# Bacterial Isolates From Blood Cultures Of Children With Suspected Sepsis In An Urban Hospital In Lagos: A Prospective Study Using BACTEC Blood Culture System

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## Abstract

Sepsis is a major cause of morbidity and mortality in children in the developing world, [1-4]. It is a systemic response to infection with bacteria, fungi, viruses, protozoa or rickettsia, [5].  Sepsis is therefore one of the causes of systemic inflammatory response syndrome (SIRS) which may manifest as hyperthermia, hypothermia, tachypnoea, tachycardia and increased or decreased white blood cell count, [5]  Sepsis can progress to severe sepsis, septic shock and multiple organ dysfunction syndrome (MODS), [5].

Definite diagnosis of sepsis is made by isolation of organism in blood specimen culture. International guidelines recommend that appropriate blood cultures should be obtained before starting antibiotics and the latter should be started as soon as possible especially within the first hour of recognising severe sepsis, [6]. The results of routine blood culture and antibiotics susceptibility tests take about a week thereby necessitating initial empirical treatment of suspected cases with broad spectrum antibiotics. Knowledge of pattern of common pathogens and the antimicrobial susceptibility pattern of these pathogens is therefore useful for guiding the initial treatment of patients.

On the other hand, the administration of antibiotics before the collection of samples may decrease blood culture yields. A previous study in Ibadan, Nigeria showed that up to one third of patients have taken antibiotics prior to presenting to the physician, [7]. The implication is that a considerable number of children with definite sepsis are likely to be misdiagnosed if they have received antibiotics before their blood sampling for cultures. The BACTEC instrumented blood culture system is impregnated with antimicrobial removal system which is proven to enhance recovery of bacteria from blood and other specimen even if there has been prior antibiotic administration, [8-9]. The current study uses the BACTEC blood culture system to study bacteriological profile in children with suspected sepsis in our practice where the incidence of pre-hospital administration of antibiotics is known to be enormous.

## INTRODUCTION

Sepsis is a major cause of morbidity and mortality in children in the developing world, [1-4]. It is a systemic response to infection with bacteria, fungi, viruses, protozoa or rickettsia, [5].  Sepsis is therefore one of the causes of systemic inflammatory response syndrome (SIRS) which may manifest as hyperthermia, hypothermia, tachypnoea, tachycardia and increased or decreased white blood cell count, [5]  Sepsis can progress to severe sepsis, septic shock and multiple organ dysfunction syndrome (MODS), [5]. Definite diagnosis of sepsis is made by isolation of organism in blood specimen culture. International guidelines recommend that appropriate blood cultures should be obtained before starting antibiotics and the latter should be started as soon as possible especially within the first hour of recognising severe sepsis, [6]. The results of routine blood culture and antibiotics susceptibility tests take about a week thereby necessitating initial empirical treatment of suspected cases with broad spectrum antibiotics. Knowledge of pattern of common pathogens and the antimicrobial susceptibility pattern of these pathogens is therefore useful for guiding the initial treatment of patients.

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blood culture system is impregnated with antimicrobial removal system which is proven to enhance recovery of bacteria from blood and other specimen even if there has been prior antibiotic administration, [8-9]. The current study uses the BACTEC blood culture system to study bacteriological profile in children with suspected sepsis in our practice where the incidence of pre-hospital administration of antibiotics is known to be enormous.

## AIMS AND OBJECTIVES:

The general aim of the study was to determine the bacteriological profile in children aged 0-15 years with suspected sepsis. The specific objectives were to determine:
1. The pattern of bacterial isolates in sick children with suspected sepsis presenting at the emergency or out-patient department of the Lagoon Hospital.
2. The sensitivity of isolated organism to one or more of amoxicillin- clavulanic acid, gentamicin and quinolones.

## PATIENTS AND METHODS

Study design and setting: The study conducted at Lagoon Hospitals, Lagos from April 2011 to March 2012 was hospital-based, prospective and cross sectional. Lagoon Hospitals is a multi-disciplinary specialist 76 bed private facility with three satellite locations across the state.
Patients:
Children aged 0 – 15 years (including neonates) presenting at the emergency room or out-patient department of the Hospital with features of systemic inflammatory response syndrome e.g. fever or hypothermia, tachypnoea, tachycardia, increased or decreased white blood cell count or with symptoms of multi- system involvement  are provisionally diagnosed as sepsis.
Blood culture:
Under asepsis, 2-5ml of venous blood was collected and inoculated into the BACTEC culture bottle (BD BACTEC 9000 blood culture system). Only aerobic cultures were done. Antimicrobial susceptibility of all isolates was determined using disc diffusion. Data was recorded specifically for amoxicillin- clavulanic acid, gentamicin and quinolones (ciprofloxacin).
Data collection
A structured data collection form was designed to obtain social demographic data and other relevant information such as clinical symptoms and signs, pre-hospital use of antibiotics, outcome of blood cultures and antimicrobial susceptibility.
Ethical issues:

Informed verbal and written consent of all participants was obtained and approval was gotten from the Ethics Committee of the Hospital.
Funding: The BACTEC blood culture system is part hospital protocol for evaluation of suspected sepsis. No external funding was required.
Competing interest: There are no competing interests.
Contributorship: All authors conceptualised and designed the study. Data acquisition, analysis and drafting of article received contribution from all authors.

## RESULTS

A total of 100 children were recruited during the study period. Of these, 32% of the children had received at least one antibiotic prior to presentation.
General characteristics of the study population
The age and sex distribution of the children are shown in table 1. Fever was present in 85% of the children. About half the study subjects (52%) were infants and 90% were under-5s. Most of the children (47%) were seen within three days of the onset of fever and only about 12% presented beyond seven days of onset of a febrile illness. The overall positive culture rate was 35% with the highest rate being among the neonates (41%). There was a 7% reduction in prevalence in older infants, a further 5% drop in older under-5s but 1.4% rise in older children. Malnutrition was very uncommon. Only 0.6% of the children in this study were at least moderately malnourished based on weight for age z- score recommendation of the World Health Organisation, [10].

**Table 1**

Age and sex distribution of the children

| Age Group | Number of children examined | | | Number (%) with positive isolate |
|---|---|---|---|---|
| | Male | Female | Total | |
| <  4 weeks | 12 | 27 | 39 | 16 (41.0) |
| > 4 weeks – 1yr | 11 | 12 | 23 | 8 (34.8) |
| > 1yr – < 5yr | 9 | 19 | 28 | 8 (28.6) |
| ≥ 5 yr. | 4 | 6 | 10 | 3 (30.0) |
| Total | 36 | 64 | 100 | 35 (35.0) |

Figures in bracket are percentages of row total.

Pattern of isolated organisms and relationship with age
Staphylococcus aureus was the commonest isolate, generally and across the various age groups (Table 2). The older child infected with Staphylococcus aureus was HIV infected with clinical stage three disease. The two cases of streptococcus

spp that occurred in the neonatal age group were beta haemolytic and manifested as early onset sepsis.

## Table 2

Age distribution of bacterial isolates from blood cultures of the children

| Bacterial isolates | < 4 wk | > 4wk – 1yr | >1yr – < 5yr | ≥ 5yr | Total |
|---|---|---|---|---|---|
| Staphylococcus aureus | 9 (56.2) | 5 (62.5) | 8 (100) | 1 (33.3) | 23 (65.7) |
| Streptococcus spp | 2 (12.5) | 3 (37.5) | 0 (0.0) | 0 (0) | 5 (14.2) |
| Klebsiella spp | 3 (9.4) | 0 (0.0) | 0 (0.0) | 1 (33.3) | 4 (11.4) |
| Escherichia Coli | 1 (6.2) | 0 (0.0) | 0 (0.0) | 1 (33.3) | 2 (5.7) |
| Enterococci | 1 (6.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.9) |
| Total | 16 (100) | 8 (100) | 8 (100) | 3 (100) | 35 (100) |

Figures in brackets are percentages of column total

Antimicrobial sensitivity of isolated organism
Table 3 shows the antimicrobial sensitivity pattern of isolated organisms. Overall, both gram positive and gram negative bacterial isolates showed highest susceptibility to quinolones (77.1% and 75% respectively). Specifically, S. aureus showed a susceptibility rate of 78% to quinolone. Gram positive organisms showed comparable resistance to amoxicillin- clavulanic acid (29.4%) and gentamicin (28.5%). On the other hand, Gram negative organisms showed the most resistance to gentamicin (75%) while equal resistance was recorded for both amoxicillin- clavulanic acid and quinolones (25%).
Neonatal age group
Of the 39 neonates, 16 (41%) had bacterial isolate on blood culture. Late onset sepsis (68.8%) was commoner than early onset sepsis (31.2%). Staphylococcus aureus was the commonest organism isolated from the neonates (69%) followed by klebsiella (12.5%), beta haemolytic streptococcus (12.5%), and E coli (6.25%). Two cases of early onset sepsis were caused by beta haemolytic streptococcus, one by Escherichia coli and the remaining two were caused by staphylococcus aureus. More than 90% of the neonates were in-born.

## Table 3

Sensitivity Pattern of the organism

| Sensitivity | Frequency (%) | | Total (%) |
|---|---|---|---|
| | Gram positive | Gram negative | |
| Sensitivity to | Amoxicillin- clavulanic acid | | |
| Sensitive | 16 (51.6) | 2 (50.0) | 18 (52.9) |
| Resistant | 9 (29) | 1 (25.0) | 10 (29.4) |
| Not Tested | 6 (19.4) | 1 (25.0) | 7 (20.0) |
| Sensitivity to | Genticin | | |
| Sensitive | 19 (61.2) | 0 (0.0) | 19 (54.2) |
| Resistant | 7 (22.5) | 3 (75.0) | 10 (28.5) |
| Not Tested | 5 (16.1) | 1 (25.0) | 6 (17.1) |
| Sensitivity to | Quinolones | | |
| Sensitive | 24 (77.4) | 3 (75.0) | 27 (77.1) |
| Resistant | 5 (16.1) | 1 (25.0) | 6 (17.1) |
| Not Tested | 2 (6.5) | 0 (0.0) | 2 (5.7) |

## DISCUSSION

The present study set out to identify bacteriological profile of children of all age groups with suspected septicaemia using an advanced technological medium (the BACTEC). To the best knowledge of the authors informed by a careful search of the literature, there has been no previous Nigerian study of sepsis in children based on this technology.

The overall positive isolation rate was 35% in our study. This is higher than 18.2% reported in Kano, [4], 30.8% in Ilorin, [11] but lower than 44.9% in Calabar, [3], Nigeria. Staphylococcus aureus was the commonest pathogen isolated in all age groups. This shows a similar pattern with the report from Calabar, [3] but differs from the report from Kano, [4], in which E. coli was the commonest isolate. However, streptococcus species were the second commonest isolated organism in our study. This combination of S.aureus and streptococcus is a deviation from the more common trend of S. aureus and E.coli reported in previous studies, [1, 3, 12]. This variation could represent an actual change in bacteriological profile due to urbanisation. This is likely so because in developed countries like the United States of America, streptococcus tends to rank high on the list of isolated organisms, [13, 14]. During the neonatal period, gram negative septicaemia is mostly associated with early onset infection, while in older children, there is close association between gram negative septicaemia and malnutrition, [15, 16]. In the current study, we found that

only 0.6% of the post neonatal age group were at least moderately malnourished based on weight for age z- score recommendation of the World Health Organisation, [10]. This may explain why gram negative organisms were rather uncommon in this age group compared with previously reported studies, [1, 3, 12].

The positive isolation rate in the neonatal age group (41%) in the current study is remarkable especially considering the fact that most of the neonates were in-born. It is higher than the rate reported in Ilorin (30.8%), [11] but lower than Calabar (50.8%), [3] and Ile-Ife (55%), [12]. However, it closely resembles that of Port Harcourt (41.6%), [17]. Interestingly, out born delivery accounted for 71.7% of the cases of neonatal sepsis in the Port Harcourt study. The fact that most of the neonates in our study (90%) were in-born gave the opportunity to draw samples for culture before commencing antibiotics. Additionally, the use of the BACTEC media must have enhanced our recovery of microbes from the few neonates who were brought from home or another facility after prior use of antibiotics.

About 32% of our study group had one antibiotic or more prior to presentation and this compares with data from a study in Ibadan [7]. The level of prior antibiotic exposure is worrisome, it draws attention to irrational and poorly regulated use of drugs in the population and this is a major challenge for sustained microbial susceptibility to available and affordable antibiotics. Increased public health education and crusades as well as necessary effective government policies are requisite if this hazard of irrational antibiotic usage is to be alleviated. Perhaps, if the technology of the BACTEC system were not deployed in this study, the bacterial isolation rate would have been much lower. Furthermore, our study recorded a trend of antimicrobial susceptibility to quinolones with increasing tendency of resistance to the very commonly available and affordable amoxicillin-clavulanic acid and gentamicin. Comparable high susceptibility of isolated organisms to ciprofloxacin had been reported in Kano and Port Harcourt, Nigeria, [4, 18]. Previous studies have also reported high susceptibility to third generation cephalosporins, [3, 4]. There is therefore a heightened concern particularly regarding choice of empirical antibiotics especially if children present with life threatening infections and first choice antibiotics are of critical value. This study highlights that quinolones are among some of the options to be considered in life threatening cases when decision on choice of empirical antibiotics is critical. Hitherto, the recommendation is for

empirical treatment with penicillin and an aminoglycoside prior to obtaining culture reports; however this study and some others highlight that a review of this guideline may be necessary especially in Nigeria, [18, 19]. The trend has also been recorded of increasing resistance of coliforms to gentamicin in Calabar, Nigeria as susceptibility of coliforms drops to 61.6% compared to 89.7%, a decade earlier. [3, 20, 21]. S. aureus isolates have shown abysmally low susceptibility to ampicillin and cloxacillin (15.8% each) in a study in Port Harcourt, Nigeria, [18]. It is therefore not surprising that its use by clinicians has been largely discouraged by the observed poorer outcome and need to treat sepsis promptly with reliable antibiotics in sick children.

Even though concerns for safety of quinolones in children have been raised, the characteristics of this drug class (e.g. excellent oral bioavailability and tissue penetration, broad antimicrobial spectrum, well characterized and predictable concentration-effect relationships, relative low incidence of development of microbial resistance) resulted in their increasing use in infants and children; initially as secondary or tertiary antimicrobial choices and three decades later, as a potential first line modality of treatment recommended in standard pediatric compendia used throughout the world (eg., ciprofloxacin monographs in Medicines for Children, Royal College of Paediatrics and Child Health and Neonatal and Paediatric Pharmacists Group, 2003; Pediatric Dosage Handbook, 16th edition, Lexicomp Corporation, 2009), [22]. Studies have shown that flouroquinolones use in children may be associated with tendon, bone and joint disorders, however, these were comparable with the occurrence in a control group, [23]. More so, these disorders also tend to be transient, [24, 25]. Monotherapy with quinolone is not being advocated however we suggest that it should be considered as a valuable option in life threatening cases when decision on choice of empirical antibiotics is critical to patient survival.

Some centres still do not have facilities to culture blood, or where they do, will have to wait for seven days for initial blood culture reports. A more universal deployment of BACTEC technology – possibly in central laboratories is highly recommended because the cost may prohibit its availability in most private and public facilities in Nigeria.

Finally, this study is not without limitations. We recognise our limitation in the tested antibiotics particularly, the cephalosporin. The sensitivity discs were limited in

antibiotics range; we therefore opted to work with the two most recurring prescription antibiotics in our facility (Amoxicillin- clavulanic acid and Gentamicin) and the uncommonly used quinolone group of drugs. Possible revision of the antibiotic policy especially in Nigeria is being advocated not based on this study alone but alongside other studies on neonatal sepsis. [18] Larger studies are recommended to inform changes in current practice in the management of children with suspected sepsis.

What is already known on the topic?

Sepsis is a major cause of morbidity in children in Nigeria. Staphylococcus aureus and Escherichia coli account for most cases of sepsis in Nigerian children.

What this study adds

Staphylococcus aureus is still the commonest cause of pediatric sepsis in urban Lagos. Streptococcal species are the second most common in this study. Resistance to gentamicin and amoxicillin-clavulanic acid is high with very high susceptibility to ciprofloxacin.

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