Journal of Advances in Medicine and Medical Research

32(8): 26-35, 2020; Article no.JAMMR.57582
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Incidence of Septicemia in Children Attending University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

Amudatu Ambali Adedokun[1*], Evelyn Orevaeghene Onosakponome[2] and Clement Ugochukwu Nyenke[2]

[1]Department of Biology, Ignatius Ajuru University of Education, Port Harcourt, Nigeria.
[2]Department of Medical Laboratory Science, Pamo University of Medical Sciences, Port Harcourt, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Authors AAA conceived the study. Author EOO designed the study protocol. Authors AAA collected the data, author CUN analyzed and author EOO interpreted the data. Authors AAA wrote the manuscript and CUN revised the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2020/v32i830463
Editor(s):
(1) Dr. Thomas I. Nathaniel, University of South Carolina, USA.
Reviewers:
(1) Meena Dias, Fr Muller Medical College Mangalore, India.
(2) Manisha N. Shah, Veer Narmad South Gujarat University, India.
Complete Peer review History: http://www.sdiarticle4.com/review-history/57582

Original Research Article

Received 25 March 2020
Accepted 01 June 2020
Published 09 June 2020

ABSTRACT

Introduction: Septicemia is an invasive infection where chemical substances released into the bloodstream causes morbidity and mortality in neonates. The developing countries carries major burden of the problem and Nigeria is not exceptional.
Objective: The study was carried out to determine age/sex-related prevalence, causative agents and antimicrobial sensitivity pattern of neonatal septicemia in children at University of Port Harcourt Teaching Hospital, Nigeria.
Methods: This retrospective study was carried out in the pediatric department for a period of twelve months. Blood culture test using thioglycollate broth and tryptone soya broth for isolation of microorganisms was adopted. Antimicrobial sensitivity pattern was done with disc diffusion method. The data was analyzed using descriptive statistics and Chi square for significance.
Results: A total of 598 children were examined, of which 394(67.9%) children showed negative blood cultures, while 204(34.1%) children had positive bacterial cultures and 2 children (0.3%)

**Corresponding author: E-mail: amudatu.adedokun@iaue.edu.ng, amudatuadedokun@gmail.com;*

were positive for *Candida albicans.* Overall, *Klebsiella* spp. was the most common pathogen, accounting for (37.8%) of the total isolates, which is followed by *Staphylococcus aureus* (28.4%), *Escherichia coli* (11.8%), unclassified Coliforms (8.3%), *Pseudomonas* spp. (4.9%), *Proteus* spp. (3.4%), *Enterococcus* spp. (2.9%) and coagulase-negative *Staphylococcus* (CONS) (2.5%) respectively. Early onset neonatal sepsis (EONNS) had *Klebsiella* spp as the most prevalent causative agent while *Staphylococcus aureus* was prevalent among the late onset neonatal sepsis (LONNS). *Klebsiella* spp. was susceptible to spafloxacin (87.0%) followed by ofloxacin (82.0%), amoxycillin-clavulanic acid (79.0%) and ceftazidime (65.0%) among the Gram negative organisms. In the category of Gram positive organisms, *Staphylococcus aureus* was highly sensitive to ofloxacin (81.0%) followed by spafloxacin (79.0%) and amoxicillin-clavulanic acid (71.0%).
Conclusion: The study showed *Klebsiella* spp. and *Staphylococcus aureus* were the prevalent bacterial organisms of septicemia in children in University of Port Harcourt Teaching Hospital. Early diagnosis with use of appropriate antimicrobial treatment will effect intervention for management of the children.

Keywords: Neonatal septicemia; antimicrobial agents; bacterial isolates; blood culture.

1. INTRODUCTION

Septicemia is a global challenge causing high morbidity and mortality among newborns [1–4]. Septicemia is the presence of viable bacteria in the circulating blood. Moreover, several risk factors have been identified both in the neonates and in the mothers who make them susceptible to infections. Neonatal septicemia has been quoted as the most common infections in this age group. The gold standard for diagnosis of septicemia is the isolation of the bacterial agent from a blood culture [5]. Unfortunately, the sensitivity of this method is low. Thus, the diagnosis of septicemia cannot be excluded even when the results are negative [6,7].

Organisms isolated from the blood stream of babies with septicemia vary from area to area. Neonates are particularly vulnerable to infections because of weak immune barrier. Some scientists explained that neonatal septicemia may be categorized as early or late onset. Onset is most rapid in premature neonates. Early-onset sepsis syndrome is associated with acquisition of microorganisms from the mother. Transplacental infection or an ascending infection from the cervix may be caused by organisms that colonize the mother's genitourinary tract, with acquisition of the microbe by passage through a colonized birth canal at delivery. The spectrum of organisms that causes neonatal septicemia varies in different countries, and sometimes changes from one center to another within the same country [8]. Group B streptococci (GBS) and *Escherichia coli* predominate in the USA and Europe, whereas Staphylococci and Gram-negative bacilli are much more common in developing countries [9].

The infant's skin, respiratory tract, conjunctivae, gastrointestinal tract and umbilicus may become colonized from the environment, leading to the possibility of late-onset sepsis from invasive microorganisms. Vectors for such colonization may include vascular or urinary catheters, other indwelling lines, or contact from caregivers with bacterial colonization [10].

Septicemia may also occur in children with focal infections or in children who have sepsis (i.e., clinical evidence other than fever of a systemic response to infection). Children with septicemia have an increased heart rate or respiratory rate and may have a change in temperature. Children with sepsis syndrome or severe sepsis have hypotension, hypoperfusion, or organ dysfunction. Septic shock occurs in children who do not respond to adequate volume resuscitation or require vasopressors or inotropes. Bacteria may be present in the bloodstream of children with focal infections, sepsis, severe sepsis, or septic shock [11].

It is noteworthy that the growing incidence of drug resistant bacteria isolates have also made treatment more difficult and costlier [12].

The pattern of distribution of neonatal septicemia should be regularly updated in order to provide sufficient information required for regular review for treatment purposes [13].

This study is aimed to determine clinical presentation, bacteriological profile of common aetiologic agents at University of Port Harcourt Teaching Hospital.

2. MATERIALS AND METHODS

2.1 Study Area

This study was conducted in University of Port Harcourt Teaching Hospital, East West Road, Port Harcourt, Rivers State of the South-South region of Nigeria. Coordinates of study area has latitude 4°53´58" N and longitude 6°55´43" E.

2.2 Study Design

This study was a retrospective evaluation of admitted children into the pediatric department (comprising of Special Care Baby Unit (SCBU), Children Emergency Ward (CHEW) and Children Medical Ward I and II (CHMW I & II), diagnosed of suspected septicemia. Children had blood cultures test carried out in the Department of Microbiology and Parasitology of the University of Port Harcourt Teaching Hospital, Nigeria between the period of January 2007 and December 2007.

2.3 Study Population

A total of 598 children of age ranged 0-18 years with septicemia were used for this study. Of the 598 children, 436(73.0%) were enrolled from SCBU while 121(20.2%) were from the CHEW and CHMW I & II had 41(6.8%) of the pediatric department. Bacteriological analysis was done following standard operating protocols in the microbiology laboratory of the hospital to determine bacterial profile involved in these conditions.

2.4 Inclusion Criteria

The study included children with clinical features and risk factors such as jaundice, electrolyte imbalance, meningitis, respiratory distress syndrome, fever, convulsions, abdominal distension, bronchopneumonia, macrosomia, omphalocoele, upper GIT obstruction, encephalocoele, hypoglycaemia, septic shock, imperforate anus, prematurity (<37 weeks of gestation age) and prolonged labor (sum of 1st and 2nd stage of labor >24 hrs.).

2.5 Exclusion Criteria

Children whose mothers did not give consent.

2.6 Sample Collection and Processing

Samples was randomly collected from the children weekly (see supplementary data). Two (2) mL of blood samples were collected from subjects with suspected septicemia and dispensed into two universal bottles containing 5 mL (in a ratio of 1:5 each) of Thioglycollate and Tryptone soy broth (This was done with great care to avoid contamination of the specimen and culture medium). The blood specimens were incubated overnight. After incubation the samples from the Thioglycollate and Tryptone soy broths were subcultured onto Chocolate and MacConkey agar. The Chocolate agar was incubated at 37°C after being placed in a canister with candle to provide 5 -10% CO_2 while the MacConkey agar was incubated aerobically. When there was no growth after the first subculture, cultures were reincubated further up to 7 days for final report, because of possible slow growth of the organisms. Following cultivation, organisms were identified using standard techniques as described by Cheesbrough [14]. Antibiotic sensitivity patterns of bacterial isolates were determined by agar diffusion method using Kirby-Bauer [15]. Control organisms such as *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 25923), *Pseudomonas aeruginosa* (ATCC 27853), *Enterococcus faecalis* (ATTC 2921) and *Streptococcus pneumoniae* (ATTC 49619) were included for interpretative standards criteria prescribed by the Clinical and Laboratory Standards Institute (CLSI) [16].

2.7 Data Analysis

Data generated were analyzed statistically using descriptive statistics and Chi square (X^2) using EPI info version 6.04 and then exported SPSS version 11.0 with 95% confidence interval and p-values of <0.05 were considered statistically significant.

3. RESULTS

Out of the 598 children examined from different units of children clinic (Fig. 1), 204 had microbial growth while comprises of males 106(52.0%) while the females had 98(48.0%). The distribution among sex-related is statistically not significant; (p >0.05). Clinical manifestations of the children were respiratory distress syndrome, meningitis, jaundice, fever, electrolyte imbalance, abdominal distension, bronchopneumonia, macrosomia, omphalocoele, upper gastro-intestinal obstruction, encephalocoele, hypoglycaemia, septic shock and imperforate anus. Respiratory distress syndrome (36.5%) were more prevalent followed by jaundice (20.2%) among the children.

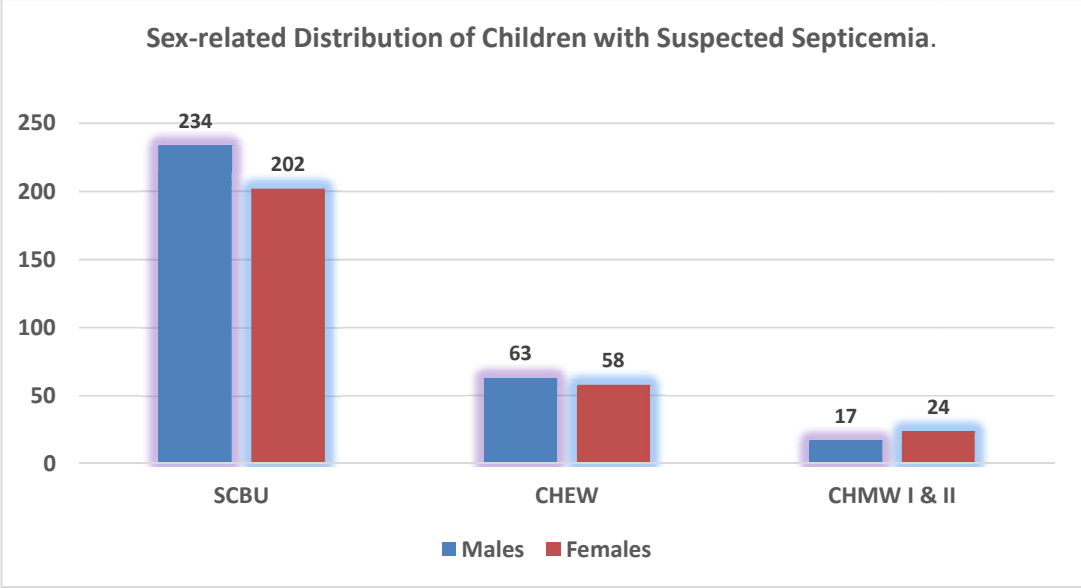

Fig. 1. Sex-related distribution of children with suspected septicemia

Children less than 1-month old had the largest number of positive bacterial growth 177(86.76%), this was followed by children between 1-12 months 11(5.40%), while others with less positive bacterial growth were 16(7.84%) of which were reduced with increased age (Table 1).

Table 1. Age and sex distributions of children with suspected septicemia

Age group (month)	Number (%) with positive bacterial cultures	Number of children examined		
		Male (%)	Female (%)	Total (%)
≤ 1	177(40.6)	234(74.3)	202(71.4)	**436(73.0)**
1-2	11(13.1)	38(12.1)	46(16.3)	**84(14.1)**
>12-24	6(33.3)	9(2.9)	10(3.5)	**19(3.0)**
>24-60	5(29.4)	9(2.9)	9(3.2)	**18(3.0)**
>60-120	5(22.0)	13(4.0)	10(3.5)	**23(3.9)**
>120-196	0(0.00)	12(3.8)	6(2.1)	**18(3.0)**
Total (%)	**204(34.2)**	**315(100)**	**283(100)**	**598(100)**

Age group distribution - (p >0.05), Sex distribution - (p >0.05)

Table 2. Prevalence of positive bacterial cultures in age groups

Bacterial isolates	Prevalence of children with positive bacterial cultures in age groups (N=204)					
	≤1 month	1 mo – 1 yr	2 yr – 5 yr	6 yr – 10 yr	10 yr -18 yr	Prevalence (%)
Klebsiella spp	71	3	2	1	0	**77(37.8)**
Staph. Aureus	45	7	5	1	0	**58(28.4)**
Escherichia coli	19	2	1	2	0	**24(11.8)**
Unclassified Coliforms	12	2	1	2	0	**17(8.3)**
Pseudomonas spp	8	1	0	1	0	**10(4.9)**
Proteus spp	4	1	2	0	0	**7(3.4)**
Enterococus spp.	5	1	0	0	0	**6(2.9)**
*CONS	4	1	0	0	0	**5(2.5)**
Total No (%)	**168(82.3)**	**18(9.0)**	**11(5.3)**	**7(3.4)**	**0**	**204(100)**

**coagulase negative staphylococcus*

Overall, *Klebsiella* spp. Was the most prevalent bacterial isolates, accounting for 77(37.8%) of the total isolates followed by *Staphylococcus aureus* 58(28.4%) and the least prevalent was coagulase-negative *Staphylococcus* 5(2.5%). The rate of possible bacterial isolates reduces with increasing age but the causative agents did not vary with age (Table 2).

Between 0-3 days of life, in EONNS the predominant pathogen was *Klebsiella* spp. In 60(61.0%) children, followed by *Staphylococcus aureus* in 39(39.0%) children in a total of 99 children (Fig. 2).

Between 4-28 days of LONNS, a total of 20 children had *Staphylococcus aureus* as the major offender with 8(40.0%). This was followed by *Klebsiella* spp. 4(20.0%), *Pseudomonas* spp. 1(5.0%), *Enterococcus* spp. 2(10.0%), unclassified coliforms 2(10.0%), *Escherichia coli* 1(5.0%), coagulase-negative *Staphylococcus* (CONS) 1(5.0%) and *Candida albicans* accounted for 1(5.0%) (Fig. 3).

Our study showed a very high degree of resistance for both Gram negative and Gram positive organisms to first line antibiotics such as tetracycline, cotrimoxazole, gentamicin, chloramphenicol and cloxacillin. For the Gram negative organisms, the antimicrobial sensitivity pattern showed that *Klebsiella* spp. Was susceptible to spafloxacin (87.0%) followed by ofloxacin (82.0%), moxicillin-clavulanic acid (79.0%) and ceftazidime (65.0%) amongst all the Gram negative organisms (Table 3).

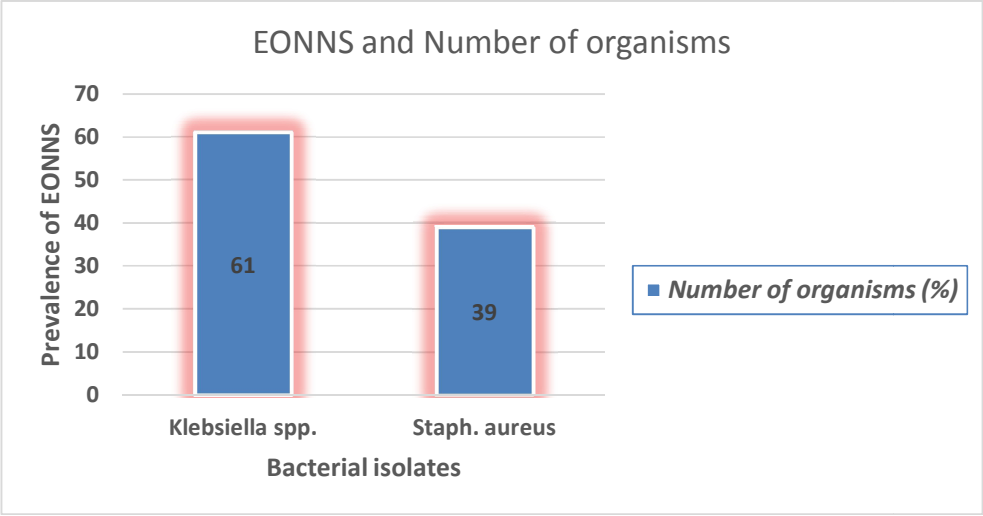

Fig. 2. Prevalence of bacterial isolates in EONNS

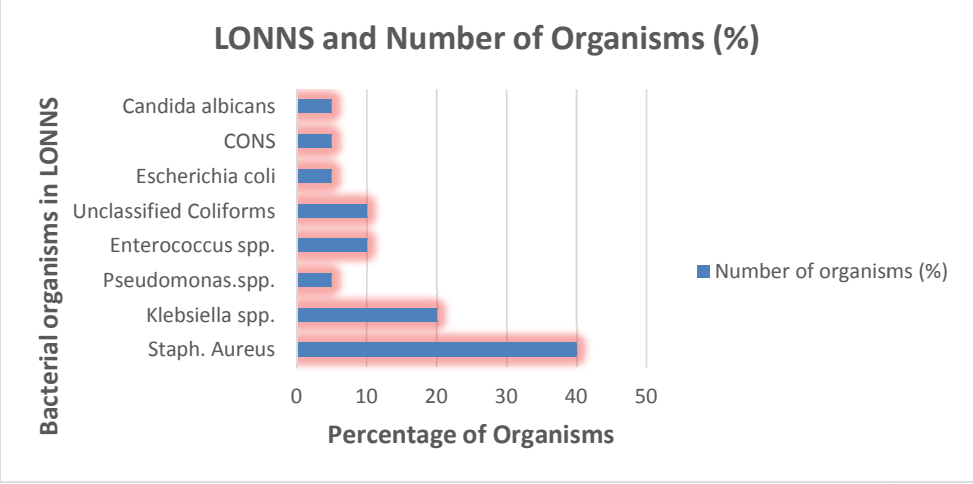

Fig. 3. Prevalence of bacterial isolates in LONNS

Table 3. Antimicrobial sensitivity pattern of gram negative organisms

Bacterial isolates	Tet	Cot	Gen	Chl	Aug	Ery	Spa	Caz	Ofl	Cxc
Klebsiella spp.	54.0	26.0	0.0	31.0	79.0	0.0	87.0	65.0	82.0	19.0
Staph. aureus	40.0	16.0	48.0	34.0	71.0	29.0	79.0	53.0	81.0	31.0
Eschericia coli	38.0	29.0	21.0	21.0	21.0	4.0	75.0	42.0	58.0	33.0
Unclassified Coliforms	29.0	29.0	35.0	12.0	35.0	0.0	47.0	0.0	35.0	18.0
Pseudomonas spp.	30.0	0.00	30.0	10.0	50.0	10.0	50.0	0.0	40.0	0.0
Proteus spp	29.0	0.0	14.0	0.0	43.0	0.0	57.0	14.0	43.0	0.0
Enterococcus spp.	0.0	0.0	0.0	0.0	0.0	0.0	67.0	17.0	17.0	0.0
CONS	0.0	0.0	0.0	20.0	0.0	0.0	40.0	20.0	20.0	0.0

Legends: Tet: Tetracycline; Cot: Cotrimoxazole; Gen: Gentamicin; Chl: Chloramphenicol; Aug: Augumentin; Ery: Erythromycin; Spa: Sparfloxacin; Caz: Ceftazidime; Ofl: ofloxacin; Cxc: Cloxacillin; CONS: Coagulase negative staphylococcus

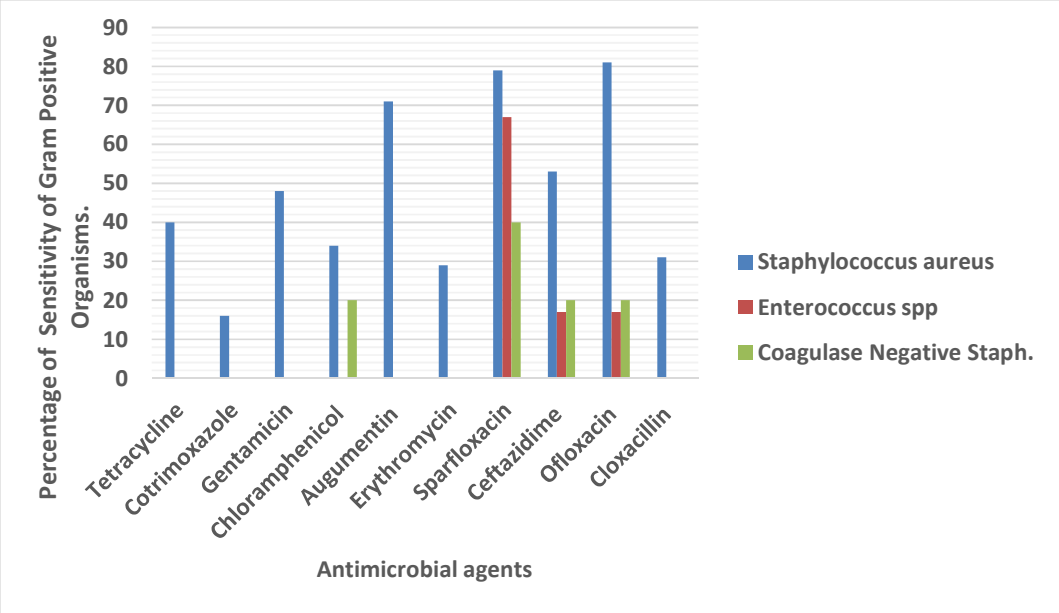

Fig. 4. Antimicrobial sensitivity of gram positive bacterial isolates

Among the Gram positive organisms, *Staphylococcus aureus* is highly sensitive to ofloxacin (81.0%) followed by spafloxacin (79.0%) and amoxicillin-clavulanic acid (71.0%) (Fig. 4).

4. DISCUSSION

Morbidity and mortality of neonatal septicemia can be prevented through early diagnosis and therapy in the pediatric unit. Antibiotic resistance has become a global threat. Reports of multidrug-resistant bacteria causing neonatal sepsis in developing countries are increasing, particularly in neonatal intensive care unit.

Bacteriological agents of blood stream infection were isolated in 204 children out of the 598 subjects indicating an incidence of 34.1%. Other studies locally had 29.7% at Enugu by Ekwochi et al. [17], 47.2% in Abeokuta by Arowosegbe et al. [18] and 21.8% in Bayelsa by Peterside et al. [19]. Elsewhere, on the incidence by Aletayeb et al. [20] in Iran had 4.1%, 14.5% in Bangladesh by Mitra et al. [21] and a study in Indonesia found 46.6% prevalence [22]. The difference in incidence of this study compared to other studies is due to the number of children with provisional diagnosis with septicemia and majority of them were neonates. This could be due to low immune response, poor hygiene practices, bottle feeding and socio-economic status of the parent. An additional effect of low socio-economic status is the inability of the indigent mother to maintain successful lactation as it is necessary for the mother to be mentally and physically healthy.

The inability of parents to pay the hospital fees charged for delivery makes them deliver at home, churches, maternity centre/herbalist shrines where there are no proper midwifery facilities. The lower prevalence of documented neonatal septicemia with positive blood culture in other studies had different reasons such as antibiotic administration in mother or neonate, difficulty in sampling, blood culture technique [23] or are likely to occur due to the improved newborn care practices by experienced mothers, particularly early initiation of breastfeeding [24] or sepsis due to anaerobic and viral or fungal pathogens [25].

Respiratory distress syndrome was the major clinical features amongst other features with 36.0% in this study which is similar to recent studies by Sathyamurthi et al. [24] 56%, 34.15% for Khante et al. [26] and 31.2% for Kurma et al. [27] respectively.

The males were more susceptible 52% while the females had 48% in all age groups. This variation had no statistical significance(p >0.05).This report is similar studies carried out in Bayelsa [19] had males 63.9% and females 36.1%, India had males 70% and females 30% and Male 64.5% and Female 35.5% [27,28]. In this study, *Klebsiella* spp. (37.8%) and *Staphylococcus aureus* (28.4%) were the prevalent causes of neonatal septicemia among the Gram negative and Gram positive organisms. These findings are especially disturbing considering a recent report of increasing incidence of Gram-negative rod septicemia in a neonatal intensive care unit [29]. This finding is in accordance with other studies findings from developing countries [30,31,32,33].

This is because *Klebsiella* spp. are ubiquitous in nature. In humans, they may colonize the skin, pharynx, or gastrointestinal tract. They may also colonize sterile wounds and urine. Carriage rates vary with different studies. *Klebsiella* spp may be regarded as normal flora in many parts of the colon and intestinal tract and in the biliary tract. Oropharyngeal carriage has been associated with endotracheal intubation, impaired host defenses, and antimicrobial use [34]. This was followed by *Escherichia coli*, Coliforms, *Pseudomonas* spp. and *Proteus* spp. respectively. The spectrum of organisms causing neonatal septicemia in this study is similar to that reported for other neonatal units in developing countries, with Gram negative organisms being responsible foremost cases, particularly early onset. *Klebsiella* spp. was found to be the predominant organisms in the early onset of neonatal septicemia (EONNS). The bacterial isolated among the EONNS were statistically significant (p <0.05). In contrast, reports by Anderson-Berry et al. [9] found coagulase-negative *Staphylococcus* (CONS) as the predominant organism in EONNS. *Staphylococcus aureus* (28.4%) was the most common isolate among the Gram positive bacteria. This was followed by *Enterococcus* spp. and coagulase-negative *Staphylococcus* (CONS). This observation is similar to those reported in studies carried out by Stoll and Shane [35], Flora et al. [36] and Tsehaynesh et al. [37]. This is because *Staphylococcus aureus* can survive in the environment for a relatively long time and is widely distributed in the hospital environment therefore has the potential for being transmitted from the environment to the patients through practices that breach infection control measures. *Staphylococcus aureus* colonizes the skin, nasopharynx, and gastrointestinal tract and spreads via the hands of health care workers [38]. Some other studies by Ghotaslou et al. [39] in Iran and Husada et al. [40] in Indonesia reported CONS to be the predominant Gram positive cocci among the Gram positive organisms.

In the late onset of neonatal septicemia (LONNS), *Staphylococcus aureus* was the most common organisms among all the organisms found. The bacterial isolated among the LONNS were not statistically significant (p >0.05). This is similar to the study in other developing countries [32,33]. The association between late onset disease and neonatal septicemia could partly be related to passive acquisition of pathogenic *Staphylococcus aureus* from adult carriers like health workers and relatives at home.

Two (2) patients were reported to have *Candida albicans* (0.3%) in this study. *Candida* spp. was also reported in studies carried out in China [41]. Premature infants with low birth weights have underdeveloped immune response and are hence predisposed to neonatal sepsis by *Candida*. This is because *Candida* colonization of the gut starts soon after birth and the administration of antibiotics and other predisposing factors such as prematurity may cause the spill-over of the organism into the blood and cause neonatal septicemia.

The result of this study showed a very high degree of resistance among the Gram negative

organisms to first line antibiotics. About 85.0% of *Staphylococcus aureus* were resistant to clotrimoxazole. There was also high degree of resistance to cephalosporins by both Gram positive and Gram negative organisms. Only 65.0% of *Klebsiella* spp. was sensitive to ceftazidime. There was low degree of resistance to quinolones, particularly spafloxacin a third generation quinolone. This is a relatively new class of antibiotics, the use of which has recently become very common; particularly in general practice. Similar results have been reported on the effectiveness of quinolones [22,23]. The resistant profile of some of the isolates suggests the presence of Extended Spectrum Beta-Lactamase (ESBL) producing organisms and a pointer to risk of nosocomial infection.

5. CONCLUSIONS

The study showed *Klebsiella* spp. and *Staphylococcus aureus* are the leading causes of septicemia in children (0-18 years) in University of Port Harcourt Teaching Hospital. Early diagnosis with use of appropriate antimicrobial treatment will effect intervention for management of the children. More so, Preventive measures need to be implemented such as hand washing.

In addition to the findings of this study that proffer solution at that time, room for more researches was created. Between the year of study to the present, the gap has been closed based on the question raised by the study by other researches. Ogundare et al. [42] in Ekiti State and Ekwochi et al. [17] in Enugu State, Nigeria in their study, apart from using other antibiotics replacing ceftriaxone, at lot of other antibiotics have been tried and are now been used in addition to the ones we discovered in our study for treatment of septicemia in children.

CONSENT AND ETHICAL APPROVAL

Ethical clearance was obtained from the Research and Ethics Committee of the University of Port Harcourt Teaching Hospital. Informed consent was obtained from parents and guardian of inand out-patients subjects used for this study at the University of Port Harcourt Teaching Hospital, Nigeria prior sample collection.

ACKNOWLEDGEMENTS

The investigators thank the medical laboratory staff of the study centre and most importantly the families of young infants who participated in the study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ullah O, Khan A, Ambreen A, Ahmad I, Akhtar T, Gandapor AJ, et al. Antibiotic sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan Arch Iran Med. 2016;19(12):866-9.
2. G/eyesus T, Moges F, Eshetie S, Yeshitela B, Abate E. Bacterial etiologic agents causing neonatal sepsis and associated risk factors in Gondar, Northwest Ethiopia. BMC Pediatr. 2017;17:37. Available:https://doi.org/10.1186/ s12887-017-0892-y
3. Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2016;28(2):135-40.
4. World Health Organization. Countdown to 2015, Maternal, newborn & child survival-fulfilling the health agenda for women and children: the 2014 report. Geneva, WHO Press; 2014.
5. Ahmed AS, Chowdhury MA, Hoque M, Darmstadt GL. Clinical and bacteriological profile of neonatal septicemia in a tertiary level pediatric hospital in Bangladesh. Indian Pediatr. 2002;39(11):1034-9.
6. Khaertynov KS, Boichuk SV, Khaiboullina SF, Anokhin VA, Andreeva AA, Lombardi VC, et al. Comparative assessment of cytokine pattern in early and late onset of neonatal sepsis. J Immunol Res. 2017;ID 8601063. Available:https://doi.org/10.1155/2017/8601063
7. Shah B, Padbury JF. Neonatal sepsis. An old problem with new insights. Virulence. 2014;5(1):17-8.
8. Désinor OY, Silva JL, Ménos MJ. Neonatal sepsis and meningitis in Haiti. J Trop Pediatr. 2004;50:48-50.
9. Palazzi D, Klein J, Baker C. Bacterial sepsis and meningitis. In: Remmington JS, Klein JO, Wilson CB, Baker CJ, editors. Infectious Diseases of the Fetus and Newborn Infant. 6th ed. Philadelphia: Elsevier Saunders. 2006;247-95.
10. Anderson-Berry AL, Bellig LL, Ohning BL, MacGilvray SS, Windle ML, Clark DA, et al. Neonatal sepsis. Am Acad Pediatr. 2006;1-11.
11. Holland BJ, Demer D, Brook I, Windle ML, Schleiss MR, Tolan RW, Jr, et al. Bacteremia. Pediatr Infect Dis. 2005;1-11.

12. Roy I, Jain A, Kumar M, Agarwal SK. Bacteriology of neonatal septicemia in a tertiary care hospital of northern India. Indian J Med Microbiol. 2002;20:156-9.
13. Shittu OB, Akpan I, Popoola TO, et al. Epidemiological features of a GIS-supported investigation of cholera outbreak in Nigeria. J Pub Health Epi. 2010;2(5):152-62.
14. Cheesbrough M. Microbiological tests. In: District Laboratory Practice in Tropical Countries. Cambridge Low-Price Editions, University Press. Cambridge. 2006;2:1-7.
15. Hudzicki J. Kirby-Bauer disk diffusion susceptibility protocol. American Society for Microbiology; 2018.
16. Clinical and Laboratory Standard Institute, author. 11th edition document M02-A11. Wayne: Clinical and laboratory standards institute. Performance standards for antimicrobial disk susceptibility tests. Approved standard. 2012;12-27.
17. Ekwochi U, Ifediora C, Osuorah CD. 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. J Clin Neonatol. 2018;7(2):80-8.
18. Arowosegbe AO, Ojo DA, Dedeke IO, Shittu OB, Akingbade OA. Neonatal sepsis in a Nigerian tertiary hospital: clinical features, clinical outcome, etiology and antibiotic susceptibility pattern. South Africa J Infect Dis. 2017;32(4):127-31.
19. Peterside O, Pondei K, Akinbami FO. Bacteriological profile and antibiotic susceptibility pattern of neonatal sepsis at a teaching hospital in Bayelsa State. Nigerian Trop Med Health. 2015;43(3):183-90.
20. Aletayeb SM, Khosravi AD, Dehdashtian M, Kompani F, Mortazavi SM, Aramesh MR. Identification of bacterial agents and antimicrobial susceptibility of neonatal sepsis: A 54-month study in a tertiary hospital. Afr J Microbiol Res. 2011;5(5): 528-31.
21. Mitra DK, Mullany LC, Harrison M, Mannan I, Shah R, Begum N, et al. Incidence and risk factors of neonatal infections in a rural Bangladeshi population: A community-based prospective study. J Health Popul Nutr. 2018;37(1):6.
22. Hasibuan B (ed). Comparison of microbial pattern in early and late onset neonatal sepsis in referral center Haji Adam Malik Hospital Medan Indonesia. IOP Conference Series: Earth and environmental science. IOP Publishing; 2018.
23. Bansal S, Jain A, Agarwal J, Malik GK. Significance of coagulase negative staphylococci in neonates with late onset septicemia. Indian J Pathol Microbiol. 2004;47(4):586-8.
24. Liben ML, Yesuf EM. Determinants of early initiation of breastfeeding in Amibara district, Northeastern Ethiopia: A community based cross-sectional study. Int Breastfeeding J. 2016;11:7.
25. Sathyamurthi B, Leela KV, Narayanababu R, Padmanaban S, Sreedevi S, Sujatha, Anandan H. Clinical and bacteriological profile of neonatal sepsis in a tertiary care hospital. Int J Sci Study. 2016;4(8): 57-60.
26. Khante SV, Raut SS. Clinical and bacteriological study of neonatal septicemia in a tertiary care hospital. Int J Res Med Sci. 2017;5(10):4455-62.
27. Kurma VR, Raju MS, Manchu T, Manchu K. Neonatal sepsis: Clinical spectrum, bacteriological profile and antibiotic sensitivity patterns in neonatal intensive care unit in a tertiary care Hospital. Int J Contemp Med Res. 2019;6(6):F1-F48.
28. Galhotra S, Gupta V, Bains HS, Chhina D. Clinico-bacteriological profile of neonatal septicemia in a tertiary care hospital. J Mahatma Gandhi Inst Med Sci. 2015;20(2): 148-52.
29. Rashmi P, Praveen BK. Clinico-bacteriological profile of neonatal sepsis. Int J Contemp Pediatr. 2019;6(2): 796-802.
30. Shrestha S, Shrestha NC, Dongol Singh S. Bacterial isolates and its antibiotic susceptibility pattern in NICU. Kathmandu Univ Med J. 2013;41(1):66-70.
31. Appiah-Korang L, Noah ON, Stephanie B, et al. Neonatal bloodstream infections in a Ghanaian Tertiary Hospital: Are the current antibiotic recommendations adequate? BMC Infect Dis. 2016;16(1):598.
32. Srinivasa S, Arunkumar D. Bacterial isolates and their Antibiotic susceptibility patterns in Neonatal sepsis. Curr Pediatr Res. 2014;18(2):83-86.
33. Basavaraj M, MrRashmiranjan R, Gagan P. Neonatal septicemia: Bacterial isolates & their antibiotics susceptibility patterns: A hospital based study. J Med Sci Clin Res. 2017;5(6).

34. Umeh O, Berkowitz LB. Klebsiella infections. Centre of AIDS Research and Education. 2009;1-11.
35. Stoll BJ, Shane AL. Infections of the neonatal infant. In: Kliegman Robert M, Stanton Bonita F., editors. Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier. 2015;909-14.
36. Flora C, Mariam MM, Martha FM, et al. Utility of qualitative C- reactive protein assay and white blood cells counts in the diagnosis of neonatal septicaemia at Bugando Medical Centre, Tanzania. BMC Pediatr. 2015; 14(248).
37. Tsehaynesh G/E, Feleke M, Setegn E. Bacterial etiologic agents causing neonatal sepsis and associated risk factors in Gondar, Northwest Ethiopia. BMC Pediatr. 2017;17(1):137.
38. Ghotaslou R, Ghorashi Z, Nahaei MR. Klebsiella pneumoniae in neonatal sepsis: A 3-year study in the pediatric hospital of Tabriz, Iran. Jpn J Infect Dis. 2007;60(2-3): 126-8.
39. Husada D, Chanthavanich P, Chotigeat U, Sunttarattiwong P, Sirivichayakul C, Pengsaa K, et al. Predictive model for bacterial late-onset neonatal sepsis in a tertiary care hospital in Thailand. BMC Infect Dis. 2020;151.
40. Sundaram V, Kumar P, Dutta S, Mukhopadhyay K, Ray P, Vikas Gautam V, et al. Blood culture confirmed bacterial sepsis in neonates in a north Indian tertiary care center: Changes over the last decade. Jpn J Infect Dis. 2009;62(1):46-50.
41. Zhang XB, Yu SJ, Yu JX, et al. Retrospective analysis of epidemiology and prognostic factors for candidemia at a hospital in China, 2000–2009. Jpn J Infect Dis. 2012;65:510-5.
42. Ogundare E, Akintayo A, Aladekomo T, Adeyemi L, Ogunlesi T, Oyelami O. Presentation and outcomes of early and late onset neonatal sepsis in a Nigerian Hospital. Afri Health Sci. 2019;19(3):2390-9.
Available:https://dx.doi.org/10.4314/ahs.v19i3.12

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/57582