	48	27.6
Jaundice	34	19.5
Vomiting	12	6.9
Abdominal Swelling	14	8.0
Convulsion	12	6.9
Poor Suck	8	4.6
Bleeding from mouth	2	1.1
Bloody Stool	2	1.1
Noisy Breathing	2	1.1
Poor weight gain	2	1.1

*Multiple responses**

Lack of ANC 41.4% and preterm ruptured of membranes 27.6% were the prevailing maternal risk factors while maternal UTI was the least commonly associated maternal risk factor. Low birth weight 57.5% and prematurity 66.1% were the most common risk factors among the neonates studied.

Table IV: Maternal and fetal risk factors in studied neonates

Risks	**Frequency**	**Percentage %**
Lack of ANC	72	41.4
PROM	48	27.6
Foul smelling liquor	14	8.0
Peripartum fever	14	8.0
Prolonged labour	10	5.7
UTI	10	5.7
Prematurity	115	66.1
Low birth weight	100	57.5
Multiple Gestation	12	6.9

Multiple responses PROM: preterm rupture of membranes, UTI: urinary tract infection, ANC: antenatal care.*

Of the 174 neonates clinically diagnosed with sepsis, bacterial isolates were obtained from the blood samples of 74 (42.5%) neonates, and the remaining 100 (57.5%) had negative blood culture.

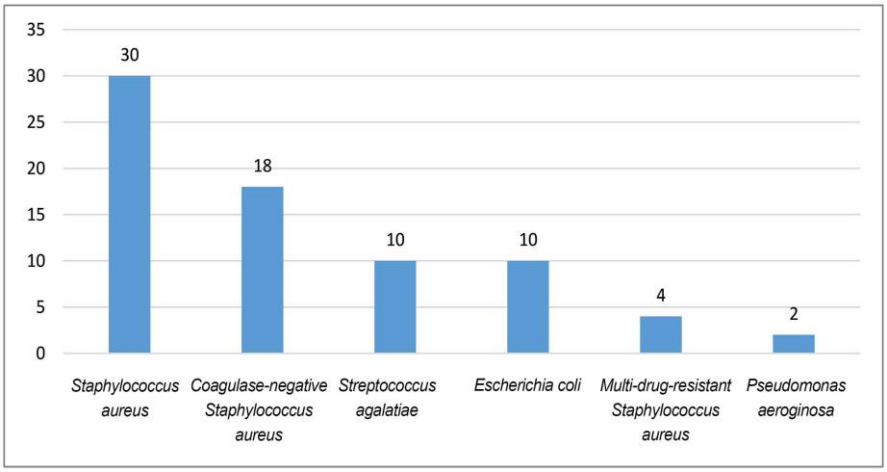

Fig. 1: Pattern of organisms Isolated from Blood culture.

Of the 74 culture-positive neonates, 52 (70.3%) were out-born. This difference is statistically significant, with a p-value of 0.015. Neonates delivered in the hospital of care (in-born) appear to have a lower incidence of sepsis than the out-born. Fifty-four percent of the male neonates tested positive for neonatal sepsis compared to 29% of the female neonates who were culture positive for neonatal sepsis. This is statistically significant, with a p-value < 0.005. Home deliveries and maternity centers had the highest positive cases of neonatal sepsis. Neonates delivered in government hospitals had the lowest positive cases. The comparison between the place of delivery and neonatal sepsis is statistically significant, $p < 0.05$. Fifty (52.1%) of the 96 neonates delivered via spontaneous vaginal delivery had positive blood cultures, as against 24 (30.8%) of 78 neonates delivered via caesarean section. The difference is statistically significant, $p = 0.005$. (Table V).

The antibiotics with the highest sensitivities are Gentamicin, levofloxacin, and others as displayed on Table VI.

Table V: Comparison between out-born and inborn delivery with neonatal sepsis

Variables	**Negative n (%)**	**Positive n (%)**	**p-value**
Outborn	52 (50.0)	52 (50.0)	0.015
Inborn	48 (68.6)	22 (31.4)	
Male	38 (45.8)	45 (54.2)	0.003
Female	62 (68.1)	29 (31.9)	
Home Delivery	0 (0)	2 (100)	0.000
Maternity Home	1 (20.0)	4 (80.0)	
Private Hospital	26 (42.6)	35 (57.4)	
Government Hospital	73 (68.9)	33 (31.1)	
Mode of delivery	Negative (%)	Positive (%)	p-value
Spontaneous Vaginal Delivery	46 (47.9)	50 (52.1)	
Caesarean section	54 (69.2)	24 (30.8)	0.005

*Chi-square**

Table VI: Antimicrobial susceptibility pattern

Antibiotics	**Staphylococcus Aureus (N=30)**		**Coagulase Negative Staphylococcus Aureus (N=18)**		**Streptococcus Agalactiae (N=10)**		**Multi drug resistant Staphylococcus aureus (N=4)**		**Escherichia coli (N= 10)**		**Pseudomonas Aeroginosa (N=2)**	
	N	**n (%)**	**N**	**N (%)**	**N**	**N (%)**	**N**	**N (%)**	**N**	**N (%)**	**N**	**N (%)**
Amoxicillin	-	-	12	0	8	2 (25)	-	-	-	-	2	0
Ampicillin	24	12 (50)	-	-	2	0	-	-	4	2 (50)	2	0
Augmentin	6	6 (100)	18	0	-	-	4	2 (50)	6	0	-	-
Cefotaxime	12	0	12	12 (100)	10	2 (20)	2	0	10	0	2	0
Cefoxilin	18	6 (33.3)	-	-	4	4 (100)	-	-	2	0	-	-
Cefuroxime	24	18 (75)	12	0	6	2 (33.3)	-	-	4	0	2	0
Ceftriaxone	6	0	-	-	2	2 (100)	-	-	4	4 (100)	2	0
Erythromycin	18	6 (33.3)	-	-	6	2 (33.3)	-	-	-	-	-	-
Gentamicin	30	18 (60)	18	0	4	2 (50)	2	2 (100)	8	4 (50)	2	2 (100)
Levofloxacin	24	12 (50)	18	12 (66.7)	8	2 (25)		-	4	4 (100)	-	-

DISCUSSIONS

Neonatal sepsis is one of the most important causes of morbidity and mortality in newborns throughout the world.[25–29] The diagnosis of neonatal sepsis can be challenging as the symptoms and signs are non-specific. Hence, a high index of suspicion and early initiation of therapy are of great importance.[5,30–32]

In this study, the prevalence of culture-proven sepsis was 25.2%. This is close to the findings of Iregbu et al (22%) northern Nigeria and Ojukwu *et al.,* (23.9%) south eastern Nigeria.[6] In contrast, Eniowo *et al.*,[33]Jatsho *et al.*,[13] and Wuni *et al.*,[34] reported a lower prevalence of 17%, 14% and 13.4%, respectively while Morad *et al.*,[1] reported a higher prevalence of 62%. This noticeable disparity in the reported prevalences from these studies could be due to varied sample sizes, different geographical locations and different study populations. In this study, majority of the studied population were outborn neonates delivered to mothers with poor obstetric care or in unhygienic delivery environments in low-standard healthcare facilities with suboptimal maternal and neonatal care.

The female gender predominance (1.1:1) among the subjects in this study is similar to the findings of Arowosegbe *et al.,* [35] in southwestern region of Nigeria but differs from studies by Roma *et al.,* [36] and Morad *et al.,* [1] who reported a male preponderance in their respective studies.

Among the neonates with culture positive results, majority were males. This is similar to findings from various studies.[1,12,13] This could be due to the X-linked immunoregulatory gene factor which favours the female gender but may increase susceptibility to infections in males.

The mean weight of neonates in this study was 2.28kg (±0.78kg), which was close to findings by Muhammad *et al.*,[37] who reported a mean weight of 2.49kg (±0.55). The close similarity in these two mean weights can be attributed to a greater number of preterm babies in both studies. However, Arowosegbe *et al.*,[3,35]Eniowo *et al.*,[33] and Joana Borges *et al.,* [38] reported higher mean weights of 2.5kg (±0.8kg), 2.92kg (±0.62kg), 3.2 kg (±0.47) respectively. This might be because their studies were done on predominantly term and late-preterm babies.

The majority of the studied neonates had early onset neonatal sepsis (EOS). This is similar to the findings of Ogundare *et al.*,[6] who reported 77.8% EOS in their study. Also, Arowosegbe *et al.,* [35] in 2017 reported that 63.5% of studied neonates had early onset neonatal sepsis. In contrast, Ako-Nai *et al.,* [39] reported a slightly higher population (53%) of neonates with late onset neonatal sepsis (LOS). A metadata analysis of the incidences of EOS/LOS from 21 studies, found a random-effects estimate of 2824 neonatal sepsis cases per 100,000 live births in the period between 1989-2018 with a 2.6 times higher incidence of early-onset neonatal sepsis than late onset neonatal sepsis.[40] This could be possibly explained by the strong association between prematurity and EOS.[11,40,41]

The mean age of the mothers of the studied neonates is 29.31 ± 5.66 years, similar to the findings of Olorukooba *et al.,* [7] from the Northern part of Nigeria, who reported 27.9 ± 6.1 years. Nabwera *et al.,* [42] reported a close mean maternal age of 28.7 ± 6.2 years from a study done in Nigeria and Kenya, and Sahu *et al.,* [41] from India reported a mean maternal age of 27.22 ± 4.31 years. Four separate studies carried out in Ethiopia by Mersha *et al.*,[43] Roble *et al.*,[44]Oumer *et al.*,[45] and Mezgebu *et al.,* [14] reported the mean ages of neonates' mothers to be 27.39 years (± 6.51 years), 26 years (± 5.09) years, 29.11 years (± 6.14) and 26.93 years (±0.45 SD) respectively. This age range falls within the reproductive age for women.[46]

Lack of ante natal care and premature rupture of membranes (PROM) were the prevailing risk factors identified among the mothers of the studied neonates. This is similar to the finding of Abnish *et al.,* [47] who reported 87.5% in Delhi, India. Similarly, Sumedha *et al.,* [2] reported a high incidence of PROM, and it has been reported to be a significant risk factor for neonatal sepsis.[48] Neonates generally have immature, defective protective mechanisms. Therefore, PROM puts them at a higher risk of ascending infection.

Other risk factors identified from this study include foul-smelling liquor (chorioamnionitis), peripartal fever, prolonged labour and UTI, all of which have been shown to predispose neonates to sepsis.

The clinical features and presentations of neonatal sepsis are non-specific. However, in this study, respiratory distress, fever, jaundice, vomiting, abdominal swelling, convulsions and poor suck were the most frequent clinical presentations in the studied neonates. Of these features, respiratory distress was the most commonly reported.[2,6,35,49]

The blood culture results from this study showed *Staphylococcus aureus* to be the commonest cause of neonatal sepsis. This is similar the finding of Osrin *et al.,* [50] in the United Kingdom. Also, in a meta-analytic study by Meduge *et al.,* [15], *Staphylococcus aureus* was reported as the most prevalent isolate. Ako-Nai *et al.,* [39] also reported similar findings.

Group B streptococcus (GBS) remains the leading isolate in the United States.[5] However, Morad *et al.,* [1] reported gram-negative bacteria (Klebsiella and E coli) as their most prevalent isolates compared to gram-positive organisms. The different profiles may be a consequence of environment. It is unclear what the role of indiscriminate use of un-prescribed antibiotics (a

prevalent problem in developing countries) may be in this regard.[15,51]

Also, the prevalence of *Staphylococcus aureus* in this study may be due to some factors like host and organism interactions. It is a common normal flora of the skin and anterior nares, especially in Nigeria, and is commonly acquired from asymptomatic carriers.[39,52].

Concerning the mode of delivery, babies delivered via spontaneous vaginal delivery had the highest number of blood culture positive results. This may be due to the fact that vaginally born babies may have been exposed to vaginal and fecal bacteria. Also, multiple vaginal examinations during labor and delivery may expose a newborn to a variety of pathogens, leading to neonatal sepsis. This finding is similar to those reported by Morad *et al.,* [1,1]Jatsho *et al.,*[13] and Abdulrahman *et al.,* [44]

CONCLUSIONS

Neonatal sepsis remains an important threat to lives of newborns. Babies delivered in the facility show significant lower incidence compared to those brought from outside the facility where asepsis measures are questionable. It is paramount to advocate preventive measures against neonatal sepsis right from antenatal periods to delivery. The labor processes including vaginal examination, rupture of membrane, and various instruments used during delivery should be in aseptic conditions to limit the occurrence and incidence of neonatal sepsis.

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