Bacteriology and Outcome of Neonatal Septicaemia: Experience from a Mission Hospital in Nigeria

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ABSTRACT

Introduction. One in every three preventable under-five deaths occur in the neonatal period and one of the leading causes of neonatal death in Low and Middle-Income Countries (LMIC) is sepsis. Organisms isolated varies between and within geographical locations, its trend changes with time. Each setting hence needs to have its antibiogram for susceptible isolates to optimize treatment outcome, the background on which this study was conducted.

Methodology. A retrospective study was done on neonates admitted to the Neonatal Intensive Care Unit of Bowen University Teaching Hospital, a missionary hospital in South West Nigeria, between January 2016 and December 2017. The medical records of these neonates were retrieved from the comprehensive electronic database for all neonates admitted into the unit.

Result. Of the 129 newborns eligible for the study, early-onset sepsis (56.6%) predominated. There were 79 (61%) males giving a M:F ratio of 1.6:1. The incidence rate of neonatal sepsis was 15 per 1,000 live births with a mortality rate of 24%. Gram-Negative Bacilli were mostly isolated in positive cultures. The likelihood of getting a positive culture was unrelated to the age and sex of patients at presentation. There was a varying resistance pattern of the isolates to commonly used empiric antibiotics.

Conclusion and Recommendation. Gram-Negative Bacilli was the commonest cause of neonatal sepsis in our center, associated with poor outcome. The high incidence of resistance to the commonly used empirical treatment calls for an urgent review of practice if the trend of high morbidity and mortality would be curtailed, as well as improved infection control practices.

Keywords: neonatal sepsis, septicaemia, antibiogram, antibiotics susceptibility testing

INTRODUCTION

Approximately 40% of mortalities for patients under five years of age in low- and middle-income countries (LMICs) occur in the neonatal period, and a leading cause is sepsis.[1,2] Morbidity and mortality following neonatal sepsis are high but preventable with appropriate antimicrobial therapy and aggressive supportive care. The higher morbidity and mortality rate in LMICs, despite the use of supposedly potent pharmacotherapy, than in developed countries may be related to isolate-treatment mismatch.

Pediatric sepsis criteria are not accurate for term neonates and have not been examined in preterm neonates for whom the developmental stage influences aberrations associated with the host immune response.[3] The clinical

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presentation of sepsis in neonates is nonspecific, ranging from subclinical infection to severe manifestations of focal or systemic disease. The gold standard for its diagnosis is laboratory isolation of the associated pathogen.[3-5] The organisms isolated vary from one geographical location to another, and the trend changes with time.[5] Neonatal pathogens within communities are not fixed, thereby necessitating frequent evaluations regarding the efficacy and safety of a chosen antibiotic regimen.[6] Infections may be acquired intrapartum, peripartum, or immediately postpartum.[5] Also, the local ecology and niche of bacteria causing neonatal sepsis is constantly changing.[7] The variation, which may be due to patterns of antibiotic use in that locality, may affect the success of empirical management. Hence, regular trend monitoring is expedient.

The initiation of appropriate antibiotics with the first 72 hours is crucial to achieving a positive outcome.[8] In 2006, the World Health Organization (WHO) reviewed five international guidelines in the management of neonatal sepsis.[9] These guidelines suggest relying on data on antibiotic resistance patterns in locally prevalent pathogens when selecting empirical treatment regimens and recommend individualizing empirical antibiotic recommendations according to local antibiotic protocols and local pathogen susceptibility. Hence, there is a need to identify the prevalent causative organisms in our locality and their antibiotic susceptibility patterns. The current protocol for the treatment of probable septicemia in most nurseries in LMICs is the use of empiric antibiotics while awaiting laboratory results, the choice of which is mostly not evidence-based. It is imperative, therefore, that data on neonatal sepsis be collated and regularly updated to provide current, relevant information for regular review of the drugs of choice in the treatment of neonatal sepsis in various geographical locations to optimize treatment outcomes and reduce mortality. This study aimed to determine the prevalence of neonatal sepsis in the study area, identify the prevalent causative organisms and their antibiotic susceptibility patterns, and review the treatment modality and outcomes in our settings.

METHODOLOGY

This is a retrospective study involving neonates admitted to the neonatal intensive care unit (NICU) of Bowen University Teaching Hospital (BUTH), a missionary hospital in Ogbomoso, Oyo State, South West Nigeria, done between January 2016 and December 2017.

Sampling Technique

The neonatal unit of BUTH has a comprehensive electronic database for all neonates admitted to the unit. This database contains detailed clinical histories and examination findings of the neonates. The vital signs and clinical changes were updated throughout hospitalization. The medical records of all neonates admitted to the neonatal unit between January 2016 and December 2017 were retrieved. All infants who met the inclusion criteria were enrolled in the study.

Inclusion Criteria

The inclusion criteria were as follows: a maternal history of intrapartum fever (> 38.0°C or > 100.4°F), chorioamnionitis, a sustained fetal heart rate > 160 beats/min, prematurity, a maternal white blood cell (WBC) count > 15,000 cells/μl, rupture of membranes > 12 h, tachypnea (> 1 h), respiratory distress, offensive lochia, a low Apgar score (< 5 at 1 min), and low birth weight (< 1500 g).[10]

Exclusion Criteria

1. Patients for whom a blood culture was not performed were excluded.
2. Neonates with an inborn error of metabolism and congenital malformations were also excluded.

Patient enrollment and conduct of the research

Demographic data and risk factors for sepsis (inclusion criteria) were extracted from the neonatal unit database. The sociodemographic data of the mother, antenatal history, labor and delivery history, medications used since birth, including pre-admission and pre-referral medications, and the use of herbal preparations were also retrieved. The presenting symptoms, examination findings, and differential diagnoses were extracted to a Microsoft Access file.

Laboratory records of blood cultures, a full blood count, and a micro-erythrocyte sedimentation rate (ESR) were retrieved from the database. Participants were categorized as early-onset sepsis (EONS) or late-onset sepsis (LONS) based on their age at presentation. Patients who presented at an age of fewer than seven days were categorized as EONS, while patients who presented at an age of seven days or older were categorized as LONS. Manual blood culture processing was performed by inoculating samples in brain heart infusion broth with 2 ml of blood. Samples were incubated for seven days, and signs of a positive culture, including the presence of air bubbles, hemolysis, and blood clots in the broth, were reviewed daily. Irrespective of whether positive signs were present, the broth was subcultured in blood agar, chocolate agar, and MacConkey agar on days 3, 5, and 7 and incubated under aerobic conditions. The colony morphology of the isolates on the solid agar was noted, and gram staining and the results of the various biochemical tests were performed to aid the identification of the organisms. Antimicrobial susceptibility testing was performed on Mueller–Hinton agar using the modified Kirby–Bauer method. The antibiotics tested were ampicillin (10 μg), amoxicillin-clavulanic acid (30 μg), cefotaxime (30 μg), ceftriaxone (30 μg), ceftazidime (30 μg), imipenem (10 μg), vancomycin (30 μg), gentamicin (10 μg), erythromycin (15 μg), ciprofloxacin (5 μg), and pefloxacin (10 μg). The others were amoxicillin (25 μg), cotrimoxazole (25 μg), cefalothin (30 μg), cefuroxime (30 μg), erythromycin (30 μg), penicillin (1.5 MU), and

chloramphenicol (33 μg). Multidrug-resistant (MDR) isolates were defined as isolates resistant to three or more antimicrobial classes.[11]

A full blood count was automated using a Sysmex® autoanalyzer, while the micro-ESR was determined by adding four drops of blood to a drop of 3.8% sodium citrate on a clean glass slide. A glass capillary tube with a 75-mm length and a 1.2-mm internal diameter was placed on the slide at an angle of 45°, allowing blood to fill the core of the tube by capillary action. After a rise of 70 mm, the tube was repositioned perpendicularly, sealed at both ends with seal paste, and kept in a vertical position for 1 h, after which the height of the plasma and the total height of blood column in the capillary tube was measured. ESR value was obtained by applying a multiplication of 200 to the ratio of the height of plasma to the height of the blood column in the capillary.

Data Management and Analysis

Data were entered into a Microsoft Access file and analyzed using the IBM Statistical Package for Social Sciences (S.P.S.S) version 23. Values are reported as proportion, frequencies tables, means and standards were generated from the data. Non-parametric variables are summarized as median and their corresponding interquartile range. Proportions were analyzed using the Chi-square test or Fischer's exact test as appropriate. The level of significance was set at $P < 0.05$.

Ethical considerations

Approval was obtained from the Bowen University Health Research Ethics Committee (NHREC/12/04/2012) with approval number BUTH/REC/-024.

RESULTS

One hundred and twenty-nine neonates (129) were enrolled in the study (Figure 1) with a median age of 5 days, range 0-28 days, majorly (56.6%) were aged <7 days old (Figure 2). There were 79 (61.0%) males giving a M:F of 1.6:1. Isolates were recovered in only 45 (35%) cases (Table 1), 40 of whom were in-borns (those given birth to at the study center). The majority of the in-borns (29/40; 73.3%) were delivered by unbooked mothers form the community. Live births within the year at the Centre were 2,642, hence, the incidence rate of 15 per 1000 live births.

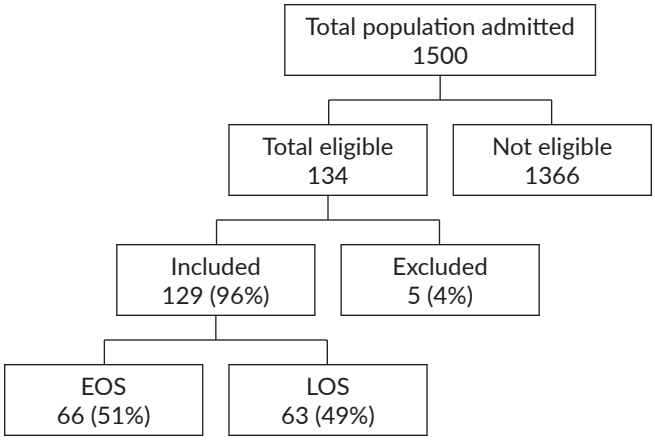

Figure 1. Flowchart showing enrollment and inclusion into study.

The likelihood of getting a positive culture was unrelated to the age and sex of the patient (Table 2), neither was the spectrum of isolate influenced by the age and sex of the patient (Table 3). Of the isolates recovered (Figure 2), 51% were Gram-Negative Bacilli which included *Klebsiella* spp (13%), *Pseudomonas aeruginosa* (11%), *Proteus mirabilis* (9%), *Escherichia coli* (9%), and other Gram-negative Bacilli that are non-enteriobacteriaceae (9%). The isolated organism was not a function of age at presentation nor the sex of the patient. (Table 3)

Isolates' susceptibility to commonly used antibiotics were tested (Table 4). All *Staphylococcus aureus* strain isolated was found to be susceptible to Augmentin, Amoxicillin, Ciprofloxacin, Ceftriaxone, Cotrimoxazole, Imipenem and Vancomycin. There were varying degrees of susceptibility to other antibiotics tested such as Ampicillin (86%), Ceftazidime (45%), Cefalothin (95%), Cefuroxime (77%), Erythromycin (50%) and Gentamycin (82%).

All *Pseudomonas aeruginosa* isolates were found to be susceptible to Chloramphenicol, Cefuroxime, Imipenem, and Vancomycin; resistant to Augmentin, Ampicillin, Amoxylcillin, and Ceftazidime while variably susceptible to Ciprofloxacin (25%), Gentamycin (25%), and Pefloxacin (25%).

Table 1. Biodata of respondent

Variable	Frequency	Percent
Age (days)		
Median (IQR)	5.00 (2.75 – 14.00)	
Range	1 – 28	
Sex		
Male	79	61.2
Female	50	38.8
Growth		
Growth	45	34.9
No growth	84	65.1

Table 2. Culture-proven cases by age and sex

Variable	Growth n = 45 (%)	No Growth n = 84 (%)	Total N (%)	χ^2	*p* value
Age (days)					
≤ 7	25 (34.2)	48 (65.8)	73	0.030	0.862
> 7	20 (35.7)	36 (64.3)	56		
Sex					
Male	32 (40.5)	47 (59.5)	79	2.837	0.092
Female	13 (26.0)	37 (74.0)	50		

χ^2: Chi square test; Y: Yates corrected Chi square

Table 3. Recovered isolates by age and sex

Variable	Organism						Total N	χ^2	*p* value
	Staph. n (%)	*Kleb.* n (%)	Other gram negative bacilli n (%)	*Pseudomonas* n (%)	*Proteus* n (%)	*E. coli* n (%)			
Age (days)									
≤ 7	13 (52.0)	1 (4.0)	8 (32.0)	1 (4.0)	0 (0.0)	2 (8.0)	25	2.690[F]	0.868
> 7	8 (40.0)	2 (10.0)	6 (30.0)	1 (5.0)	1 (5.0)	2 (10.0)	20		
Sex									
Male	12 (37.5)	3 (9.4)	11 (34.4)	2 (6.3)	1 (3.1)	3 (9.4)	32	3.947[F]	0.559
Female	9 (69.2)	0 (0.0)	3 (23.1)	0 (0.0)	0 (0.0)	1 (7.7)	13		

χ^2: Chi square test; F: Fisher's exact test

Table 4. Distribution of sepsis cases according to outcomes

Sepsis Cases	No. (%)
Died	31 (24)
Cured	98 (76)
Total	129 (100)

Proteus mirabilis strains isolated were all sensitive to Augmentin, Amoxicillin, Chloramphenicol, Cefuroxime, Ceftriaxone, Gentamycin and Penicillin. Likewise, all strains were resistant to ampicillin and variably sensitive to Ceftazidime (50%), Ciprofloxacin (25%), Ofloxacin (50%) and Pefloxacin (25%).

The *E.coli* recovered from the patients were all sensitive to Augmentin, Amoxycillin, Ceftazidime, Ciprofloxacin, Cotrimoxazole, Ceftriaxone, Cefuroxime, Gentamycin, Imipenem, and Vancomycin. They demonstrated varying degrees of resistance to other tested antibiotics which were Ampicillin (25%) and Pefloxacin (50%).

Klebsiella species isolates were all susceptible to Ciprofloxacin, Imipenem, Nitrofurantoin, and Pefloxacin. Percentage susceptibility to Ampicillin was 83%, likewise to Chloramphenicol, Cotrimoxazole, to Ceftriaxone, to Erythromycin and Vancomycin; 67% to Augmentin and 50% to Gentamycin. For other Gram-Negative Bacilli, however, susceptibility to Ceftazidime is by all isolated strains, as well as susceptibility to Imipenem and Vancomycin. Percentage susceptibility to Amoxicillin, Cotrimoxazole, and Gentamycin was 25% while susceptibility to Pefloxacin, Ciprofloxacin, Ceftriaxone, Cefuroxime was 50%. Seventy-five percent of the isolates were susceptible to Augmentin and a mortality rate of 24% was noted (Table 5).

Table 5. Antibiotic Susceptibility Profile of Isolates to Commonly Prescribed Antibiotics

Antibiotics	Organisms								
	Staphylococcus aureus			*Proteus mirabilis*			*Klebsiella* spp		
	S	R	N/A	S	R	N/A	S	R	N/A
Augmentin (AUG)	22 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	4 (67)	2 (33)	0 (0.0)
Ampicillin (AMP)	18 (86.0)	4 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	5 (83)	1 (17)	0 (0.0)
Amoxylcillin (AMX)	22 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	5 (83)	1 (17)	0 (0.0)
Ceftazidime (CAZ)	10 (45.0)	12 (55.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (100.0)
Cefalothin (CF)	21 (95.0)	1 (5.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	6 (100.0)
Ciprofloxacin (CIP)	22 (100)	0 (0.0)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)	6 (100)	0 (0.0)	0 (0.0)
Cefuroxime (CTX)	17 (77.0)	5 (23.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (100)
Cotrimoxazole (COT)	22 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	5 (83)	1 (17)	0 (0.0)
Ceftriaxone (CRO)	22 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	5 (83)	1 (17)	0 (0.0)
Erythromycin (ERY)	11 (50.0)	11 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	5 (83)	1 (17)	0 (0.0)
Gentamycin (GEN)	18 (82.0)	4 (18.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	3 (50.0)	3 (50.0)	0 (0.0)
Imipenem (IPM)	22 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	6 (100)	0 (0.0)	0 (0.0)
Vancomycin (VA)	22 (100)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	4 (67)	2 (33)	0 (0.0)
Chloramphenicol (C)	0 (0.0)	0 (0.0)	22 (100)	4 (100.0)	0 (0.0)	0 (0.0)	5 (83)	1 (17)	0 (0.0)
Pefloxacin (PEF)	0 (0.0)	0 (0.0)	22 (100)	1 (25.0)	3 (75.0)	0 (0.0)	6 (100)	0 (0.0)	0 (0.0)
Ofloxacin (OFL)	0 (0.0)	0 (0.0)	22 (100)	2 (50.0)	2 (50.0)	0 (0.0)	6 (100)	0 (0.0)	0 (0.0)
Penicillin (PEN)	0 (0.0)	0 (0.0)	22 (100)	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (100)
Nitrofurantoin (NIT)	0 (0.0)	0 (0.0)	22 (100)	0 (0.0)	0 (0.0)	4 (100.0)	6 (100)	0 (0.0)	0 (0.0)

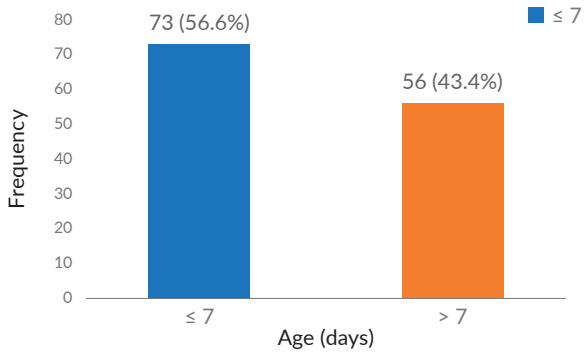

Figure 2. Age of patient.

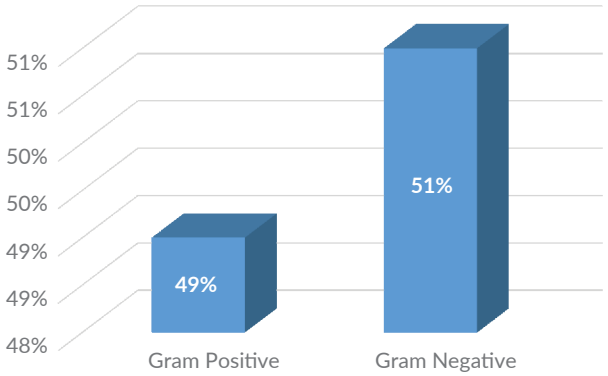

Figure 4. Frequency of isolation of organisms.

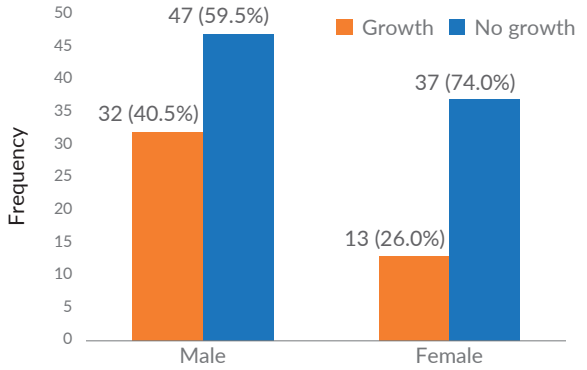

Figure 3. Rate of isolate recovery by sex.

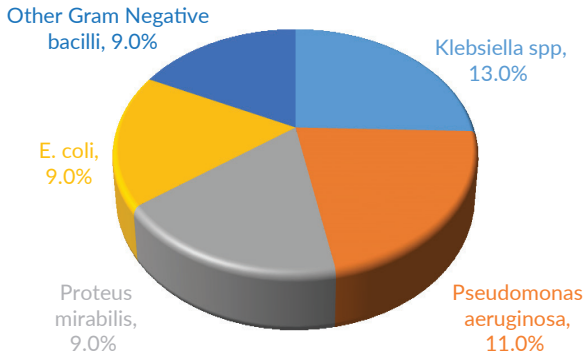

Figure 5. Spectrum of gram negative organisms isolated.

Table 5. Antibiotic Susceptibility Profile of Isolates to Commonly Prescribed Antibiotics *(continued)*

Antibiotics	Organisms								
	Pseudomonas auruginosa			*Escherichia coli*			Other GNB		
	S	R	N/A	S	R	N/A	S	R	N/A
Augmentin (AUG)	0 (0.0)	5 (100.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	3 (75.0)	1 (25.0)	0 (0.0)
Ampicillin (AMP)	0 (0.0)	5 (100.0)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)
Amoxylcillin (AMX)	0 (0.0)	5 (100.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)
Ceftazidime (CAZ)	0 (0.0)	5 (100.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)
Cefalothin (CF)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)	0 (0.0)	4 (100)
Ciprofloxacin (CIP)	4 (80.0)	1 (20.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	2 (50)	2 (50)	0 (0.0)
Cefuroxime (CTX)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	2 (50)	2 (50)	0 (0.0)
Cotrimoxazole (COT)	0 (0.0)	0 (0.0)	5 (100.0)	4 (100.0)	0 (0.0)	0 (0.0)	1 (7.1)	3 (75.0)	0 (0.0)
Ceftriaxone (CRO)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	2 (50)	2 (50)	0 (0.0)
Erythromycin (ERY)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)
Gentamycin (GEN)	4 (80.0)	1 (20.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	1 (25.0)	3 (75.0)	0 (0.0)
Imipenem (IPM)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)
Vancomycin (VA)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100)	0 (0.0)
Chloramphenicol (C)	5 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)
Pefloxacin (PEF)	4 (80.0)	1 (20.0)	0 (0.0)	2 (50.0)	2 (50.0)	0 (0.0)	2 (50)	2 (50)	0 (0.0)
Ofloxacin (OFL)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)
Penicillin (PEN)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)
Nitrofurantoin (NIT)	0 (0.0)	0 (0.0)	5 (100.0)	0 (0.0)	0 (0.0)	4 (100.0)	3 (75.0)	1 (25.0)	0 (0.0)

DISCUSSION

The diagnosis of neonatal sepsis is daunting as a result of the atypical response of newborns to infections. The clinical features are often subtle and nonspecific, culture confirmation of the diagnosis is thus expedient.

A culture-proven sepsis rate of 35% obtained in the study was similar to the reported incidence of 34% in Lagos University Teaching Hospital,[12] and a private tertiary hospital located in the same geopolitical zone as the study area.[7] The reported rate is also in tandem with a 30.8% rate documented in Ilorin,[13] a 33.1% reported in Port Harcourt, Nigeria[14] and 37% reported by Mugalu et al. in Uganda.[15] This less than 100% rate of culture-proven sepsis may contribute to high antibiotic consumption in neonatal units as neonatologists would rather treat infants with suspected sepsis though not confirmed with a positive blood culture.[16] The lower rate isolates observed among subjects with probable sepsis in these studies may, however, be due to history of prior use of antibiotics by caregivers and the use of herbal remedies some of which may have antimicrobial properties.[12-15]

The neonatal sepsis incidence rate of 15 per 1000 live birth reported in this study is higher than 7.04 per 1000 live births recorded in the nearby urban center, Ilorin.[13] This was probably due to the community settings in the study area, which is not as urban and the hospital setting and services which are not as advanced as its obtainable in larger tertiary health facilities. Compared with reports from the developed world such as the EU and the USA, this rate is on the high side as the incidence rate of 0.25–0.38 per 1000 population in the European Union, 3.0 cases to occur per 1000 in the United States have been reported.[17,18] Neonatal sepsis in hospitals are to a large extent nosocomial,[19] mirroring the level of asepsis in the hospital and infection control practices at the Centre.

Hospital-born babies in developing countries are at increased risk of neonatal infections because of poor intrapartum and postnatal infection-control practices.[20] Defects in infection control practices evident in developing countries are likely responsible for the high incidence rate. Ninety-nine percent of the approximate 1 million annual neonatal deaths from life-threatening invasive bacterial infections occur in developing countries, at least 50% of which are from home births or community settings, such as is obtainable in the study location, hence the high incidence rate and mortality recorded in this study.[21,22] Neonatal mortality was estimated to be about 34% in developing countries and about 5% in developed countries by the WHO with most of these deaths occurring in the first week of life.[22] These rates vary between and within continents as well as between different countries in these regions and within the countries themselves. Neonatal deaths accounted for 52% of all under-5 child mortality in South Asia, 53% in Latin America and the Caribbean, and 34% in sub-Saharan Africa.[23,24] Neonatal mortality for different African countries ranges from 11% in South Africa to 68% in Liberia.[25] Discrepancies in rate may be due to under-reporting, likewise, culture-negative sepsis is not usually considered by many while reporting on neonatal sepsis. The large number of neonates treated for culture-negative sepsis is largely ignored in epidemiological studies, thus, there is a paucity of data on this condition.[26]

Financial constraints, sociocultural beliefs that negatively influence health-seeking behavior of parents and caregivers, hence prevent them from seeking medical care for their newborn or lead them to refuse hospital admission when advised are also factors that may favor high rate of neonatal mortality in this environment.[6] Limited access to hospital-based facilities, financial constraints or sociocultural, delays in the administration of appropriate antibiotics when eventually they get to the healthcare facility and or inadequate courses of antibiotics are common features in LMIC which may render hospitalization of the newborn for medical treatment fruitless or ineffective as reflected by the high case-fatality rates in hospitals in LMIC.[6]

In a review article by Zaidi et al. on pathogens causing neonatal sepsis in the developing world, Gram-Negative Bacilli were noted to be the major pathogen in EOS, majorly *Klebsiella* spp while Gram-positive cocci essentially GBS and *Staphylococcus aureus* predominate the pathogens implicated after the first week of life.[27] The findings from this study are in concordance with this international perspective as gram-negative bacilli predominantly were isolated. In a study carried out at Ile Ife, South West Nigeria, Gram-positive bacteria were found to be the most prevalent causative organisms in deviant to the findings in this study.[28] This might be associated with a difference in the distribution of regional microorganisms.[6,21,22] This is a pointer to the fact that geographical location alone isn't enough to influence the spectrum of microbes an individual is exposed to in the environment. Other factors such as unsafe birthing practices such as delivery on an unsterilized floor, cutting the cord with a non-sterile instrument and potentially unsafe cultural customs such as spreading dung on the newborn's umbilicus. Other predisposing risk factors for infection in neonates include low birth weight, prematurity, prolonged rupture of membranes and a long delivery period are an important determinant of the resident microbial flora of an environment.[29]

Although early-onset sepsis is commonly considered maternally-acquired,[22] the overwhelming majority of Gram-negative organisms, such as *Klebsiella*, *Pseudomonas*, isolated in various studies and the frequency of *S. aureus* isolated in the first week of life among the studies reviewed, suggests that these infections may be acquired from the hospital or community environment due to poor hygienic practices intrapartum and during postnatal care, rather than reflecting vertical transmission to the infant from exposure to vaginal tract flora. Lack of hygiene during and after delivery, poor cord care, and unhygienic newborn care practices in hospitals are major factors in the acquisition of these infections in

both hospital and community settings.[20] This has important implications for the treatment and prevention of early-onset neonatal infections as an institution of optimal infection control practices will probably reduce the incidence of serious bacterial infection in neonates.

Varying degrees of resistance to commonly prescribed antibiotics noted in this study are in tandem with the report of Pradipta et al. where an average resistance of above 50% to commonly prescribed antibiotics was recorded.[30] Likewise, a report of Adediwura et al. in a tertiary facility in Nigeria[31] and Tadesse et al. in a study carried out in Africa.[32] Commonly used antibiotic in the empirical treatment of neonates with presumed sepsis in the study area is ceftazidime. This study reported 45% of *staphylococcus* spp isolated, 100% of *Pseudomonas aeruginosa* isolated and 50% of *Proteus mirabilis* isolated were resistant to this drug.

Although WHO recommends ampicillin with gentamicin for empiric treatment of suspected neonatal sepsis, penicillin or cloxacillin if *staphylococcal* infection is suspected, the observation from the present study shows the contrary as widespread high level of resistance to these drugs by prevalent bacterial isolates was reported. This rather raises the need for individualized antimicrobial treatment based on local susceptibility pattern.[9]

CONCLUSION

The incidence rate of sepsis in the neonate in the study was high, the outcome of infection poor as evidenced by the high mortality rate reported. The resistance of many of the implicated isolate to the first drug of choice in the empirical treatment of suspected cases was also noted, necessitating the need to review the drug for empirical therapy of suspected cases as well as improve infection control practices. An alternative to hospital-based administration of antibiotics should also be considered to mitigate against the negative influence of sociocultural practices negatively influencing the health-seeking behavior of the locality.

Recommendation

There is a need for regular antimicrobial surveillance to develop and update local antibiogram to significantly reduce neonatal morbidity and mortality from septicaemia. Culture-independent diagnostics technique to confirm diagnosis should be instituted due to the low rate of culture-proven sepsis. Improved infection control practices should be advocated as well as the development of preventive measures such as maternal vaccines to reduce transmission from mother to child.

Statement of Authorship

1. Study concept and design: **JAA**
2. Acquisition of data: **AMA, OT**
3. Analysis and interpretation of data: **JAA, AMA**
4. Drafting of the manuscript: **JAA**
5. Critical revision of the manuscript for important intellectual content: **JOA**
6. Statistical analysis: **PGO**
7. Administrative, technical, and material support: **JOA**
8. Study supervision: **JAA**

Author Disclosure

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APPENDIX

Study Proforma

Socio-demographic details:
Fill or circle as appropriate.

1. Serial Number:
2. Date:
3. Name/ Identifier
4. Age (in months):
5. Gender: 0. Female 1. Male
6. School: 0. Public School 1. Private School
7. Class:
8. Years of Education:
9. Primary Care Giver: 0. Father 1. Mother 2. Grandparent 3. Nanny 4. Others
10. Address:
11. Previous Addresses:
12. Tribe: 0. Yoruba 1. Igbo 2. Hausa 3. Others
14. Family Status: 0. Single 1. Married 2. Separated 3. Divorced
16. Father's Education:
    1. University graduate or equivalent
    2. School certificate holders who also have teaching or other professional training
    3. School certificate or grade II teachers certificate holders or equivalent
    4. JSS 3 and primary six certificate holders
    5. No formal education

17. Father's Occupation:
    1. Senior public servants, professionals, managers, large-scale traders, contractors
    2. Intermediate grade public servants, senior schoolteachers
    3. Junior schoolteachers, drivers and artisans
    4. Petty traders, messengers, labourers and similar grades
    5. Unemployed, full-time housewives, students and subsistence farmers
18. Mother's Education:
    1. University graduate or equivalent
    2. School certificate holders who also have teaching or other professional training
    3. School certificate or grade II teachers certificate holders or equivalent
    4. JSS 3 and primary six certificate holders
    5. No formal education
19. Mother's Occupation:
    1. Senior public servants, professionals, managers, large-scale traders, contractors
    2. Intermediate grade public servants, senior schoolteachers
    3. Junior schoolteachers, drivers and artisans
    4. Petty traders, messengers, labourers and similar grades
    5. Unemployed, full-time housewives, students and subsistence farmers

History:

20. Symptoms check:

Fever 0. Yes 1. No
Convulsions 0. Yes 1. No
If yes, how many times? ..... How long did each episode last for on the average? .....
Yellowness of eyes in the past 0. Yes 1. No
Vomiting 0. Yes 1. No
Loss of consciousness 0. Yes 1. No
Difficulty in breathing 0. Yes 1. No
coloured urine, past or present 0. Yes 1. No
If yes, 0. Bloody urine 1. Brown coloured urine

21. Examination findings:

Weight: ..... Height: ..... Dehydration: 0. Yes 1. No Pallor: 0. Yes 1. No
Pulse: ..... BP: ..... SpO_2 ..... GCS ..... Pedal oedema 0. Yes 1. No Periorbital oedema 0. Yes 1. No
Urine output ..... ml/kg /hr

22. Investigations:

FBC & Diff .....
RBS ..... RVS ..... ESR .....
Urinalysis:
Appearance: 1. Normal 2. Abnormal
SG: pH: Blood: Protein Glucose: Nitrite:
Serum E, U & Creatinine:
Serum bilirubin:
G6PD Status:
Haemoglobin genotype: