Childhood Septicemia; Retrospective Analysis of Bacterial Pathogens and Antimicrobial Susceptibility Pattern in Maiduguri, Nigeria

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Abstract: Childhood septicemia remains the leading cause of morbidity and mortality among children aged less than 5 years in sub-Saharan African countries. Appropriate choice of antimicrobial agents for treatment and management will depends on adequate knowledge of the bacterial agents and their antimicrobial pattern recovered from positive blood culture in the hospital. The retrospective study determined the bacterial pathogens and their antimicrobial susceptibility pattern in suspected cases of childhood septicemia presented at the hospital over the study period. A total of 2134 patients aged less than 12 years admitted into the Pediatrics department with suspected cases of childhood septicemia were recruited into the study. 255(11.5%) yielded significant bacterial growth, high bacterial isolation rate was recorded within the age-group 12-60months (29.8%), followed by 1-3months (28.2%), and <1 month (27.5%) respectively. Gram-negative bacteria accounted for 66.7% pathogens isolated compared to gram-positive bacteria (33.3%). *Staphylococcus aureus*, *Klebsiella* spp, and *Salmonella spp* were isolated at the following frequency, 66.7%, 12.9%, and 7.5%.High sensitivies were observed with ofloxacin, ciprofloxacin, gentamicin, ceftazidime, cefuroxime and erythromycin and resistance with ampicillin-cloxacillin, co-trimoxazole and augmentine. In conclusion, this retrospective study identified the common bacterial pathogens associated with childhood septicemia, their antimicrobial susceptibility pattern and possible factors influencing negative blood cultures results.However,periodic studies should be encouraged for better understanding of the local epidemiology of the clinical conditions and the antibiotic therapy approach.
[Okon KO, Askira UM, Ghamba PE, Isyaka TM, Hamidu IM, Kankop JW, Aguoru CO. **Childhood Septicemia; Retrospective Analysis of Bacterial Pathogens and Antimicrobial Susceptibility Pattern in Maiduguri, Nigeria.** *N Y Sci J* 2014;7(6):9-13]. (ISSN: 1554-0200). http://www.sciencepub.net/newyork. 2

Keywords: Childhood septicemia, bacterial pathogens, antimicrobial susceptibility pattern, Maiduguri.

1. Introduction

Childhood septicemia remains the leading cause of morbidity and mortality among children less than 5 years of age in developing countries, particularly in sub-Saharan Africa (Berkowitz 1984, Sykes 1987, Lepage and Bogart 1987, Ayoola et al, 2003, Mulagu et al 2006, Meremikwu et al,2005). It is mostly community-acquired infections with poor prognosis as there might be no clear definitive signs and symptom in some cases(Alausa et al, 1977, Alausa 1977, Sykes 1987, Lepage and Bogarts 1987). Nevertheless, clinical diagnosis can be based on factors such as the age of the patient, suspected aetiological agents, and underlying clinical conditions, as these factors are reported to influenced the prevalence and outcomes of the episodes (Fowlie and Schmidt 1998, Molyneux 2004). In Malawi, Molynuex (2004) reported higher frequent episodes of bacteremia in HIV-infected children accompanied with high mortality than HIV-negative ones.

In most documented studies, gram-negative bacteria of the family Enterobactericeae accounts for majority of bacterial pathogens responsible for high mortality rate due to gram-negative septicemic shock (Karlowsky et al, 2004). In Europe and USA, *S. aureus* and *Escherichia.coli* were reported as the two most common pathogens that are clinically significant causes of bloodstream infections (Karlowsky et al 2004, Diekema et al 2000, Fluit et al 2000), in contrast to *S.aureus*, *Klebsiella spp* and *Salmonella spp* in sub-Saharan Africa(, Berkowitz 1984, Sykes, 1987, Molyneux, 2004).

Clinical diagnosis of childhood septicemia depends on the blood culture positivity, but in most cases only 50% of all positive blood culture represent true blood stream infection(Diekema et al, 2000). To achieve effective treatment and management of childhood septicemia through prescription/administration of appropriate antimicrobial agents, adequate knowledge of the

bacterial pathogens and their antimicrobial susceptibility pattern recovered from blood culture in the hospital is important. Based on this knowledge, we decided to undertake this retrospective study to determine the bacterial pathogens isolated and their antimicrobial susceptibility pattern from in suspected cases of childhood septicemia presented in our hospital.

2.Materials and Methods

The study was conducted in the department of Medical Microbiology, University of Maiduguri Teaching Hospital, Maiduguri between January 2008-December 2009. Bacteriological data of blood culture analysis from patients aged less than 12 years old presented at the hospital with suspected cases of childhood septicemia. Demographic variables extracted from the laboratory records and entered into the study database includes, age, sex, bacterial pathogens isolated and antimicrobial susceptibility pattern.

Five milliliter of venous blood was aseptically drawn and injected into two blood culture bottles (Robertson cooked meat medium). In the case of neonates, approximately 2-3ml was collected due to the inherent difficulty in their blood collection. The blood culture bottles were incubated at 37^0C for 24 hours. The bottles were checked regularly for signs of turbidity, an indication of bacterial growth, and sub cultured on blood, chocolate and MacConkey agar plates incubated aerobically and anaerobically at 37^0C for 24 hours. Suspected bacterial colonies were isolated and identified by standard bacteriological techniques(Barrow and Fetthan 1993).Blood culture bottles with no evidence of bacterial growth after 7 days of incubation and subculturing is regarded as negative.

Antimicrobial susceptibility testing was determined by disc diffusion method using Mueller-Hinton agar(Bauer et al, 1966).The following antimicrobial discs were tested against the bacterial isolates, ampicillin-cloxacillin(APX), Co-trimoxazole (SXT), augmentine(AU), erythromycin(E), gentamicin (CN), cefuroxime(CXM), Ceftazidime (CAZ), chloramiphenicol(CH), ciprofloxacin(CIP) and ofloxacin (OFX). The zone of inhibition diameter was measured using a calibrated ruler to classify the bacterial isolates into either sensitive, intermediate or resistant.

Data analysis; The demographic variables of positive blood culture and isolated bacterial pathogens were collated and analysed using SPSS version 16.0. The values were expressed in means and percentages. Comparison of demographic variables was determined by chi-square test. The level of significance of $p<0.05$ was employed.

3.Results

Of the 2134 patients seen and their blood culture specimens analyzed, 255(11.9%) yielded significant bacterial growth, while 1879(88.1%) showed no evidence of bacterial growth. The mean age of the patient was 2.87 ± 1.34 months, gender distribution of 137(53.7%) males and 118(46.3%) females giving male to female ratio of 1.2:1.Gram-negative bacteria accounted for 66.7% of the total bacterial pathogens isolated and 33.3% for gram-positive bacteria. The distribution of bacterial pathogens isolated as presented in figure 1, *S.aureus* accounted for 66.7%, followed by *Klebsiella spp* (12.9%), *Salmonella spp* (12.9%) and the least *Streptococcus spp* (0.4%). No anaerobic or polymicrobial bacterial isolates occurred in the study.

The distribution of bacterial isolates in accordance with the age-group of the patients(table1), the peak of bacterial isolation was observed within the gae-group 12-60months,(29.8%) followed by 3-12 months (28.2%) and <1 month(27.5%). Statistical significant difference was observed between the age-group and bacterial pathogens isolated(<0.001).

The antimicrobial susceptibility pattern presented in figure 2, the bacterial isolates exhibited high sensitivity to ofloxacin, ciprofloxacin, chloramphenicol, ceftazidime, cefuroxime and erythromycin, while pattern resistance pattern was observed with ampicillin-cloxacillin, co-trimoxazole and augmentine.

4.Discussion

In this study, gram-negative bacteria accounted for 66.7% of the bacterial isolated compared to 33.3% due to gram-positive. This pattern is consistent with the findings of other similar studies(Martin et al 2005, Iregbu et al 2006, Nwadioha et al, 2010), this is indication of the fact that gram-negative bacteria are major causative agents of both hospital and community-associated infections(Sykes 1987, Berkowitz 1984). In contrast, The Surveillance Network (TSN)Database-USA which comprised of 269 laboratories reported an overall isolation rate of bloodstream infection of 78.1% due to gram-positive bacteria and 21.9% gram-negative(Karlowsky et al, 2002). The bacterial isolation rate was 11.9%, which is relatively low, when compared to 18.2% reported in Lagos(Uzodimma et al, 2013), 30.8% in Kano (Nwadioha et al, 2010) and 44.9% in Calabar (Meremikwu et al,2005) of studies conducted in Nigeria and 24.7% in Bangladesh(Chattopadhyay et al, 2010). Several factors like geographical location, studied population, antibiotic medication before blood sampling, underlying clinical conditions, and methodology employed are known to influence the blood culture outcome and bacterial isolation rate

(Dellinger 2008, Chattopadhaya et al, 2010). In addition, we observed the male to female ratio of 1.25:1, which was comparable to 1.2:1 reported in similar study in Bangladesh (Chattopadhaya et al, 2010), an indication of gender factor in susceptibility to sepsis.

In this study, *S. aureus*, was the predominate pathogens followed by *Klebsiella spp*, similar pattern was reported in Bangladesh(Chattopadhaya et al, 2010), but differs to *S.aureus /E.coli* combination in studies conducted in Lagos(Uzodimma et al, 2013) and in Kano(Nwadioha et al, 2010). While the pattern was at variance with the pattern reported in Europe, Canada, Latin America, in which coagulase-negative staphylococci, *E. coli, Klebsiella pneumonia*e, and *Enterococcus faecium* accounted for >80% of blood culture isolates(Diekema et al, 2000, Fluit et al, 2000, Karlowsky et al 2004). The overall isolation rate among the neonates was 27.5%,in which 55.7% were due to *S.aureus* isolates and 21.4% *Klebsiella spp*, this rate was comparable to 24.4% in Bangladesh (Chattopadhaya et al, 2010,but differs in the pathogens rate, 37.1% due to *Klebsiella pneumonae* and (31.74%) methicillin-resistant *S.aureus.* The isolation rate reported was lower when compared to different levels reported in Nigeria, 30.8% in Ilorin (Mokuolu et al, 2001), 50.8% in Calabar(Meremikwu et al,2005), and 55% in ile-ife(Komolafe et al, 2008). These observed differences could be attributed to

several factors like underlying clinical conditions, virulence factors of the bacterial pathogens and the immune status of the patients(Akpede et al 1995, Ako-Nai et al 1999). Also, the cross infection due to the level of hygienic standard in the wards, and contamination during blood collection cannot be ruled out (Bingen et al 1995).

The high blood culture negative result recorded in 1874 blood culture bottles is a common phenomenon associated with blood culture method. Factors that might be responsible for such high negative result could be due to administration of antibiotic prior to blood culture samples or infection due to non-culturable agents. Due to lack of facilities in most laboratory isolation of other fastidious pathogens like Erysipelothrix spp, Leptospira spp and Listeria monocytogenes, that have been implicated in childhood septicemia might be limited(Grieco and Sheldon 1980, Hoeden 1989, Ako-Nai et al 1999). However, the timing and volume of blood specimen are crucial in childhood septicemia diagnosis. Therefore, some studies suggested that blood specimens are best collected when the body temperature is $>38^0$C, or white blood cells is $>15,000$mm^3/ml or <10000mm^3/ml and approximately 3-5ml /bottle (Bennette and Beeson 1954, Washingston and Ilstrup, 1986).
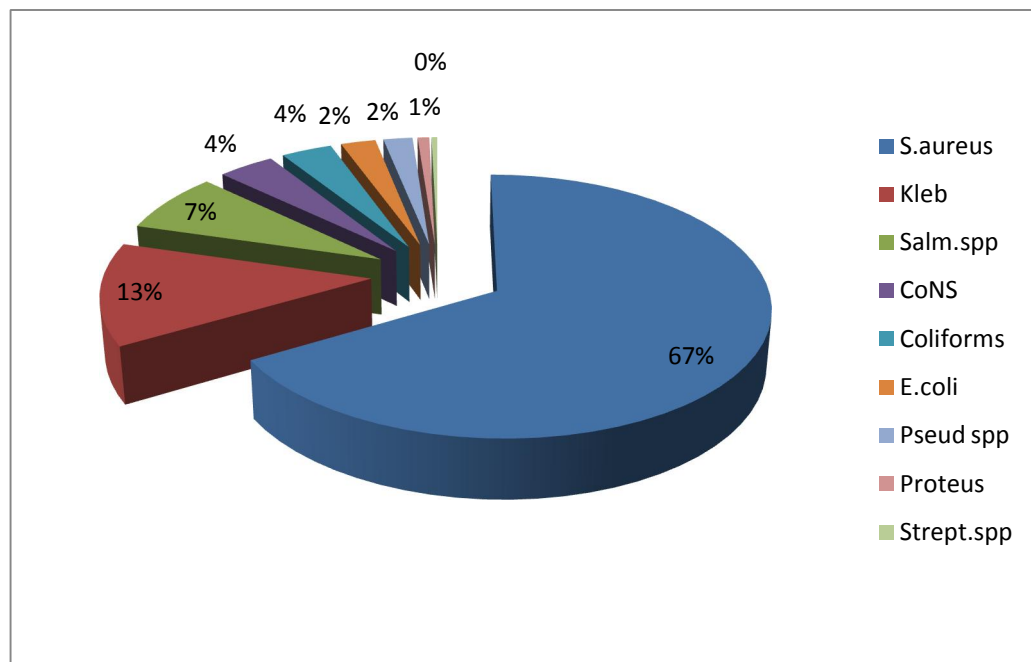

Figure 1; Frequency of occurrence of the bacterial pathogens isolated

Table 1; The distribution of bacterial isolates according to age-group

Bacteria	<1month	1-3months	3-12months	12-60months	60-144months
Gram-positive bacteria					
S.aureus	39	9	56	51	15
Coagulase-negative staphylococci	1	2	3	3	1
Streptococcus spp					1
Gram-negative bacteria					
Klebsiella spp	15	2	4	12	
Salmonella spp	1		4	8	6
E.coli	6				
Pseudomonas spp	2		2	1	
Proteus spp	1			1	
Coliforms	5	1	3		
Total	**70(27.5)**	**14(5.5)**	**72(28.2)**	**76(29.8)**	**23(9.0)**
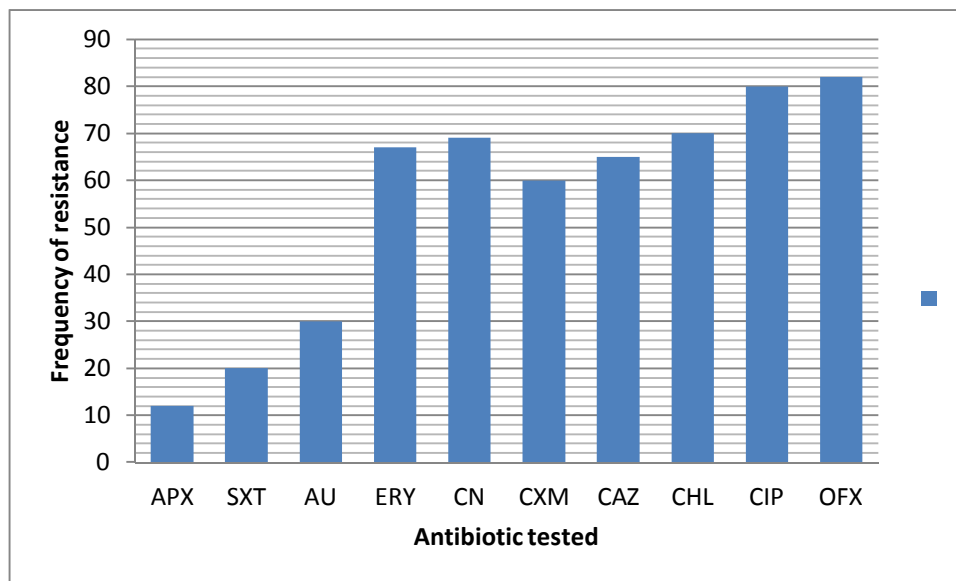
Figure 2; Antimicrobial resistance pattern of bacterial pathogens isolated(%)

The overall antimicrobial susceptibility pattern of the bacterial isolates revealed similar reported in other studies in which high resistance pattern were observed with commonly prescribed and administrated antibiotics like ampicillin-cloxacillin, co-trimoxazole and augmentine and sensitivity with the quinolones like ofloxacin and ciprofloxacin (Nwabuisi et al 2000, Aboderin et al 2004, Nwadioha et al 2010). But,the chemotherapeutic usage of quinolones in pediatric population are limited because of their contradiction and complication associated with the agents. Other agents like gentamicin and erythromycin are still been used as single or in combination therapy in the management of childhood septicemia(Nwabuisi et al 2000, Aboderin et al 2004, Nwadioha et al 2010).

In empirical therapy approach in the management of childhood septicemia, combination therapy becomes paramount as it provides a broad spectrum approach of other possible pathogens that might not be distinguished clinically and also prevent emergence of resistant strains(Karloswsky et al 2004).

In conclusion, this study revealed the prevalent bacterial pathogens associated with childhood septicemia and their antimicrobial susceptibility pattern. This findings provides a baseline information as a guide in empirical therapy in management of childhood septicemia in our hospital. Nevertheless, periodic studies for better understanding of the local epidemiology of childhood septicemia would formed the template for antibiotic policy for the hospital and early signal for emergence of resistant strains.

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5/23/2014