Original Article

A 4-Year Prospective Study of Clinico-bacterial Profile and Antibiogram of Neonatal Bacterial Sepsis at a Tertiary Health Facility in a Resource-limited Setting

Uchenna Ekwochi, Christian Ifediora[1], Chidiebere D. I. Osuorah[2]

Department of Paediatrics, Enugu State University of Science and Technology, Enugu, Nigeria, [1]Griffiths University Medical School, Gold Coast, Australia, [2]Child Survival Unit, Medical Research Council UK, Gambia Unit, Fajara, The Gambia

ABSTRACT

Background: In the developing countries, neonatal sepsis (NNS) contributes significantly to neonatal admissions and deaths. Its symptoms are usually nonspecific, and definitive laboratory diagnosis can be challenging in a resource-limited setting. Therefore, early empirical antibiotic therapy antibiotics are important in these localities, and this makes it important to document local organisms and their antibiotic sensitivity pattern. Unfortunately, no previous study in our setting has documented these. **Methods:** This study involved newborns (inborn and outborn) admitted with sepsis (cases) within the 1st month of life at the Enugu State University Teaching Hospital (ESUTH), Enugu, Southeast Nigeria. Controls were included for the analysis, and data were collected over a 4-year period from January 2013 to December 2016. **Results:** In all, 1920 newborns were admitted to the Special Care Baby Unit of ESUTH during the study period. Fifty-seven were managed for culture-proven sepsis, resulting in an in-hospital incidence rate of 29.7 per 1000 admitted newborns (95% confidence interval 21.9–37.4). A total 228 newborns were recruited (57 cases and 171 controls; ratio of 1:3). The most common presenting symptom and sign were fever (84.2%) and depressed primitive reflexes (50.9%), respectively. A case-fatality rate of 7.4% was observed. Newborn's place of birth ($P = 0.02$) and the final outcome ($P = 0.004$) were significantly associated with the development of sepsis, while gender ($P = 0.12$), birth weight ($P = 0.33$), gestational age ($P = 0.53$), and mode of delivery ($P = 0.74$) were not. Nearly 60% of the organisms implicated were coliforms, while one-quarter were *Staphylococcus aureus*. The most sensitive antibiotics were the fluoroquinolones, particularly ciprofloxacin, while amoxicillin, ampicillin, and clindamycin were generally not effective. **Conclusion:** NNS in our environment is commonly caused by coliforms and *S. aureus* and being outborn is a significant determinant. Antibiotic resistance follows recognized patterns, but the quinolones, despite their inconclusive safety profile in children, are most sensitive.

KEYWORDS: *Antibiogram, clinical features, Enugu, neonates, sepsis*

INTRODUCTION

Sepsis is a systemic inflammatory response syndrome due to infection.[1] Neonatal bacterial sepsis specifically refers to sepsis caused by bacteria in the first 28 days of life. Systemic inflammatory syndrome includes two or more of the following clinical features: fever, hypothermia, tachycardia, tachypnea, and abnormal white blood cells in immature

forms.[1] Globally, neonatal deaths are caused by infections (which include sepsis/pneumonia, tetanus, and diarrhea) which account for 36%, preterm 28%, and

Address for correspondence: Dr. Chidiebere D. I. Osuorah,
Child Survival Unit, Medical Research Council UK,
Gambia Unit, Fajara, The Gambia.
E-mail: chidi.osuorah@gmail.com

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birth asphyxia 23%. Altogether, they are responsible for 87% of neonatal deaths.[2,3] In the developing countries, neonatal sepsis (NNS) contributes 30%–50% of neonatal deaths.[4] It accounts for 61% of neonatal admissions and 29.4% of neonatal death in the current study center.[5,6] It is described as early-onset sepsis (EOS) when it occurs within the first 72 h of life and late-onset sepsis (LOS) when it occurs after 72 h.[7] The causative organisms in EOS are mainly the organisms in the maternal genital tract, labor rooms, or operating theaters, while the nosocomial and the community-acquired organisms are usually responsible for LOS.[8] Risk factors for NNS include, but are not limited to prematurity, low birth weights, prolonged rupture of membrane, asphyxia, and maternal perinatal fever.[9,10] It is important to note that the clinical symptomatology of NNS are subtle and nonspecific,[10] and its definitive diagnosis using positive blood culture, which is the gold standard, could be quite challenging. This is so because in the study setting, a minimum wait period of 48-h is usually required for result of blood culture to be released to clinicians.[11] Secondly, the cost of blood culture test in our setting is usually borne by patients and their care-givers which is mostly unaffordable for majority of them.[6] Early commencement of antibiotics in NNS enhances good prognosis;[10] it is therefore recommended that every locale should document the organisms predominantly implicated in their newborn infections and their antibiotic sensitivity pattern. Using this pattern, an early empirical antibiotic therapy could be started in cases of sepsis awaiting the blood culture and antibiotic sensitivity to substitute as necessary.[12] In our setting, there is no study documenting the clinical symptomatology, bacterial profile, and antibiotic sensitivity for newborn sepsis, upon which effective empirical therapy could be formulated. The latter strongly underscores the need for this study.

METHODS

Study area

The study was done at the Special Care Baby Unit (SCBU) of Enugu State University Teaching Hospital (ESUTH), Park Lane, Enugu, Southeast Nigeria. This is a state-owned tertiary health facility that serves as a referral center for specialized medical services for Enugu and the neighboring states. The SCBU cares for sick newborns delivered within the hospital (inborn) or referred from other health facilities (outborn) who presented within the first 28 days of life. It has separate sections for inborn and outborn babies. Each section has a separate complement of medical facilities for the care of the sick babies. The unit is being manned by consultant neonatologists, pediatrics, residents,

and nurses, some of which have undergone training in pediatric nursing.
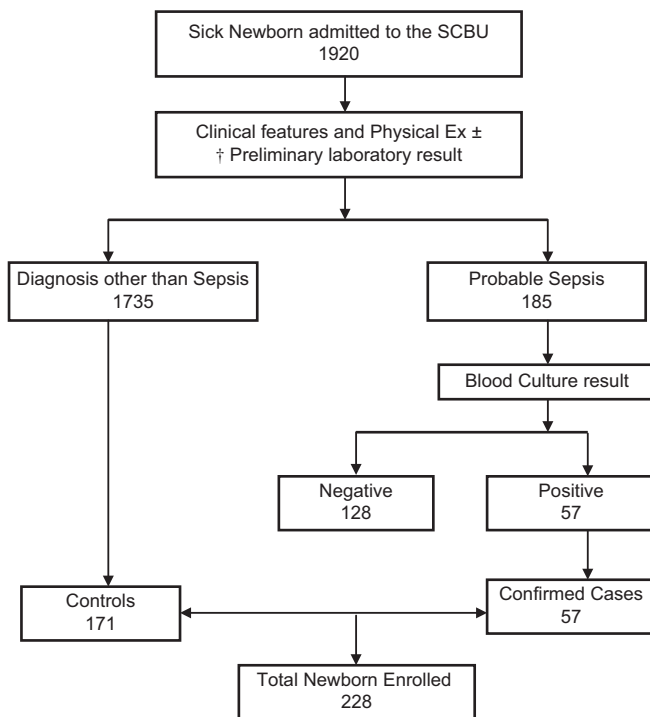
Case definition and recruitment

This was a case–control and prospective study carried out over a 4-year period from January 2013 to December 2016. Newborns suspected of having septicemia based on clinical symptoms such as fever, refusal to suckle, weakness, vomiting, and abdominal distension are admitted to the sick baby unit of the ESUTH.

After admission, a thorough history is taken documenting the onset of illness, presence of maternal risk factors for NNS such as maternal illnesses, prolonged rupture of membrane (> 24 hours to delivery of baby), lower abdominal pain, vaginal discharge, instrumental delivery, place of birth, gestational age at birth, and absence of spontaneous and sustained respiration at birth.

A thorough physical examination is carried out noting signs such as irritability, state of the anterior fontanel, lethargy, jaundice, pallor, organomegaly, depressed primitive flexes, erythema, induration, and umbilical and other orificial discharge. Concurrently, relevant laboratory specimens for sepsis screen are collected. These include complete blood count, swabs where indicated, urinalysis, Gram stain, and blood culture. Further investigations are also carried out as indicated. Because it takes 3–7 days for culture result to be available, a presumptive diagnosis of NNS is made in the presence of suggestive clinical features and/or physical findings, with a supportive preliminary laboratory results. However, the presence of positive bacterial isolate in the blood culture is regarded as confirmatory.

Once a presumptive diagnosis of sepsis is made, and samples taken for relevant laboratory investigations including blood culture, the baby is commenced on empirical broad-spectrum antibiotics. This may be changed depending on sensitivity result upon the retrieval of the blood culture antibiogram, particularly when there are no clinical improvements with the initial antibiotic treatment.

For the purpose of this study, only sick newborns with positive blood culture result were recruited as cases [Figure 1]. For each case, unmatched controls were enrolled under the following measures; gender, birth weight, gestational age at birth, mode of delivery, and place of birth. Each case under the aforementioned measures was matched with its controls in the ratio of at least 1:3. For the purpose of this research, the findings of the general and systemic physical examination for the cases were documented in the Microsoft Excel sheet of the study. The bacteria isolated in the blood culture and their drug sensitivity patterns were also documented.

Figure 1: Overview of case definition and recruitment processes of surveyed newborns †Complete blood Count, Urinalysis or Gram stain

Data analysis

Analysis was performed using the IBM® SPSS version 24.0 (SPSS Inc., Chicago, IL, USA). Both descriptive (presented as absolute data or as percentages) and inferential analyses were adopted (using both the Pearson Chi-square statistics and logistic regression as indicated). Binary logistic regression (BLR) was preferred regression method (variables were dichotomized where necessary), and two different analyses were carried out.

The first BLR attempted to identify associations with "cases of sepsis," which was the outcome (dependent) variable, while there were six predictor (independent) variables. These predictor variables include birth weight in kg (≥2.5 vs. <2.5), place of birth (inborn or outborn), gestational age in completed weeks (≥37 vs. <37), gender (male and female), mode of delivery (cesarean vs. vaginal), and final outcome (dead vs. alive).

The second set of BLR analysis was done to identify potential associations between various patient characteristics and some clinical features found the cases and included eight outcome (dependent) variables and six predictor (independent) variables. The eight outcome variables, dichotomized as necessary, were birth weight in kg (≥2.5 vs. <2.5), place of birth (inborn or outborn), prolonged rupture of membrane, PROM (yes or no), mode of delivery (cesarean required or not required), gestational age in completed weeks

(≥37 vs. <37), gender (male and female), age at onset of sepsis (≤72 vs. >72), and finally, age at presentation to the SCBU, (≤72 vs. >72). On the other hand, the six predictor variables include the presence or absence of clinical features, including asphyxia, hypertonia, jaundice, hepatomegaly, abdominal distention, and primitive reflexes.

It should be noted that, in all cases of the BLR, variables with numbers <5 were excluded, and only $P < 0.05$ was considered statistically significant.

Ethical consideration

The study was approved by the Ethical Committee of ESUTH. Written informed consent was obtained from the parents and or caregivers of the subject before recruitment. They were assured that participation is voluntary and withdrawal at any stage of the research is guaranteed. Moreover, all clinical and laboratory findings on their babies will be confidential and can only be utilized in the management of their babies. They were further assured that refusal to participate in the study will not cause any bias in the care of their babies.

RESULTS

In all, 1920 newborns were admitted to the SCBU of ESUTH during the study period. Fifty-seven were managed for culture-proven sepsis, resulting to an in-hospital incidence rate of 29.7 per 1000 admitted newborns (95% confidence interval [CI] 21.9–37.4). Table 1 summarizes the characteristics of all these participants and shows that 140 or 61.4% of them were males, while the mean birth weight was 2.70 ± 1.02 kg. Most (44.3%) were born at term, but 39% and 5.3% were born pre- and post-term, respectively. Majority of the newborns were either born inside within ESUTH (58.4%), delivered by spontaneous vaginal delivery (SVD) (59.7%), and survived (78.9%). Tables 2-4 show the characteristics of the cases only.

As shown in Table 2, majority (70.2%) of those who developed sepsis were males, most (56.6%) had normal weights ranging from 2.5 to 4.2 kg, and unlike in the overall group, majority (71.9%) were born outside ESUTH. Furthermore, 59.6% were born at term, one-third developed asphyxia, and while 84.2% of the cases developed within 72 h of birth, only 18.0% were admitted to ESUTH after 72 h of birth.

The clinical features of the newborns with sepsis are summarized in Table 3 and revealed that fever was the most common symptom, with 84.2% of the presentations manifesting as such. Poor suckling (39.3%), fast breathing (43.6%), jaundice (39.3%), lethargy (31.6%), and poor cry (30.4%) were other fairly common

Table 1: Characteristics of all newborns presenting at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria, from January 2013 to December 2016

Characteristic	Variable	n (%)
Gender (n=228)	Male	140 (61.4)
	Female	88 (38.6)
Birth weight (kg) (n=216)	Large (>4.2)	13 (6.0)
Mean=2.70	Normal (2.5-4.2)	112 (51.9)
Range=4.9 (0.6 to 5.5)	Low (1.5-2.4)	63 (29.2)
	Very LBW (≤1.5)	28 (13.0)
SD=1.019		
Median=2.75		
Gestational age (weeks) (n=228)	Postdate (≥41)	12 (5.30)
	Term (37-40)	127 (44.3)
	Preterm (≤36)	89 (39.0)
Place of birth (i.e., whether inside the tertiary hospital or outside of it) (n=226)	Inborn	94 (41.6)
	Outborn	132 (58.4)
Mode of delivery (n=221)	Spontaneous vagina delivery	132 (59.7)
	Cesarean section	89 (40.3)
Outcome (n=218)	Alive	172 (78.9)
	Dead	46 (21.1)

LBW – Low birth weight; SD – Standard deviation

Table 2: Demographic, pregnancy, and birth characteristics newborns presenting with sepsis at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Characteristic	Variable	n (%)
Gender (n=57)	Male	40 (70.2)
	Female	17 (29.8)
Birth weight (kg) (n=53)	Large (>4.2)	3 (5.7)
	Normal (2.5-4.2)	30 (56.6)
	Low (1.5-2.4)	17 (32.1)
	Very LBW (≤1.5)	3 (5.7)
Gestational age (weeks) (n=57)	Postdate (≥41)	4 (7.0)
	Term (37-40)	34 (59.6)
	Preterm (≤36)	19 (33.3)
Place of birth (i.e., whether inside the tertiary hospital or outside of it) (n=57)	Inborn	16 (28.1)
	Outborn	41 (71.9)
Mode of delivery (n=57)	Spontaneous vagina delivery	33 (57.9)
	Cesarean section	24 (42.1)
PROM (n=57)	Yes	16 (28.1)
	No	41 (71.9)
Asphyxia (n=57)	Yes	19 (33.3)
	No	38 (66.7)
Age at presentation to baby unit (h) (n=50)	≤72	41 (82.0)
	>72	9 (18.0)
Mean=61.1		
SE of mean=14.7		
Range= 0 to 528		
Median=24		
Age at onset of sepsis (h) (n=57)	≤72 h	49 (84.2)
	>72 h	9 (15.8)
Mean=64.2		
SE of mean=15.1		
Range=0-528		
Median=24.0		

PROM – Premature rupture of membrane; SE – Standard error; LBW – Low birth weight

symptoms, while vomiting (17.5%), diarrhea (1.8%), abdominal distention (15.8%), excessive cry (12.5%), and bleeding from the cord (3.5%) were not very common.

As shown in Table 4, depressed primitive reflexes were the only other common physical finding, present in just over half (50.9%) of the cases, but hepatomegaly (21.1%), splenomegaly (1.8%), pallor (12.5%), and hypertonia (26.3%) were not common. Table 4 also shows that about 9-in-10 (92.6%) of the septic cases survived.

Table 5 reveals the findings of the comparisons between key characteristics of the Cases and those of the Controls using the Chi-squared analysis. It was found that the place of birth ($P = 0.02$) and the final outcome ($P = 0.004$) were significantly associated with the development of sepsis, while gender ($P = 0.12$), birth weight ($P = 0.33$), gestational age ($P = 0.53$), and mode of delivery ($P = 0.74$) were not. Using the BLR, these associations were re-tested, and both associations identified earlier retained their respective significances [Table 6]. As shown, newborns who developed sepsis were 59% less likely to be born within ESUTH, i.e. to be "inborn" (odds ratio [OR] 0.41; CI 0.20–0.88; $P = 0.02$), and were also three-and-half times likely not to survive (OR 3.46; CI 1.11–10.78; $P = 0.03$). Again, no associations were found between the development of sepsis and birth weight, gestational age, gender, and mode of delivery.

The associations between various patient characteristics and some clinical features found among newborns presenting with sepsis are summarized in Table 7. It was observed that, among newborns with sepsis, whose birth weights were ≥2.5 kg were eight-and-half times more likely to develop asphyxia (OR = 8.47; CI = 1.69–42.48; $P = 0.05$) and five times more likely to develop hypertonia (OR = 5.14; CI = 1.01–26.10; $P = 0.05$) than those whose birth weights were <2.5 kg. In addition, those of them who were born at term or more (≥37 weeks) were 74% less likely to develop hepatomegaly (OR = 0.26; CI = 0.07–0.98; $P = 0.05$) relative to those born preterm (<37 weeks).

It was also found that septic newborns who developed sepsis at ≤72 h of birth were 86% less likely to develop

Table 3: Clinical features of newborns presenting with sepsis at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Characteristic	Variable	n (%)
Temperature (*n*=57)	Yes	48 (84.2)
	No	9 (15.8)
Vomiting (*n*=57)	Yes	10 (17.5)
	No	47 (82.5)
Diarrhea (*n*=57)	Yes	1 (1.8)
	No	56 (98.2)
Poor suckling (*n*=56)	Yes	22 (39.3)
	No	34 (60.7)
Fast breathing (*n*=55)	Yes	24 (43.6)
	No	31 (56.4)
Convulsion (*n*=57)	Yes	15 (26.3)
	No	42 (73.7)
Jaundice (*n*=56)	Yes	22 (39.3)
	No	34 (60.7)
Weakness/lethargy (*n*=57)	Yes	18 (31.6)
	No	39 (68.4)
Abdominal distension (*n*=57)	Yes	9 (15.8)
	No	48 (84.2)
Excessive cry (*n*=56)	Yes	7 (12.5)
	No	49 (87.5)
Poor cry (*n*=56)	Yes	17 (30.4)
	No	39 (69.6)
Bleeding from umbilical cord (*n*=57)	Yes	2 (3.5)
	No	55 (96.5)
Heart rate (per min) (*n*=56)	90-160 (normal)	45 (80.4)
	<90 (bradycardia)	0
	>160 (tachycardia	11 (19.6)
Respiratory rate (per min) (*n*=56)	30-53 (normal)	15 (26.8)
	<30 (bradypnea)	40 (71.4)
	>53 (tachypnea)	1 (1.8)

Table 4: Physical features found in newborns presenting with sepsis at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Characteristic	Variable	n (%)
Hepatomegaly (*n*=57)	Yes	12 (21.1)
	No	45 (78.9)
Splenomegaly (*n*=57)	Yes	1 (1.8)
	No	56 (98.2)
Full anterior fontanelle (*n*=57)	Yes	14 (24.6)
	No	43 (75.4)
Pallor (*n*=56)	Yes	7 (12.5)
	No	49 (87.5)
Hypertonia (*n*=57)	Yes	15 (26.3)
	No	42 (73.7)
Hypotonia (*n*=56)	Yes	4 (3.6)
	No	52 (96.4)
Depressed primitive reflexes (*n*=57)	Yes	29 (50.9)
	No	28 (49.1)
Outcome (*n*=54)	Alive	50 (92.6)
	Dead	4 (7.4)

abdominal distension (OR = 0.14; CI = 0.03–0.72; *P* = 0.02), while those admitted to the SCBU at ≤72 of birth were 85% less likely to develop abdominal distension (OR = 0.15; CI = 0.03–0.73; *P* = 0.02).

Finally, those born in ESUTH were about five times more likely to develop jaundice compared with those born outside (OR = 4.83; CI = 1.36–17.16; *P* = 0.02).

Table 8 shows the causative organisms implicated in the cases of sepsis, as well as their patterns of antibiotic sensitivities. It reveals that approximately 3-in-5 of the cases (59.6%) involved coliforms, while one-quarter were from *Staphylococcus aureus*. The most sensitive antibiotic in the study center is ciprofloxacin with a sensitivity of 49.1% for coliforms, 15.8% for *S. aureus*, and 7.0% for *Streptococcus* spp. Other fluoroquinolones had similarly high sensitivity. Next to fluoroquinolones are the ceftriaxone and gentamicin while drugs such as amoxicillin, ampicillin, cefixime, and clindamycin were not effective against the common pathogens in the study center [Table 8].

DISCUSSION

The incidence of culture-proven sepsis in our center was 29.7/1000 newborn admitted to the SCBU of the ESUTH. Another similar study reported an incidence rate of 5.5/1000 birth in a community-based study in developing communities around the world.[13] The far higher incidence rate reported in our study may be related to the fact that it was hospital based as opposed to the community-based method in the referenced study. The high incidence rate of NNS reported in this study could explain the continued high under-5 children mortality rate seen in Sub-Saharan Africa.[14] The World Health Organization in 2004 reported that neonatal death accounted for over a third of deaths in under-5 children in Africa. Among the neonatal deaths reported, NNS and prematurity accounted for more than 80% of all neonatal mortality.[14] The male to female ratio of 6:1 showing a male preponderance in this study is in line with other reports that have documented male predominance in neonatal infections.[15,16] Higher susceptibility of males to infection from earlier studies is said to be genetically mediated.[17,18]

More babies who had sepsis were delivered through SVD compared to cesarean section though this did not attain statistical significance possibly due to small sample size. A similar finding was documented by Veerendra *et al*.[19] in a hospital-based study where they found that newborns who had normal vaginal deliveries are 2.29 times more at risk of developing NNS compared to those delivered via cesarean section. The latter is an aseptic surgical procedure and entails strict observance of asepsis compared to the former which is a natural

Table 5: Comparison of the characteristics of newborns with sepsis (cases) and those without sepsis (controls) for all those admitted at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria, from January 2013 to December 2016

Characteristic	Variable	Number of cases (%)	Number of controls (%)	χ^2 statistic	P
Gender	Male	40 (70.2)	17 (9.9)	2.47	0.12
	Female	17 (29.8)	100 (90.1)		
Birth weight (kg)	Large (>4.2)	3 (5.7)	10 (6.1)	3.41	0.33
	Normal (2.5-4.2)	30 (56.6)	82 (50.3)		
	Low (1.5-2.4)	17 (32.1)	46 (28.2)		
	Very LBW (≤1.5)	3 (5.7)	25 (15.4)		
Gestational age (weeks)	Postdate (≥41)	4 (7.0)	8 (4.7)	1.29	0.53
	Term (37-40)	34 (59.6)	70 (52.6)		
	Preterm (≤36)	19 (33.3)	93 (42.7)		
Place of birth	Inborn	16 (28.1)	78 (46.2)	5.74	0.02*
	Outborn	41 (71.9)	91 (53.8)		
Mode of delivery	Spontaneous vagina delivery	33 (57.9)	99 (60.4)	0.11	0.74
	Cesarean section	24 (42.1)	65 (39.6)		
Outcome	Alive	50 (96.6)	122 (74.4)	8.06	0.004*
	Dead	4 (7.4)	42 (25.6)		

*Statistically significance is set at *P*≤0.05. LBW – Low birth weight

Table 6: Binary logistic regression showing associations between the development of sepsis and some characteristics of newborns at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Outcome (dependent) variables	OR	95% CI of OR		Significance (*P*)
		Lower	Upper	
Birth weight (kg) (≥2.5 vs. <2.5)	1.09	0.39	3.07	0.87
Gestational age (weeks) (≥37 vs. <37)	0.91	0.31	2.65	0.86
Gender (male vs. female)	0.74	0.37	1.50	0.40
Final outcome (dead vs. alive)	3.46	1.11	10.78	0.03*
Mode of delivery (caesarean vs. vaginal)	1.23	0.60	2.51	0.57
Place of birth (inborn vs. outborn)	0.41	0.20	0.88	0.02*

*Statistically significance is set at *P*≤0.05. OR – Odds ratio; CI – Confidence interval

process, and newborns delivered through it are exposed to organisms which naturally inhabits the mother's birth canals. Such organisms have long been implicated as causes of early-onset NNS.[17]

In our study, it was observed that most newborns with sepsis were delivered outside the study center. This finding corroborates a study in Nepal which documented a higher prevalence of sepsis among outborns compared to inborn babies.[20] The explanation given in the referenced study which is also true in our environment was that some of these deliveries done outside could occur at home or maternity homes where basic aseptic procedures during childbirth may not be followed. In addition, these babies delivered outside and referred to our facility are more likely to have been exposed to microorganism in the environment during transportation further increasing the likelihood of infectivity.

The proportion of newborns who died from NNS in the current study is lower (7.4%) compared to 19% documented by a similar hospital-based study on bacteriologically proven cases of NNS at the University of Calabar Teaching Hospital in Southern Nigeria.[21] These figures are still unacceptably high in both scenarios compared to figures in developed climes. These high case-fatality rates reported in both studies are particularly troubling because these newborns had blood culture and antibiogram which should enhance the use of the most sensitive antibiotics in their treatment. However, factors such as late presentation noted in our study,[22] particularly among newborns delivered outside, may have contributed to the high mortality rate seen in this study.

None of the clinical features encountered in newborns with sepsis in our study was significantly correlated with the diagnosis of sepsis. However, fever and depressed primitive reflexes were the most frequently encountered clinical presentation in septic neonates. This re-affirms the long documented nonspecific and subtle signs and symptoms of NNS[10] and underscores the importance of careful evaluation of neonates with suspected sepsis and the need for a culture in the definite diagnosis of NNS.

Table 7: Binary logistic regression showing associations between various patient characteristics and some clinical features found in among newborns presenting with sepsis at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Outcome (dependent) variables	Predictor (independent) variables	OR	95% CI of OR		Significance (*P*)
			Lower	Upper	
Birth weight (kg) (≥2.5 vs. <2.5)	Asphyxia (yes vs. s no) (*n*=53)	8.47	1.69	42.48	0.01*
	Hypertonia (present vs. absent) (*n*=53)	5.14	1.01	26.10	0.05*
	Jaundice (present vs. absent) (*n*=52)	3.16	0.98	10.24	0.06
Gestational age (weeks) (≥37 vs. <37)	Asphyxia (yes vs. no) (*n*=57)	3.88	0.97	15.59	0.06
	Hepatomegaly (present vs. absent) (*n*=57)	0.26	0.07	0.98	0.05*
	Hypertonia (present vs. absent) (*n*=57)	4.42	0.88	22.14	0.07
Age at onset of sepsis (≤72 vs. >72)	Abdominal distention (yes vs. no) (*n*=50)	0.14	0.03	0.72	0.02*
Age at presentation to hospital (h) (≤72 vs. >72)	Abdominal distention (yes vs. no) (*n*=57)	0.15	0.03	0.73	0.02*
	Diminished primitive reflexes (yes vs. no) (*n*=57)	4.50	0.85	23.95	0.08
Place of birth (inborn vs. outborn)	Jaundice (present vs. absent) (*n*=56)	0.46	0.24	0.87	0.02*

**Statistically significance is set at *P*≤0.05; Only results with *P*<0.10 are included

Coliform bacteria were the most common isolated organisms in the study center followed by *S. aureus*. *Escherichia coli* was the most common coliform seen. Our diagnostic laboratory lacks the facilities to specifically isolate other forms of coliforms; hence, they were all reported as coliforms. Similar bacteriological profile was reported in another, hospital-based study, which isolated *E. coli* as the most common causative organism followed by *Staphylococcus*.[23] The former is a common flora in the genitourinary tract and is vertically transmitted to newborn *in utero* or at time of birth, while the latter is commonly transmitted by hospital workers and relatives.[24] Contrary to our finding, another hospital-based study in a Neonatal Intensive Care Unit reported a higher incidence of *S. aureus* than coliform bacteria such as *Klebsiella*.[25] The variation in the isolated organism among centers strongly supports the need for health facilities caring for these vulnerable newborns to document the predominant cause of sepsis that could guide the initiation of antibiotics empirically in suspected cases.

Finally, our study showed that drugs such as ceftriaxone and gentamicin recorded intermediate sensitivity, while ampicillin, amoxicillin, and clindamycin had almost zero sensitivity to cultured bacteria. It is not surprising to note the rising tide of resistance to previously sensitive, available, and affordable penicillin-like the amoxicillin. In the study environment, it is common practice for antibiotics to be dispensed and purchased over the counter without prescription. The authors have previously documented very high prevalence of use and misuse of antibiotics by caregivers in the treatment of common childhood illness in the same environment.[26,27] Such practice could greatly enhance the emergence and spread of resistant strains of microbes.

It is worrisome to note from our study that quinolones, such as ciprofloxacin, ofloxacin, and pefloxacin, were the most sensitive antibiotics to the predominant isolates seen in our study. Although there are concerns for possible adverse effects such as arthropathy and tendinitis associated use of quinolones, several large retrospective studies in children have not associated use of fluoroquinolones with long-term joint abnormality or growth impairment.[28-30] However, more data from controlled trials are needed to further elucidate the safety profile of these drugs in children. The general recommendation has been that its use should be guided by clear medical rationale and careful monitoring. Hence, authors recommend them only when benefits outweigh the potential risk, especially to organism that has demonstrated multidrug resistance.

CONCLUSION

Our study reported a high incidence and mortality rate of NNS in Enugu. None of the clinical features reported in septic neonates were strongly correlated with a diagnosis of septicemia in surveyed newborns. Coliforms and *S. aureus* accounted for majority of bacterial isolated in the culture samples of these septic neonates. A high incidence of bacterial resistance to commonly available antibiotics such as penicillins and cephalosporins was also noted in our environment. Quinolones with an inconclusive safety profile in children remain the most sensitive antibiotics for NNS in our environment.

Conflicts of interest

There are no conflicts of interest.

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Table 8: Organisms and patterns of antibiotic responses among newborns presenting with sepsis at the Special Care Baby Unit, Enugu State University Teaching Hospital, Enugu, Southeast Nigeria

Organism	n†	Ciprofloxacin	Ofloxacin	Pefloxacin	Levofloxacin	Ceftriaxone	Chloramphenicol	Clarithromycin	Erythromycin	Amoxicillin	Ampicillin	Clindamycin	Gentamicin	Cefixime
Coliform spp.	36	49.1	42.1	29.8	19.2	24.6	22.8	10.5	7.0	3.5	0	0	0	0
Staphylococcus spp.	14	15.8	12.2	1.8	14.0	7.0	5.2	0	0	0	0	0	5.7	0
Streptococcus spp.	6	7.0	5.2	3.5	5.2	5.2	3.5	0	0	0	0	0	3.5	0
Salmonella spp.	1	-	-	-	-	-	-	-	-	-	-	-	-	-

†Number of neonates on whom organism was isolated

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