

# Asymptomatic Bacteremia in Children Infected with Human Immunodeficiency Virus in Calabar, South-South, Nigeria

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**Abstract:** *Background:* Asymptomatic Human Immunodeficiency Virus (HIV) infected children are prone to serious bacterial infection as a result of poor immunity.

*Objective:* This was to determine the common pathogenic organisms responsible for bacteremia among asymptomatic HIV infected children attending the outpatient clinics at the University of Calabar Teaching Hospital, Nigeria.

*Subjects and Methods:* This prospective non randomized cross-sectional study was conducted over 6 months from January 1st to 30th June 2014 among cohorts of HIV infected Anti-retroviral (ARV) naive and experienced children attending the clinic. Ethical approval was obtained from the ethical committee of the institution. Blood culture specimens were collected from all HIV infected patients who met the criteria for enrollment. All specimens with isolated bacteria organisms were treated with antibiotics according to the sensitivity pattern, in addition to administered Anti-retroviral drugs.

*Results:* Out of the total of 109 patients recruited, 38(34.9%) had bacteremia. There were more males (57.9%), and most of them (63.2%) had Highly Active Anti-Retroviral Therapy (HAART) for more than 24 weeks. Bacteremia was inversely proportional to the CD4 count. The commonest organism isolated was unclassified *Coliforms* (47.3%) followed by *Staphylococcus aureus* (39.5%).

*Conclusions:* HIV infected children are prone to bacteremia especially among those with low CD4 count. *Coliform* was the commonest organism isolated. We recommend that HIV infected children be routinely investigated for bacteremia.

**Keywords:** Organisms, ARV, gentamycin, Blood culture, CD4.

## INTRODUCTION

The World Health Organization (WHO) estimates that approximately 3.4 million children were living with HIV at the end of 2011 with 91% of them in Sub-Saharan Africa. Each year in Sub-Saharan Africa, 4.6 million children die before reaching the age of 5 years, and the vast majority of these deaths were not fully investigated [1]. Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS) are responsible for 4% of the causes of death among children under 5 years [2]. Bacterial infection was responsible for the immediate cause of death of up to 26% of patients with HIV infections [3]. HIV-infected children are at high risk for serious bacterial infections with encapsulated organisms [4] particularly during the early years of life in contrast to HIV-infected adults with predominant Opportunistic Infections (OIs). In Nigeria, bacteremia is an important cause of morbidity and mortality among HIV-infected children [2].

There is paucity of data on bacteremia in HIV positive children in Calabar, Nigeria. Therefore, this study was conducted to determine the common pathogenic organisms responsible and their sensitivity

pattern. It is aimed to guide health care providers to initiate appropriate antibiotic treatment.

## SUBJECTS AND METHODS

This prospective non randomised cross-sectional study was conducted from January 1<sup>st</sup> to 30<sup>th</sup> June 2014 at the Children Outpatient Clinics (CHOP) of the University of Calabar teaching hospital (UCTH), Calabar, Nigeria. The tertiary health care facility provided treatment and care at no cost to all HIV infected children less than 15 years. An average of 3 new patients per week and total of 10-20 children attended the thrice weekly clinic. The children were treated with Highly Active Antiretroviral drugs (HAART) in accordance with the current Integrated National Guidelines for HIV Prevention, Treatment and Care (2014). These children were without fever or any other illnesses during their clinic visit. The CD4 count did not determine the inclusion or exclusion into the study. Excluded from the study were children on steroids, chemotherapy, those with skin sepsis, ear discharge. Also excluded were children on antibiotics except patients on routine prophylactic co-trimoxazole. The very ill patients excluded from the study were admitted into the paediatric ward of the hospital for treatment and care.

Ethical clearance was obtained from the Ethical Committee of the institution as well as signed consent

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from the parents or caregivers. Each patient that met the inclusion criteria was recruited. A filled proforma form was opened for each patient; information recorded included the age, sex, anthropometry, CD4 count etc. After explanation of procedure to the parents/caregivers, three millilitres (3mls) of blood was collected from each subject under aseptic condition and put into the culture bottle for aerobic blood culture. The samples were taken within 30 minutes to the medical laboratory department of the hospital for analysis by a certified laboratory scientist. Children with positive blood culture samples were treated for 7 days in accordance with the sensitivity results. The study was terminated if the patient requested for transfer to another centre, requested for discharge against medical advice, voluntarily withdrew consent after initial approval and death of the patient during the study.

Data was analysed using Statistical Package for Social Students (SPSS) version 20. Continuous variables were summarized using means, median and ranges as appropriate. Proportions were compared using Chi-square test of significance. A probability (P-value) of less than 0.05 was considered statistically significant.

## RESULTS

Of the 109 children recruited into the study, 38(34.9%) had bacteremia. There were more males 57.9%. The mean age was  $\pm 6.3$  years ( $X^2 = 0.421$ ; P-value 0.516). The mean weight and height were 19.1kg (8.9-34.5; SD 6.66) and 107.2cm (73.5-137; SD 16.6) respectively. The mean BMI was 15.7, below the 50th percentile. Twenty four 24(63.2%) had HAART for more than 24 weeks (Table 1). Most of the parents of the children studied were in social class II and III

according to the classification by Oyediji *et al.* [5]. The parents of 28 (73.7%) and 10 (26.3%) children were from the low and high socioeconomic classes respectively.

The relationship between CD4 count and bacteremia is shown in Table 2. Proportionately, the lower the CD4 count the higher the percentage of bacteremia except CD4 count  $>1,500$  cells/mm<sup>3</sup>.

The organisms isolated were unclassified *Coliforms* 47.3%, *Staphylococcus aureus* 39.5%, *Streptococcus pyogenes* 7.9%, and *Serratia* species 5.3%.

## DISCUSSION

The prevalence rate of 34.9% obtained from this study was similar to 37.1% recorded by Imade *et al.* [6] in Benin Nigeria from the same geopolitical zone like Calabar. It was however higher than 21% reported by Kolo *et al.* [7] in Minna, North-Central Nigeria and 21.4% reported by workers in Uganda and Zimbabwe [8, 9]. It is much higher than 12.8% reported by Berkley *et al.* [10] in Kenya. Our findings were corroborated by results of hemoculture antimicrobial susceptibility tests from HIV infected patients at Siriraj hospital, Bangkok, Thailand. The percentages of positive hemocultures though slightly lower were 24.6%, 21.4%, 23.9%, and 28.5% in 1996, 1997, 1998, and 1999, respectively [11]. The high prevalence observed in this survey could be attributed to the vicious cycle of the disease, poverty and ignorance that is common in the sub region which is also in keeping with our findings. Surprisingly, bacteremia was common among children aged 6-12 years. One would have expected a higher level of immunity among this age group. This observation could be due to the slow progression of the disease in some

**Table 1: Age, Sex and Duration of HAART among 38 HIV Positive Children with Bacteremia**

Characteristics	Bacteremia		No Bacteremia		Risk ratio	$\chi^2$	P value
	N	%	N	%			
<b>Age</b>							
2-6yrs	17	(44.7)	21	(55.3)			
6-12yrs	21	(55.3)	17	(44.7)	1.24	0.421	0.516
<b>Sex</b>							
M	22	(57.9)	16	(42.1)			
F	16	(42.1)	22	(57.9)	0.73	0.947	0.330
<b>Duration of HAART</b>							
<24wks	14	(36.8)	24	(63.2)			
>24wks	24	(63.2)	14	(36.8)	1.71	2.63	0.105

children identified as slow progressors or poor adherence to Anti-retroviral drugs.

**Table 2: Relationship between Bacteria and CD4 Count in HIV Positive Samples**

D4 Count Range (cells/mm <sup>3</sup> )	No Examined	No Positive (%)
≥1500	13	4 (30.8%)
>750 – 1500	30	7 (23.3%)
>500 – 750	38	12 (31.6%)
>350 – 500	18	9 (50%)
<350	10	6 (60%)
Total	109	38 (34.9%)

Majority of the infected children had been on HAART for more than 24weeks. It is expected that after commencement of HAART for 24weeks and beyond there should be increased immunological response to more than 50% of baseline, CD4 count and viral load should be undetectable. Surprisingly, our study showed that children who received HAART for greater than 24 weeks were more infected with HIV. The reason for this is unclear; however adherence could not be entirely excluded as a possible reason for this observation. There are no facilities in our centre to measure the blood levels of the drugs to objectively determine and measure level of adherence. It is recommended that a study to measure blood levels of drugs and bacteremia be conducted.

The inverse relationship between bacteremia and CD4 count could be due to improvement in the immunological status following the use HAART and corresponding decline of co-morbidities and other opportunistic infections. The commonest organism isolated from this study was *Coliforms* and closely followed by *Staphylococcus aureus*. In Benin *Staphylococcus aureus* was the commonest isolate in their study followed by *Escherichia coli* [6]. In Abuja, Obaro *et al.* [12] identified *Staphylococcus aureus* as the most common organism causing bacteremia. These findings were entirely at variance with the Watoto (ARROW) clinical trial in Uganda and Zimbabwe where *Salmonella* specie was the most common pathogen isolated, followed by *Escherichia coli* and *Staphylococcus aureus* [8]. *Coliforms* are normal commensals of the digestive system while *Staphylococcus aureus* are common on the skin. These are potential sources of acquisition of infection due to poor personal hygiene.

Most of the organisms were sensitive to Gentamycin which had been one of the first line drugs of our institutional antibiotic policy [13]. Gentamycin is a parenteral antibiotic, so its abuse is less compared to other oral antibiotics. However, in Benin Gentamycin was the second most sensitive antibiotic after ceftriaxone.

## CONCLUSION

This study showed that *Coliforms* and *Staphylococcus aureus* were organisms responsible for bacteremia in HIV-infected children in our centre. Children with low CD4 count were more predisposed to bacteremia. Clinicians therefore should have high index of suspicion in this group of children hence the need for regular blood culture. In addition, parents should be educated on nutritional therapy as an adjuvant to treatment in HIV infected children.

## LIMITATIONS

Inability to perform anaerobic culture.

## COMPETING INTEREST

Authors have no financial relationship with Presidents Emergency Plan for AIDS Relief (PEPFAR).

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