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Prevalence of bacteraemia in febrile, under-five children in the children's outpatient clinic of University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria

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Abstract: *Background:* Bacteraemia is the presence of viable bacteria in the circulating blood. The most common manifestation of bacteraemia is fever. Untreated bacteraemia can progress in 10% of children to focal infection and sepsis which can be fatal. Knowledge of the organisms implicated in causing bacteraemia would help in the right choice of antibiotics while awaiting blood culture results.
Objective: This study determined the prevalence and aetiology of bacteraemia among febrile non neonatal, under–five children seen in the Children's Clinic of the University of Port Harcourt Teaching Hospital.
Method: Febrile Children, aged 29 days to < 60 months, who presented in the outpatient clinic and whose parents gave consent were recruited from September 2010 to January 2011. Information on their weight, bio-data, and blood culture results were collected and analysed.
Result: A total of 362 children (M:F 1.1:1) were studied. Bacteraemia was found in 32 (8.8%) children. The prevalence rate of bacteraemia was highest in children aged 1-12months (12.1%) and higher in males 13(10.2%) compared to females 19(7.4%). *Staphylococcus aureus* was the commonest (56.3%) organism isolated.
Conclusion: The prevalence of bacteraemia in febrile post-neonatal under-five children in the Children's Outpatient Clinic of University of Port Harcourt Teaching Hospital was 8.8% with *Staphylococcus aureus* being the commonest organism implicated. It is recommended that antibiotics active against Staphylococcus aureus should be among the drugs that need to be commenced in this group of children while blood culture result is being awaited.

Key words: Fever, blood culture, bacteremia, under-five children,

Introduction

Bacteraemia is the presence of viable bacteria in the circulating blood[1]. Bacteraemia can present with fever as the only symptom, it can also present with focal infections (such as meningitis, osteomyelitis, endocarditis, epiglottitis, cellulitis, pneumonia, septic arthritis, etc) or as a systemic infection causing sepsis[2,3]. The most common manifestation of bacteraemia is fever[2,4]. Fever is also one of the most common presenting symptoms in the emergency room, accounting for 20% of paediatric emergency room visits as reported by Nelson et al in Boston[5]. In the United States of America, bacteremia occurred in <2% of febrile children[6,7]. In Nigeria, bacteraemia was found in 38.2% of febrile infants in Ibadan.[8]Bacteraemia is of clinical significance because if untreated it can progress to focal infection in 10% of children and to sepsis, which can be fatal[1,9]. Ispahani et al[10], found mortality directly related to bacteraemia to be 19.5 %. Berkley et al[11] reported a threefold increase in mortality among children with severe malaria and bacteraemia compared with those without coexisting bacteraemia(33.3% vs 10.4%). An early diagnosis of bacteraemia in a febrile child is crucial in reducing childhood mortality. Knowledge of the organisms implicated in causing bacteraemia would also help in the right choice of antibiotic while awaiting blood culture results. This will help in effective management of febrile children and decrease childhood morbidity and mortality.

Objectives

The aim of this study was to determine the prevalence and aetiology of bacteraemia among febrile post-neonatal, under–five children seen in the Children's Clinic of the University of Port Harcourt Teaching Hospital (UPTH). The specific objectives were to determine the percentage of febrile children aged 29 days to < 60 months with bacteraemia and identify the organisms implicated in bacteraemia.

Ethics

Ethical clearance for the study was obtained from the Ethics Committee of the UPTH. A signed or thumb printed written informed consent was obtained from parents/guardians of each child, after adequate explanation.

Method

This was a prospective study done in the Children's Out -patient Clinic of UPTH from September 2010 to January 2011. UPTH is a tertiary health institution located in Port Harcourt, a cosmopolitian city in the southern part of Nigeria. It serves as a referral centre for patients within and outside its locality. The sample size was calculated[12] using a bacteremia prevalence rate of 38.2%[13]. Children aged 29 days to <60 months, with axillary temperature ≥37.5°C and those whose parents or guardian gave informed-consent were consecutively recruited till the calculated sample size of 362 was reached. Those that had taken antibiotics within three days of presenting to the clinic were excluded. Their parents or guardians were interviewed and blood culture was done for all the patients under sterile condition. The blood culture bottles were in pairs, each containing thioglycollate for anaerobic organisms and tryptone soy broth for aerobic organisms, respectively. 2mls of venous blood was injected into each of the two blood culture bottles and kept in an incubator (Triup inter Corp U.K) set at 37^0C. By 24 hours after incubation the bottles were examined for signs of bacterial growth which include turbidity, haemolysis, gas bubbles and clots[14,15]. A sterile wire loop was used to get some broth from the blood culture bottles. The broth was then inoculated on Chocolate agar (5% heated human blood) and MacConkey plates by streaking the plates horizontally in one direction (i.e. subculture). Many single horizontal streaks were made to cover the plates. Each time the loop was used to inoculate plates it was sterilised by heating over a Bunsen burner till it was red hot and was then allowed to cool before repeating the inoculation of the plate. The chocolate agar plate was incubated in a CO_2 enriched environment (candle light in extinction). Both chocolate and MacConkey plates were incubated at 37^0C and examined the following day for presence of colonies. All bottles were subcultured daily up to seven days. The Colonies on the plates were identified by morphology, gram stain and biochemical tests (coagulase, oxidase, catalase)[14,15]. Bacteraemia was considered positive if blood culture yielded growth of any organism within seven days incubation period, except all isolates of likely contaminants (*coagulase negative Staphylococcus, epidermidis,* and *Bacillus sp*)[16.17]. It was considered negative if no growth was detected during the 7-day incubation period. Data was collected and analysed using Epi info version 3.5.1. Statistical analysis was also done using chi-square test and Fisher's exact test for variables that are ≤ five. Statistical significance of 95% confidence interval was set at $p < 0.05$.

Result

A total of 438 children aged 29days to <60 months presented to children outpatient clinic with fever over the 3months period. Seventy four (16.9%) children who had taken antibiotics within three days of presenting in the clinic and two children whose parents did not give consent were excluded while 362 febrile children were recruited for the study.
There were 186 (51.4%) males and 176 (48.6%) females (M:F ratio, 1.1: 1), the age range was 1 to <60 months (mean 21± 16 months, mode 24 months). Bacteria was cultured from blood samples of 32(8.8%) febrile children. The prevalence of bacteraemia was highest in children between the ages of 1-12months (12.1%) and decreased with increasing age, although, the difference was not statistically significant (Table 1).

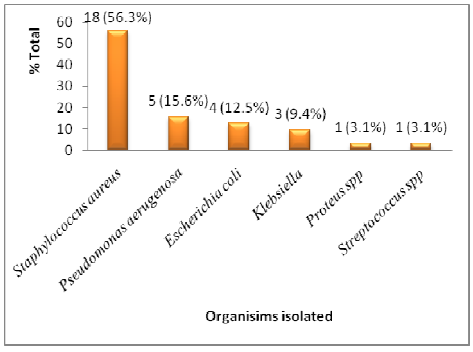
Table 1: Prevalence of bacteraemia according to age groups

Age-groups (Months)	Positive--blood Culture No (%)	Negative--blood Culture No (%)	Total No (%)
1-12	17(12.1)	123(87.9)	140(100)
>12-24	11(9.6)	104(90.4)	115(100)
>24-36	3(5.3)	54(94.7)	57(100)
>36-48	0(0)	18(100)	18(100)
>48-<60	1(3.1)	31(96.9)	32(100)
Total	32(8.8)	330(91.2)	362(100)

(χ^2= 5.9,df = 4,p = 0.205)

The commonest organism isolated from the blood cultures was S*taphylococcus aureus* in 18(56.3%) children while *Proteus mirabilis* and S*treptococcus* spp were isolated in 1(3.1%) child each (Fig.1).

Fig 1: Organisms isolated from blood culture



The prevalence rate of bacteraemia was higher in males 13(10.2%) compared to females 19(7.4%). However, the observed gender difference among children with bacteraemia was not statistically significant (p=0.343). All the isolates were more in males than females except Pseudomonas aerugenosa which was more in females than in males. There was however no statistically significant difference in the organism pattern according to gender (p>0.05), Table 2.

Table 2: Organisms Isolated according to gender

Organisms isolated	Gender Female (%)	Male(%)	Total	Pvalues
Staphylococcus aureus	8(42.1)	11(57.9)	19(100)	0.55
Pseudomonas aerugenosa	3(60)	2(40)	5(100)	0.47
Escherichia coli	1(33.3)	2(66.7)	3(100)	0.52
Klebsiella	1(33.3)	2(66.7)	3(100)	0.52
Proteus spp	0(0)	1(100)	1(100)	0.51
Streptococcus spp	0(0)	1(100)	1 (100)	0.51
Total	13(40.6)	19(59.4)	32(100)	

Discussion

The prevalence of bacteraemia among febrile, non-neonatal under-five children was 8.8%. This is similar to the 8.2% prevalence rate reported by Rattanaphone et al[18] in Vietnam and comparable to 7.8% reported by Berkley et al[11] in Kenya. While both studies were done in developing countries with similar demographic data, the prevalence of 8.2% found by Rattanaphone et al[18] was among hospitalized infants. The present study had a predominantly infant population 140(38.7%), which could also account for the similarity in prevalence rates between the studies. Berkley et al[11] had a prevalence rate of 7.8% and though the age distribution of their study population was not stated, they had a mean age of 31 months which is within the age range of the present study. Besides the age of their study population, both studies were done in malaria endemic areas, and that can account for the similarity seen in the prevalence rate in both studies. Malaria may predispose to bacteraemia because plasmodium falciparum impairs T-lymphocyte proliferative responses and causes a reduction in the number of circulating T-cells[19,20].

Higher prevalence rates of bacteraemia were reported in other Nigerian studies by Meremikwu et al[21] (48.9%), Ayoola et al[l8] (38%), Onipede et al[22] (27%) and Prada et al[23] (16%). While these studies were done among hospitalized children, the present study was done in an outpatient clinic where the severity of illness of most of the patients was less, which might explain the lower prevalence of bacteraemia in our study.

A lower prevalence rate of 1.9% was found by Alpern et al[7] in Philadelphia USA. Besides the fact that the study was done in a developed economy with better sanitation and health facilities which would contribute to decreasing incidence of bacteraemia[24], the methodology used by Alpern et al[7] excluded children with chronic disease, those with focal infection and all children that required admission within 24 hours of presenting to the hospital. As a result, children that were at higher risk of bacteraemia [25,26] were excluded from the study, possibly accounting for the lower prevalence rate in their study. The present study did not exclude children based on the severity of their illness.

The higher prevalence of bacteraemia found among infants (12.1%) in the present study. compares to previous studies [2127,28]. Enwere et al[28] in Gambia reported a high incidence of invasive bacterial disease which was highest in the first one year of life and thereafter decreased with increasing age in both children vaccinated with pneumococcal vaccine and unvaccinated children. Similarly, Berkley[27] in Kenya reported a minimal annual incidence of community acquired bacteraemia of 1457 cases per100,000 children among infants. Also, Meremikwu et al[21] in Calabar found the prevalence rate of bacteraemia among children hospitalized with features of sepsis to be 49.1% among neonates and 20.5% among those aged 2 to 5 years and 2.9% among those aged 11 to 15 years. Young age has been documented as a risk factor for bacteraemia[29,30]. The reason for higher prevalence of bacteraemia in younger children which we found in our study could be due to the immaturity of the immune system which causes poor humoral and cell mediated immune response[31,32]. Lee and Harper[33] however, found a lower risk of occult pneumococcal bacteraemia in children aged 3 to 6 months when compared to older children aged 6 to 36 months, they attributed the low rate of nasal colonization by *streptococcus pneumonia* in the younger age group less than 6 months of age as a possible explanation for their findings.

All the organisms isolated in this study have been implicated as causes of bacterial infection in children [7,11,18,22,23]. This study showed a preponderance of gram positive organisms (59%) compared to gram negative organisms as reported in previous studies[7,11,18,21,24]. *Staphylococcus aureus* was the commonest organism isolated in the present study, confirming the increasing role of this pathogen in childhood bacterial infection as documented by other studies [11,12,18,21,24]. The presence of poor personal hygiene, overcrowding and recurrent skin abrasions could explain the high frequency of staphylococcal infection found in our study, as they have been documented as some of the risk factors for *staphylococcus aureus* infection[34,35]. While the earlier two factors could be due to the poor socioeconomic demography in Nigeria, the latter factor could be due could be caused by frequent mosquito bites (which is common in the area) that bridge the skin epithelium, increasing staphylococcal infection, which is a skin commensal. Other organisms isolated in this study were *Pseudomonas* (15.6%), *Escherichia coli* (12.5%), and *Klebsiella spp* (9.4%). This was similar to results found by Ayoola et al[8] and Rottanaphone et al[18] among febrile Nigerian children and hospitalized Vietnamese children respectively, where the common organisms were

Staphylococcus aureus, Escherichia coli and *Klebsiella spp*

Although, *Pseudomonas aerugenosa* has been found to cause bacteraemia in previous studies in Nigeria[11,21,24], South Africa[24] and Vietnam[18], it has contributed to less than 6% of the causative organisms in these studies. The reason for the relatively high prevalence of pseudomonas isolated in this study (15.6%) compared to previous studies[11,18,21,24] could not be readily explained, as none of the children from which it was isolated from had any known underlying illness and none was severely malnourished. These factors would have decreased their host immunity and predisposed the children to pseudomonasinfection[36].

The presence of Streptococcus spp as a causative organism of bacteraemia in our study is similar to findings in Asia[18] , Kenya[11], South Africa[24], Nigeria[8,21,22,28], and during pre- pneumococcal conjugate vaccine (PCV) era in the USA[37]. This is because these studies were done where PCV vaccine was not administered routinely. The absence of Salmonella spp among the isolated organisms is similar to other Nigerian studies by Ayoola et al[8] and Johnson et al[38], and differs from other African studies[11,24] where *Salmonella* spp has been reported to contribute significantly to bacteraemia. The fact that salmonella infection is more prevalent in children aged 5 to 11years[39] could account for lack of salmonella isolate in the present study which involved only children under 5 years old.

A higher male prevalence for bacteraemia was found in our study. This observation is similar to the findings by Berkowitz[24] in South Africa and Berkley et al[27] in Kenya who reported a higher prevalence in males of 6.1% and 6.4% compared to 5.5% and 6.3% in females, respectively. The cause of the gender disparity in favour of the males could be due to over representation of males in the general study population. The gender disparity could also be attributed to the presence of androgen hormones in males, which has been found to have an immunosuppressive effect on humoral and cell mediated immune response[40,41,42]. This effect of androgens has been postulated to predispose males to higher risk of infection than their female counterparts, although this effect has been documented in adults and there are limited studies done in children. Isaacman et al[43], however found females to be at increased risk for bacteraemia compared to males in a retrospective review of febrile children aged 3-36 months in an emergency room in Virginia,. The authors[43] acknowledged that the reason for the higher of risk bacteraemia among females could not be explained.

Conclusion

In conclusion, the prevalence of bacteraemia in febrile post-neonatal under-five children in the Children's Outpatient Clinic of University of Port Harcourt Teaching Hospital is 8.8%. Staphylococcus aureus is the commonest organism implicated. We recommend therefore, that antibiotics active against Staphylococcus aureus should be among the drugs that need to be commenced in febrile under-five children at risk for bacteraemia while blood culture result is being awaited.

Conflict of Interest: None
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