

Pediatric Blood Culture Isolates and Antibiotic Sensitivity Pattern in a Nigerian Tertiary Hospital

T. O. Ogunkunle¹, M. B. Abdulkadir², O. S. Katibi², S. O. Bello¹, R. A. Raheem³, R. Olaosebikan⁴

Departments of ¹Paediatrics and ³Microbiology, University of Ilorin Teaching Hospital, ²Department of Paediatrics and Child Health, University of Ilorin/University of Ilorin Teaching Hospital, Ilorin, Kwara State, Nigeria, ⁴Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Abstract

Introduction: There is a significant variation in the bacterial pathogens implicated in childhood septicemia and their antibiotic sensitivity pattern from place to place. Sustained monitoring of this dynamics is therefore critical to rational antibiotic use. **Materials and Methods:** This study was thus conducted to determine the etiology of childhood septicemia and their antibiotic sensitivity pattern. Blood culture results (contaminants excluded), age, and sex of all pediatric patients with suspected septicemia between January 2013 and December 2014 were retrieved. Data were analyzed using SPSS version 20. **Results:** Over a 2-year period, a total of 3680 blood samples were processed. Pathogenic bacteria were isolated in 701 samples (19%). *Staphylococcus aureus* was the most common isolate (41.4%) and was most sensitive to ampicillin-sulbactam (89%). *Klebsiella* species (21.7%), coagulase-negative *Staphylococcus* (14.7%), and *Pseudomonas aeruginosa* (11%) were other common organisms isolated. Virtually, all the isolates demonstrated a reliable susceptibility to ciprofloxacin except for *S. aureus* and *Klebsiella* species which were most sensitive to ampicillin-sulbactam and imipenem, respectively. **Conclusion:** In conclusions, *S. aureus* is the leading cause of childhood septicemia in this locale. The significant rate of isolation of the supposedly less virulent organisms calls for an urgent review of potential risk factors and an appraisal of the hospital infection control policies and structures.

Keywords: Antibiotics, isolates, paediatric

INTRODUCTION

The bacterial infection is a major cause of morbidity and mortality globally, but the greatest burden is borne by the developing countries.^[1] Bacteremia is the predominant cause of sepsis, i.e. systemic inflammatory response syndrome.^[2-5] Delayed recognition and treatment of bloodstream bacterial infection significantly increase the risk of morbidity and mortality as they progress to sepsis, severe sepsis, septic shock, and multiple organ dysfunction syndromes.^[6,7]

Diagnostic criteria of sepsis (i.e. fever, tachycardia, tachypnea, leucopenia/leukocytosis, or presence of >10% immature neutrophils) are less sensitive and not specific to bacterial infection.^[8] Bacterial isolation from blood specimen and antibiotic sensitivity testing thus provides the definitive diagnosis upon which antimicrobial therapy should be based.^[9] However, these investigations are either not available or the results are delayed, especially in resource-poor settings; consequently, overuse and misuse

of antibiotics are prevalent with the attendant risk of antimicrobial resistance.^[10]

There are wide variations in the bacterial pathogens implicated in childhood septicemia as well as their sensitivity pattern to antibiotics.^[5,11-17] The knowledge of epidemiology and antimicrobial susceptibility pattern of bacterial isolates in a given area is thus crucial to rational, empirical antibiotic use. The pattern of bacterial isolates and the antibiotic sensitivity of isolated organisms in children with clinical suspicion of bloodstream bacterial infection seen at a tertiary health-care facility in North Central Nigeria is thus presented in this study.

Address for correspondence: Dr. T. O. Ogunkunle,
Department of Paediatrics, University of Ilorin Teaching Hospital, Ilorin,
Kwara State, Nigeria.
E-mail: taopheeqsheun@yahoo.com

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MATERIALS AND METHODS

It was a retrospective study of all cases of suspected septicemia in pediatric patients (0–18 years) over a 2-year period (January 1, 2013, and December 31, 2014). The minimum sample size of 363 was calculated with the Fisher formula using a previous prevalence rate of 38.2%.^[5] The results of blood culture (contaminants excluded) and antibiotic sensitivity pattern of the subjects were extracted alongside their ages and sex. The extracted information was analyzed using SPSS version 20 (SPSS IBM Corp. New York, USA).

Routine blood culture during the period under review was manual using cooked meat. Aerobic cultures were mounted on the same day and subcultured within 48 h if there was growth. Eosin methylene blue and blood agar plates were used for subculture and incubated at 37°C. Identification of organisms and antibiotic sensitivity patterns of bacterial isolates was made using standard methods.^[18]

RESULTS

A total of 3680 blood culture results of children with suspected bacteremia over a 2-year period were studied. The isolates and sex distribution of the patients are shown in Table 1. Bacteria isolation rate was 701 (19%). More males (396 [56.5%]) than females (305 [43.5%]) had a positive blood culture result.

The types and pattern of bacterial isolates in age groups are shown in Table 2. Overall, Gram-positive organisms (coagulase-negative *Staphylococcus* [CoNS], *Enterococcus*, *Staphylococcus aureus*, and β -hemolytic and nonhemolytic *Streptococcus*) accounted for most of the isolates 410 (58.5%). The most frequent isolate across all age groups was *S. aureus* (41.4%), this is followed by *Klebsiella* species (21.7%), CoNS (CoNS; 14.7%), *Pseudomonas aeruginosa* (11%), and *Escherichia coli* (5.6%). The prevalence of the latter organisms was however nonuniform across all age groups though *E. coli* septicemia occurred more frequently in the neonatal age group. Septicemia occurred more frequently among under-five ($n = 508$), notably in the neonatal age group.

Table 1: Bacterial isolates and sex of children with suspected bacterial sepsis

Isolates	Male	Female	Total, n (%)
CoNS*	52	51	103 (14.7)
<i>Escherichia coli</i>	25	14	39 (5.6)
<i>Enterococcus</i>	10	2	12 (1.7)
<i>Klebsiella pneumoniae</i> *	82	70	152 (21.7)
<i>Pseudomonas</i>	47	30	77 (11)
<i>Staphylococcus aureus</i>	162	128	290 (41.4)
Proteus	10	3	13 (1.9)
Others*	8	7	15 (2.1)
Total, n (%)	396 (56.5)	305 (43.5)	701 (100)

**Klebsiella* species, *Others: Aerobic spore-forming bacilli ($n=1$), β -hemolytic *Streptococcus* ($n=2$), *Streptococcus pneumoniae* ($n=1$), nonhemolytic *Streptococcus* ($n=2$), *Salmonella* species ($n=3$), *Acinetobacter* species ($n=7$). CoNS: Coagulase-negative *Staphylococcus*

Antimicrobial sensitivity pattern of the isolated organisms is displayed in Table 3. *S. aureus* had the highest susceptibility to ampicillin-sulbactam (89%), cefuroxime (86.5%), imipenem (86.5%), amoxicillin-clavulanate (85.8%), ciprofloxacin (82.9%), and gentamicin (77.7%). *Klebsiella* species was most reliably susceptible to imipenem (70.4%) and to a lesser extent ceftazidime (68.1%). CoNS was most sensitive to Unasyn (ampicillin/sulbactam) (95%), while the susceptibility of *P. aeruginosa* was highest to imipenem (95.8%), followed by ciprofloxacin (92.8%) and gentamicin (79.4%).

DISCUSSION

The prevalence rate (19%) of septicemia in this study is comparable to the 15% rate found in a 7-year surveillance study in Kano.^[19] However, it was remarkably low compared to the 38.2% rate found by Adedoyin *et al.*^[5] in the same center about 8 years earlier. A higher rate of 35% was also found in Lagos.^[12] In the latter studies, however, a smaller study population and shorter span of study may also have resulted in higher rates given the seasonality of bacterial etiology of sepsis.^[19]

Gram-positive pathogens predominate in this report with the leading etiologic agent across all age groups being *S. aureus* (41.4%). This is in consonance with reports from previous studies.^[5,12,13,20] However, Obaro *et al.*,^[19] in a recent multicenter study, revealed that *Salmonella* species are the most common cause of childhood bacteremia in the Central (Abuja) and North Eastern (Kano) part of Nigeria. The study, however, did not report the prevalence of associated risk factors (e.g. malnutrition, malaria, HIV infections, and level of hygiene) which could have been responsible for the preponderance of *Salmonella* species.^[21] Nwadioha *et al.*^[22] have previously documented the preponderance of enteric pathogen, i.e. *E. coli* as the causative agent of bacteremia from the same region, which further suggests a peculiar predisposition to feco-orally acquired pathogens.

Noteworthy is the contribution of *Klebsiella* species, CoNS, and *P. aeruginosa* to the burden of septicemia and their pattern of distribution across different age groups. Previous studies have reported the etiologic role of *Klebsiella* species and *P. aeruginosa* in childhood septicemia, but the duo has been found to be more common in neonates.^[13,22] In a study by Uzodimma *et al.*,^[12] *Klebsiella* species accounted for 11.4% of organisms isolated from children with suspected septicemia mostly from the neonatal age group. However, in this report, these organisms were most prevalent among children aged one to 5 years. They also constitute a sizeable proportion of organisms isolated (32.7%; *Klebsiella* species 21.7% and *Pseudomonas* 11%) contrary to report by Adedoyin *et al.*^[5] from the same center about a decade earlier.

Increasing rates of antibiotic-resistant bacteria isolates have been observed globally.^[23] Most WHO member states have reported up to 60% resistance in *Klebsiella pneumoniae* against third-generation cephalosporins.^[23] In this study, imipenem

Table 2: Age distribution of bacterial isolates

Isolate	Age				Total, n (%)
	≤4 weeks	>4 weeks-1 year	>1 year-5 years	>5-14 years	
CoNS	23	27	26	27	103 (14.7)
<i>Escherichia coli</i>	20	7	3	9	39 (5.6)
<i>Enterococcus</i>	0	5	5	2	12 (1.7)
<i>Klebsiella</i> [†]	36	32	46	38	152 (21.7)
<i>Pseudomonas</i>	12	12	24	29	77 (11)
<i>Staphylococcus aureus</i>	78	67	65	80	290 (41.4)
Proteus	3	5	2	3	13 (1.9)
Others*	4	2	4	5	15 (2.1)
Total	176	157	175	193	701 (100)

[†]*Klebsiella* species, *Others: Aerobic spore-forming bacilli (n=1), β-hemolytic streptococcus (n=2), *Streptococcus pneumoniae* (n=1), nonhemolytic *Streptococcus* (n=2), *Salmonella* species (n=3), *Acinetobacter* species (n=7). CoNS: Coagulase-negative *Staphylococcus*

Table 3: Percentage susceptibility of bacterial isolates

	Isolates									
	AZT	AMC	SAM	ERY	IPM	GM	CIP	CXM	CEF	CAZ
CoNS	46.5	85.7	95.0	61.7	89.7	77.8	90.8	85.3	69.1	50.0
<i>Escherichia coli</i>	20.0	54.5	75.0	NT	62.5	90.3	81.5	69.7	72.2	69.7
<i>Enterococcus</i>	71.4	100.0	66.7	83.3	100.0	77.8	87.5	55.6	57.1	0.00
<i>Klebsiella</i>	25.0	27.9	44.0	0.00	70.4	50.4	65.4	34.4	38.7	68.1
<i>Pseudomonas</i>	70.0	58.3	79.1	NT	95.8	79.4	92.8	56.7	59.7	67.7
Proteus	NT	72.7	0.00	NT	75.0	55.6	70.0	70.0	69.2	60.0
<i>Staphylococcus aureus</i>	63.4	85.8	89.0	59.4	86.5	77.7	82.9	86.5	54.8	28.6

NT: Not tested, AZT: Azithromycin, AMC: Amoxicillin-clavulanate, SAM: Ampicillin-sulbactam, ERY: Erythromycin, IPM: Imipenem, GM: Gentamicin, CIP: Ciprofloxacin, CXM: Cefuroxime, CEF: Ceftriaxone, CAZ: Ceftazidime, CoNS: Coagulase-negative *Staphylococcus*

appears to be the antibiotic of choice when confronted with *Klebsiella* septicemia, as the resistance to ceftriaxone was as high as 61.3%, a third-generation cephalosporin which had hitherto been the standard intravenous treatment for severe *Klebsiella* infections in hospitals. Furthermore, imipenem also stood out as the antibiotics of choice against *P. aeruginosa* ahead of other commonly used antibiotics. The economic cost of the compelling need to use imipenem as a first-line option will certainly be challenging, especially in a resource-poor setting.

CONCLUSION

Septicemia constitutes a significant disease burden among children under the age of 5 years. The predominant causative agent is *S. aureus* but with a significant contribution of supposedly less virulent organisms. This finding might suggest some form of suboptimal immunity or hospital-associated infections. This calls for an urgent review of factors that may be causally related to this development, including an appraisal of the hospital infection control policies and structures.

Ciprofloxacin seems to be a rational initial empirical antibiotic of choice when confronted with a possibility of septicemia among pediatric patients in this environment. The potential

danger of the widespread use of ciprofloxacin, however, is the emergence of resistance to *Enterobacteriaceae* and *Mycobacterium tuberculosis* due to its association with a high incidence of extended-spectrum β-lactamase enzyme production among these organisms.^[24] Therefore, where septicemia due to *S. aureus* is plausible (i.e. staphylococcal skin infection), the use of ampicillin-sulbactam will be the most rational choice. In addition, the presence of ecthyma gangrenosum in a septicemic child raises a strong suspicion of *Pseudomonas* infection^[25] and would warrant the use of imipenem as a first-line antibiotic.

Limitations: The bacterial yield from culture may have been affected by the volume of blood drawn for analysis, this could however, not be controlled for given the retrospective study design. Also, the clinical correlates were not assessed.

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Conflicts of interest

There are no conflicts of interest.

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