Bacteremia in Children Infected with HIV/AIDS in Minna, Niger State, Nigeria

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Authors' contributions

This work was carried out in collaboration between all authors. Author OOK designed the study, performed the statistical analysis, wrote the first draft of the manusript and managed literature searches. Authors MG, SYD, MEA and TBS managed the analyses of the study and literature searches. All authors read and apprroved the final manuscript.

Original Research Article

ABSTRACT

Bacterial infection was reported to be one of the leading causes of high mortality among children. Bacteremia is a frequent complication found among HIV infected children and usually associated with a poor prognosis. This study was aimed at determine the spectrum of bacterial agent that cause bacteremia among HIV infected children in Minna, Niger State and thus determine the difference between the frequency of occurrence of the isolates from HIV infected with HIV uninfected children. The experimental design adopted was simple randomized non-block design. This study was carried out children attending General Hospital, Minna Niger state, pediatric out-patient department between June 2013 and December, 2013. 91 HIV infected children and 100 uninfected were included in this study. Their ages range from two years to 12 years. Blood culture samples were used to determine the profile of bacterial infection. All isolates from the cultures were identified using Microbact identification kit. The prevalence rate of bacteremia among HIV infected and HIV uninfected children was found to be 21% and 8% respectively. *Staphylococcus aureus (11.88%)* was the most common gram positive while *Klebsiella pneumoniae* (13.86%) was the most common gram negative organism from both HIV infected and uninfected participants. There was an

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increase in non-typhoidal *Salmonella* spp. without any *S. typhi* isolated. Bacteremia infection among HIV infected children was found to be significantly higher than those found from HIV negative children (p < 0.05). Bacteremia infections in children are basically caused by gram-positive cocci and gram-negative bacilli. The prevalence rate of bacteremia was found to be significantly higher among HIV infected participants than HIV uninfected children.

1. INTRODUCTION

Bacteremia with the human immunodeficiency virus (HIV) co-infection were frequent complications found among children in developed and developing countries (Nigeria included), and data on this problem are limited. Children with HIV/AIDS compared to immune competent ones present with infection patterns that are different in nature, severity and/or frequency [1]. Bacterial infections are very common among children both immune-suppressed and immune-competent individual. Bacteremia are frequent complication found among immune-suppressed children and is usually associated with poor prognosis and are responsible for high mortality for up to 32% among HIV infected children especially under a very low immune suppression (CD4 T-cell count) [2] and unhygienic conditions [3]. A lot of studies have shown that there are variable distributions of bacterial agents causing bacteremia. This variation could be as a result of different life styles, seasonal variation, and geographical variation. The most common pathogen as described by previous studies was *Streptococcus pneumoniae, Staphylococcus aureus and Klebsiella pneumoniae.* Bacterial infections are common causes of high mortality among children and adults infected with HIV infection because of abnormalities in humoral, cellular, and mucosal immunity. HIV-infected children have an increased risk of bacteremia during bacterial infections which could disseminate into different organ or even systemic [4]. Many studies have demonstrated that the prevalence of bacteremia in HIV-infected patients who have fever and are hospitalized ranges from 5 to 28% [5,6]. The common sources of infections are pneumonia or respiratory tract infection and gastroenteritis but most of them are unknown [7,8,9,10]. In this study we aimed to determine the prevalence of bacteremia in both HIV positive and HIV seronegative children in Minna, Niger state.

2. METHODOLOGY

The general hospital in Minna, North-central geopolitical zone of Nigeria and it serves as a referral center for HIV care in Minna and neighbouring communities. The clinic provides care including antiretroviral therapy for HIV-infected children and is sponsored by the Government of Niger State. Ethical approval was obtained from the hospital research board and informed consent from the parents of the participants. The participants were children between the ages of two and twelve years. 91 HIV infected children and 100 HIV uninfected children attending out-patient department of government hospital met the criteria and were enrolled for this study. HIV seronegative participants include exposed children and unexposed children.

Blood was taken following cleansing of the skin with isopropyl alcohol; 5 ml of blood was drawn through vein puncture and was inoculated into blood culture vial with appropriate media. Blood cultures were incubated and continuously monitored by using a seven-day period. Positive vials were sub-cultured and resulting isolates were identified by standard bacteriological methods using Microbact identification kit (Oxoid, UK). Bacteremia or blood stream infection (BSI) was diagnosed when a blood culture grew an organism with (secondary BSI) or without (primary BSI) any obvious focus of sepsis. Bacteremia was considered when one or more blood cultures showed at least one recognized pathogenic and other opportunistic bacteria. Blood isolates of coagulase negative staphylococci, *Corynebacterium* spp, *Bacillus spp*, *Clostridium* spp, and any other potential contaminants were excluded from our analysis. Fungal or mycobacterial positive blood cultures were excluded from this study. The CD4 cell count was recorded for all the HIV infected children.

3. RESULTS AND DISCUSSION

Table 1 shows the distribution of bacteremia in relation to CD4 counts. There was an increase in bacteremia among participants with lower CD4 up to 86% prevalence rate. This report was similar to report of several studies in this region that there is an increase in prevalence rate of bacterial infection among HIV infected patient

with low CD4. The prevalence rate of infection seems to have an inverse relation with the CD4 count. Table 2 shows the frequency of occurrence of different pathogenic bacteria. 101 different Gram-negative and Gram-positive were identified from both HIV infected and HIV uninfected children. The frequency of Gram-negative bacilli observed was higher than Gram-positive from all the participants. *Klebsiella pneumoniae* (13.86%) was the most common gram-negative bacilli observed, followed closely by non-typhiodal salmonella spp (10.89%). The prevalence rate of infection among HIV infected participants 62(61%) was found to be higher than prevalence rate among the HIV uninfected participants 39(39%).

The frequency of occurrence of gram negative bacteria isolated in relation to gender and HIV status was shown in table 3. This table shows that HIV male participants had higher number of isolated bacteria compared with HIV infected female and HIV uninfected participants.

3.1 Discussion

The public health significance of diagnosis of the bacterial agent incriminating the immune suppression of HIV infected children is important and was demonstrated in this study. This setting is one of the resource limited setting where there is higher rate of indiscriminate use of drug, unavailability of clean and portable water, poverty and abuse of drug is common. This study was sited at Minna, Niger state, north central Nigeria. The spectrum of bacterial agents identified from bacteremia differs from report from other part of country, although not from the same age groups. In this study, *Klebsiella pneumoniae* and *E. coli* were the leading cause of bacteremia among the subject, while in Lagos State, south west Nigeria, non typhoidal Salmonella spp and *S. aureus* as been shown to be prevalent [11]. Higher rate of bacteremia was found among participants with low CD4 counts as most participants with CD4 count were infected with HIV infection [12]. In a study from Akwa, Anambra State, it was discovered that there was an inverse relationship between prevalence of infection and CD4 count [13]. CD4 counts indicate the effectiveness of immune system and the level of HIV infection among infected individual. The participants with CD4 count lower than 100 cell/ul were reported to the hospital on their first visit, with severe fever and were later diagnosed with poly microbial and HIV infections. The result is also similar to findings of

Heather et al. [1], who discovered that late diagnosis of HIV infection increases the rate of polymicrobial infections and a recent review of studies on co-infections in HIV found strong evidence of increased HIV viral load with bacteremia and as hoped, decreased viral load following treatment [14]. The rate of infection reduces as the CD4 count increases in most participants. This could be as a result of improvement in the competent level of their immune system or the effect of antiretroviral drugs been administered and/or prevention of some opportunistic infections.

Table 1. Distribution of bacteremia in relation to CD4 count in HIV positive samples

CD4 count (cell/ul)	No. examined	No. positive	% positive
<100	7	6	85.71 [a]
100 - 200	15	6	40.00 [b]
201 - 400	19	4	21.05[abc]
401 - 600	14	4	28.57[ab]
> 600	36	8	22.22[abc]
total	91	28	30.77

Means on the same column with different superscripts are significantly different ($p < 0.05$)

Klebsiella pneumoniae was the most common gram-negative bacilli observed (13.86%) while *Staphylococcus aureus* were the most common gram-positive cocci observed (11.88%) as major cause of bacteremia in this study shown in table 2. Non typhoidal Salmonella spp. was also found to be one of the major causes of bacteremia among the subject, without any record of *S. typhi*. The profile of bacteria identified was similar to the findings in other part of the country. In a study in Ibadan, where almost the same conventional methods were used [15], pneumococcus and Klebsiella ssp. was predominantly identified while in another study in Abuja, *S. aureus* and *S. typhi* was found to be the leading cause of bacteremia among the participants selected. The frequency of occurrence of bacteria among HIV infected participants were found to be higher than those found among HIV uninfected participants [16]. Difference in disease epidemiology between HIV seropositive and seronegative participants could also be affected by the unhygienic practices, sanitary conditions and socio-economic impact. This study can be underestimated because the participants studied were only from out-patient department, not considering children that were on admission or those that attend other private

hospitals. In North America and European countries, Staphylococcus species was reported to be the most common causes of bacterial infections and bacteremia due to the high rate of intravenous drug use, central venous catheters, and neutrophil defects [1]. In Minna, Niger State, indiscriminate use of drugs and blind therapy due to availability of drugs over the counter could be responsible for increase in *Klebsiella pneumoniae* and *Staphylococcus aureus* which could be community acquired infection since all the participants were from the out-patient department of the hospital. Gram-negative bacteria are also common in HIV-infected patients, especially non-typhoidal salmonella with the relative risk being between 20 and 100 times that of the general population. In this study, the difference between Gram-positive bacteremia

and Gram-negative bacteremia was much less and did not reach the statistical level. This may be explained by the low and unhealthy personal hygiene, unavailability of clean portable water and poor environmental sanitation observed in this region. These results are similar to those found in the study of Heather et al. [1], performed at a different hospital and different country and geographical locality. Nonetheless, the role of pneumococcal bacteremia cannot be ignored in this study. In some other Africa studies, pneumococcal bacteremia had been reported to be the leading cause of bacteremia [7]. It was observed in this study that 8% of bacteremia was cause by *Steptococcus pneumoniae* and this percentage is of great public health importance.

Table 2. Profile of pathogenic bacteria isolated

Organism	No from HIV infected	% positive	No from HIV uninfected	% positive	Total no	% positive
Klebsiella pneumoniae	10	71.43	4	28.57	14	13.86
Klebsiella oxytoca	5	100.00	0	0.00	5	4.95
Serratia marcescens	2	33.33	4	66.67	6	5.94
Salmonella paratyphi	4	36.36	7	63.64	11	10.89
Salmonella arizonae	5	71.43	2	28.57	7	6.93
Serratia rubidaea	3	100.00	0	0.00	3	2.97
Pseudomonas aeruginosa	1	25.00	3	75.00	4	3.96
Proteus mirabilis	4	80.00	1	20.00	5	4.95
Hafnia alvei	1	100.00	0	0.00	1	0.99
Cirobacter freundii	0	0.00	2	100.00	2	1.98
Escherichia coli	1	12.5	7	87.50	8	7.92
Staphylococcus aureus	9	75.00	3	25.00	12	11.88
Streptococcus pneumoniae	5	62.50	3	37.50	8	7.92
Streptococcus pyogenes	4	57.14	3	42.86	7	6.93
Viridans Streptococcus	3	100.00	0	0.00	3	2.97
Anaearobic Streptococcus	2	100	0	0.00	2	1.98
Mircococci	4		0	0.00	4	3.96
Total	63	61.39	39	38.61	102	

Frequency of occurrence of gram negative bacteria isolated in relation to gender and HIV status was shown in Table 3. The variance in frequency between gender groups could be as a result of the mode of selection of participants. It has been reported that HIV-infected children have greater risk of gram negative bacteremia than their negative counterparts, and these infections might be more invasive. Antiretroviral therapy have marked decreased on morbidity and mortality due to bacteremia in developed countries; but it still remains a great problem in resource limited settings and underdeveloped countries.

Increase in prevalence of bacteremia in HIV infected male participants as shown in Table 4 could be as a result of mode of participant selection and different level of immuno-suppresion which might increase the rate of infection. Bacteremia among children was found to be not gender sensitive with prevalence rate varied and cross across gender. Previous studies have reported varied ratios of male to female infection rate. This is similar with to the findings by Heather et al. (2012) that there is male predominance in increase rate of infection but did not agree with Nwozor and Nwarkwo in 2013 that of the CD4 count analysed in Akwa, Anambra state, male to female ratio of infection is 1;2.2. More studies from Africa on similar aspect would shed light on role of male gender preponderance to bacterial infection.

Table 3. Frequency of occurrence of gram negative bacteria isolated in relation to gender and HIV status

Organism	HIV infected				HIV uninfected			
	Male		Female		Male		Female	
	No. isolated	%	No isolated	%	No. isolated	%	No isolated	%
Klebsiella pneumoniae	7	33.33	3	20.00	1	6.25	3	21.43
Klebsiella oxytoca	2	9.52	3	20.00	0	-	0	-
Serratia marcescens	2	9.52	0	-	3	18.75	1	7.14
Salmonella paratyphi	3	14.29	1	6.67	5	31.25	2	14.28
Salmonella arizonae	3	14.29	2	13.33	0	-	2	14.28
Serratia rubidaea	1	4.76	2	13.33	0	-	0	-
Pseudomonas aeruginosa	0	-	1	6.67	1	6.25	2	14.28
Proteus mirabilis	3	14.29	1	6.67	0	-	1	7.14
Hafnia alvei	0	-	1	6.67	0	-	0	-
Cirobacter freundii	0	-	0	-	2	12.50	0	-
Escherichia coli	0	-	1	6.67	4	25.00	3	21.43
Total	21	31.82	15	22.73	16	24.24	14	21.21

Table 4. Occurrence of Bacteraemia in Relation to HIV status

HIV status		HIV positive sample						
	Total sample	Male				Female		
	Examined	No. examined	No. positive	% positive	No. examined	No. positive	% positive
HIV infected	91	56	32 [a]	42.86	35	14 [a]	63.36
HIV uninfected	100	78	6b	7.69	22	2b	9.09

Means on the same column with different superscripts are significantly different (p < 0.05)

4. CONCLUSION

Bacteremia infections among HIV infected children in Niger State are basically caused by gram-positive cocci and gram-negative bacilli. *Klebsiella pneumoniae* was the most common gram-negative bacilli identified and *Staphylococcus aureus* was the most common Gram-positive cocci observed. This study found an increase in prevalence of non typhi salmonella spp without any *S. typhi* isolated. The finding suggested that the spectrum of bacterial agents identified from blood samples of children for bacteremia in Minna were not different from some isolates in most other part of the country. This may be due to socoi-economic impact of the parents; unhygienic practises by the participants as the participant were school age children, unavailability of portable and clean water and intake of contaminated food and fruits. The prevalence rate of bacteremia was found to be significantly higher among HIV infected participants than HIV uninfected children. There is need to expand the surveillance study to include more local government areas of the state and compare the rate of infection among hospitalized HIV infected children and hospitalized HIV uninfected children.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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