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CHILDHOOD HIV ADMISSIONS AT A NIGERIAN TERTIARY HOSPITAL

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ABSTRACT

Objective: To describe the clinical and laboratory profiles of paediatric (Human Immunodeficiency virus) HIV admissions and their outcomes post scale up era.

Method: Information on the clinical profiles, immunology and outcome was obtained from the case notes of HIV infected children admitted between the year 2007 and 2010 at a Nigerian teaching hospital. Data was analyzed with the SPSS 18 software.

Results: Of the 2523 paediatric admissions 42(1.7%) were HIV infected. The 42 were made up of 21 boys and 21 girls and their mean age was 3.7±2.9years. Pneumonia, septicaemia, Tuberculosis, malaria, meningitis, otitis media, osteomyelits, pharygotonsilitis and septic arthritis was the diagnosis in 10(23.8%), 10(23.8%), 10(23.8%), 7(16.7%), 1(2.4%), 1(2.4%), 1(2.4%), 1(2.4%) and 1(2.4%) children respectively. Sequelae followed all neurological and bone infections. Of the total 191 childhood deaths recorded on the paediatric wards 9(4.7%) were due to HIV. A case fatality rate of 9(21.4%) was recorded. Tuberculosis, septicaemia, bacterial pneumonia and immune reconstitution syndrome accounted for more than 60% of the deaths. Ten patients were on Highly Active Anti-retroviral Therapy (HAART) while the remaining 32 were not. No deaths were recorded among the patients on HAART in contrast to the 9 deaths amongst patients not on HAART ($p = 0.04$, OR = 1.41 CI= 1.12 – 1.77). Four of the 5 patients on HAART had sequelae compared with the single case of sequela amongst the 30 not on HAART ($p<0.01$, OR=0.07, CI= 0.01 – 0.71).

Conclusion: Human Immunodeficiency Virus infection is an important cause of morbidity and mortality in childhood. Super imposed bacterial infections are important reasons for admissions. Bone and neurologic infections are commonly associated with sequelae amongst survivors. Administration of HAART was protective against mortality.

Key Words: Clinical, Immunologic, Characteristics, HIV-infected, Children

INTRODUCTION

The disease HIV is probably the most dreaded pandemic in human history with an estimated 33.8 million people infected globally in the year 2008.[1] Sub-Saharan Africa has been disproportionately affected, accounting for 91% of new paediatric infections in the year 2008.[1] Nigeria being the most populous African nation has also had its own share of this pandemic recording 220,000 infections in the year 2007, thus making the country the second largest country in Africa with paediatric infections.[2] An improvement in the national response to this pandemic in Nigeria has recently been witnessed. This has resulted in the scaling up of diagnostic and treatment services coupled with the training of health personnel.[3] Diagnostic and treatment are also currently offered free to the citizenry.

Reports on paediatric HIV admissions in Nigeria are few, with respect to the burden imposed by the disease in the country.[4,5] Furthermore, all of these studies were conducted before the scaling up of services.[4,5] Thus, a knowledge gap currently exists on paediatric HIV admissions in the scale up era. The aim of the present study is to give an update on the clinical profile, immunology and outcome of paediatric HIV infected admissions at the Ladoke Akintola University of Technology Teaching Hospital, Nigeria.

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METHODS

This is a retrospective study of all paediatric HIV admissions at the Ladoke Akintola University Teaching Hospital, Osogbo, Nigeria between 1st January 2007 and 31st December 2012. The hospital is situated in Osogbo, which is the capital of Osun state, located in the South West Nigeria. This hospital provides tertiary health services to the inhabitants of the state which was recorded to have a population of 3.2 million in 2006.[6] The inhabitants of the neighbouring states such as Ondo, Kwara and Ekiti also patronize the facility. The hospital provides free care for HIV infected children and it is supported by the government of Nigeria and the United States President's emergency plan for AIDS relief program. All principles governing ethical research were complied with in the research.

Diagnosis of HIV was based on a positive ELISA reaction and confirmed by a Western blot in children aged 18 months and older. Infections in children aged less than 18 months were established using the HIV DNA polymerase chain reaction kit. The voluntary counselling and testing method was used to diagnose all infected children with symptoms suggestive of HIV infections or those whose mothers or siblings presented with symptoms.

Information was extracted from the case notes of all paediatric HIV admissions. Details obtained include age, sex, clinical presentation, diagnoses, CD4 count on admission and outcome. Chronic cough was taken as a cough persisting more than 21 days. [7] Frequent watery stools lasting more than 14 and 30 days classified as persistent and chronic diarrhoea, respectively. Generalized lymph node enlargement was lymph node enlargement involving more than 2 contiguous sites. [8] Fever lasting for more than 14 days was regarded as prolonged fever. Children whose mother were HIV positive and no other risk factors for HIV were identified were classified to be vertically infected, while those whose mothers were HIV negative with risk factors for HIV infection were classified as horizontally infected

Diagnosis of tuberculosis was based on the WHO guidelines for national tuberculosis programs for children.[8] Pneumocystis jeroveci pneumonia was based on clinical and radiological features.[9] Age appropriate absolute CD4counts for severe immune suppression was used to classify the immunologic status and clinical staging on admission was based on HIV clinical staging [8]

The data obtained was analyzed with PASW statistics version 18 using simple descriptive statistics such as range, mean and percentages for continuous variables. Associations for categorical variables were tested with chi–square and values less than 0.05 were regarded as statistical significant.

RESULTS

Population studied

Of the 2,523 admissions in the paediatric ward (excluding neonatal ward) over the study period, forty two (1.7%) were HIV infected. A total number of 191 deaths occurred amongst these 2,523(7.6%) admissions.

Age and sex distribution

The mean age of the children studied is 3.7±2.9 with their ages ranging between 2 months and 10 years. Of the 42 children studied 7(16.7%) were aged between 2 months and 1 year, while 23(54.8%) were aged between >1 – 5 years. The remaining 12(28.6%) were aged between >5 – 10 years. Twenty one boys and 21 girls were studied giving a male to female ratio of 1:1. The age and sex distribution of the children is shown in Table 1.

Clinical features

The common features at presentation were fever, weight loss, cough, thrush, generalized lymph node enlargement. Prolonged fever was recorded in 20 children, while fever lasting than 20days was recorded in 15. Chronic cough was noted in 7 children, while cough persisted for less than 21 days in 14. Diarrhoea was chronic in 10, acute in 6 and persistent in 2. The 7 cases of skin rashes were made up of 2 cases of scabeitic rashes, and one case each of a chest wall furuncle, cellulitis of a finger, tinea facei, tinea unguim and a case of sebhoroheic dermatitis. The other clinical features are shown in table 2.

Mode of transmission

Of the 42 children studied, the mode of acquisition of HIV was presumed vertical in 41(97.6%) and horizontal form a blood transfusion in one (2.4%). Of the 41 children presumed to be vertically infected, 38(92.7%) mothers and their babies missed out on prevention of mother to child strategies because their mothers were not aware of being HIV infected, two (4.8%) of the remaining mothers who knew there retroviral status were not aware of the PMTCT interventions and the remaining one(2.4%) mother gave no reasons. Of the total 42 admissions 40(97.6%) were previously diagnosed and registered for care at the paediatric anti-retroviral clinic prior to this study, while the remaining 2(2.4%) admissions were newly diagnosed during the course of this study.

Diagnoses and microbiologic etiologies of some diseases

Pneumonia, septicaemia, malaria, pulmonary tuberculosis, disseminated tuberculosis, meningitis, bilateral chronic secretory otitis media, osteomyelits, pharygotonsilitis and

right hip septic arthritis were seen in 10(23.8%), 10(23.8%), 7(16.7%), 6(14.3%), 4(9.5%), 1(2.4%), 1(2.4%), 1(2.4%), 1(2.4%) and 1(2.4%) children respectively. Table 5 shows the diagnoses in the children studied. The seven cases of malaria were uncomplicated in 4(57.1%) and due to severe anaemia, protracted vomiting and cerebral malaria in each of the remaining respective cases. Of the 10 cases with pneumonia, 3 were presumed to be caused by pneumocystis jeroveci and the etiologies of the others could not be ascertained either because of no growth bacteriological studies in 3 or inability to carry out the required tests because of financial constraints in 4

Staphylococcus aureus was recovered from the blood culture and joint aspirate of a child with septicaemia and the child with arthritis respectively. No organisms were recovered in four and the remaining 5 could not afford the blood culture investigation. Plasmodium falciparum was detected in the blood film of all the patients with malaria. Candidiasis was responsible for airway obstruction in the child with croup.

Complications and sequelae in the children admitted

Bronchopneumonia was complicated with bilateral effusion and febrile convulsion in one child. In addition hearing impairments complicated the case with bilateral chronic secretory otitis media. Auto-digital amputation complicated the case of the osteomyelitis of the right index finger, while the child with the right hip arthritis developed ankylosis and shortening of the right leg. Hemiparesis complicated both cases of cerebral malaria and meningitis. In addition the child with meningitis developed facial palsy. Immune reconstitution syndrome complicated the treatment of three of the five children with disseminated tuberculosis. Table 3 shows the diagnoses and complications of the admitted children

Clinical staging and immune status.

Concerning the clinical staging of HIV disease in the admitted children, 9 were in stage II, 32 in stage III and one in stage IV. No child was in stage I. The clinical staging at admission was the clinical staging at HIV infection detection. The mean CD4 count of the patients studied was 758ul. Twenty (47.6%) of the children had a severe immunosuppression (CD4<15%), while the remaining 22(57.6%) did not have severe immune suppression (CD4>15%)

Nutritional status

Nine(21.4%) of the 42 children were well fed and 33(78.6%) were malnourished. Amongst the 30 children aged 5years and less, failure to thrive was recorded in 20(66.7%), marasmus in 8 and under weight in 2.Stunting was recorded in 10 children, however none of the children had kwashiorkor or marasmic kwashiorkor.

Association between nutritional status and CD4 count

Of the 33 children with severe malnutrition 19(57.6%) had severe immunosuppression while one(11.1%) child had immunosuppression amongst the nine well nourished. The differences between these two groups are statistically significant. (p=0.01, OR= 0.09, CI=0.01-0.82)

Drug administration

HAART was administered to 12 of the 42 children. Of the 12 on HAART four(25.0%) had initiated treatment before admission and the remaining eight(75.0%) while on admission. HAART administration was initiated after the intensive phase of anti-tuberculous drugs in those co-infected with tuberculosis. Four of the 5 patients on HAART had sequelae compared with the one with single case of sequela in the 30 not on HAART (p<0.01, OR=0.07, CI= 0.01 – 0.71). No deaths were recorded among the patients on HAART in contrast to the 9 deaths amongst patients not on HAART (p = 0.04, OR = 1.41 CI= 1.12 – 1.77).

Ceftriaxzone was administered to all those with bacterial pneumonia and septicaemia and co-trimoxazole was administered those with presumed Pneumocystis pneumonia. Ampicillin and cloxacillin combinations were administered to those with bone and soft tissue infections.

Adverse drug reaction and immune reconstitution syndrome

One of the patients developed toxic epidermal necrolysis to administration of co-trimoxazole. This was later complicated by acute renal failure in the same patient and ultimately death. Immune reconstitution syndrome was recorded during the initial phase of anti-tuberculous drug treatment in three of the five children with disseminated tuberculosis. The children were on rifampicin, isoniazid, pyrazinamide and ethambutol.

Outcome

Of the 42 children studied 33(78.6%) survived while 9(21.4%) died. The 9 deaths represent 4.7% of the total 191 deaths amongst the paediatric admissions, excluding neonatal admissions. The cause of death in the nine are immune reconstitution syndrome in patients treated for disseminated tuberculosis, pneumocystis jeroveci pneumonia, bacterial bronchopneumonia with heart failure, septicaemia and severe malaria in 2,2,2,1,1 and 1 cases respectively. Acute renal failure secondary to toxic epidermal necrolysis with thrombocytopaenia from hypersensitivity reaction to co-trimoxazole administration complicated deaths among one of the previously recorded cases of mortality.

A significant difference exists between the eight(40.0%)

deaths recorded amongst the 20 children with severe immune suppression (CD4<15%) compared with the one(4.5%) death amongst the 22 without severe immunosuppression (CD4>15%).(p<0.01, OR=0.07, CI= 0.01 – 0.64). None of the patients on HAART died compared with the 9 mortalities recorded in the group not on HAART.

Duration of hospitalization

The duration of hospitalization ranged from 3 to 45 days and the mean duration of hospitalization was 13.4days. The average time spent on admission by those with septic arthritis, tuberculosis, septicaemia, meningitis and malaria was 63,35,15,14 and 3 days respectively.

DISCUSSION

The present study shows that HIV is an important cause of morbidity and mortality in children. Our hospital prevalence of 1.7% is smaller in comparison to the 5.7 and 8.3 percent estimates obtained at two Nigerian tertiary hospitals in Abuja, and Sokoto respectively. [5,10] Similarly, the 4.7% mortality estimate obtained in the present study was smaller compared to the 28.6 and 22.4 percent at Abuja and Sokoto. The lower admission and mortality rates recorded in the present study may be attributed to differences in times when study was conducted and the study locations. The Abuja and Sokoto study were carried before the scaling up of treatment for HIV specifically 6 and 11 years ago.[5,10] Abuja and Sokoto are located in Central and Northern region of Nigeria respectively, while the present study was conducted in South west Nigeria.

A vertical mode of transmission was the most common mode of acquisition of HIV in this study and this finding is consistent with most studies.[4,5,10] However, it contrasts sharply with the study conducted in East Nigeria where 68% of the children contacted HIV through by blood transfusion.[11] The average at presentation varied from available studies, it was higher than the 16 months reported at Abuja and lower than the 5.7 years obtained in India.[5,12] The differences obtained in the mean age estimates between the Abuja and India study may be explained by the variances in the age composition. Children aged below 18months were excluded at India, while there was a predominance of infants in the Abuja study. Most of the children in the present study were in the age category between 1 -5years.

No adolescents were recorded in this study this and the reason might not be unconnected with the fact that early access to anti-retrovirals is just taking its root in Nigeria and perinatally infected children are likely to have died before attaining adolescence without access to these drugs. Anti-retrovirals have been documented to be important for survival of perinatal infected children to adolescents.[13] No gender predilection was noted in this study, indicating both sexes have equal chances of admissions.

The predominant clinical features in the present study were fever, generalized lymph node enlargement, hepatosplenomegaly, cough, skin disease, failure to thrive, weight loss, diarrhoea and pallor and they accounted for more than 70% of the findings. The preponderance of skin disease such as candidiasis and other non specified rashes further underscores the point that the presence of cutaneous disease may be a pointer to underlying HIV infection. Treatment of identified cutaneous disease is important from the point of managing the patient holistically and for cosmetic reasons. Pneumonia, septicaemia and tuberculosis were the most common indications for admissions. Previous studies have reported similar clinical features and diagnoses.[9,10, 11,12,14].

Most of the children studied presented with advanced HIV disease, probably because advanced disease is associated with more severe secondary infections that may necessitate admissions. Some of the secondary or opportunistic infections were associated with complications and duration of admission in this study is similar to previous studies.[5,14] Isolation of bacterial pathogens and Pneumocystic Jeroveci was a challenge in the present study, because of financial constraints and non-availability of broncheo-alveolar lavage respectively as previously documented. [5,9,12]

Severe malaria was a common diagnosis in the present study and it manifested with life threatening manifestations like severe anaemia that could have acutely lead to death and neurologic sequelae in the child with cerebral malaria. It is important to note that sequelaes complicated all bone and neurologic infections. Our findings in this present study shed light on sequelaes that follow infective conditions. Severe malaria as an important cause of morbidity in HIV infected children which were hitherto not reported in previous reports.[4,5,9,12,14]The absence of information on sequelaes in previous reports may be related to restricted access or inability to access HAART at that time and this could have led to death.

The mortality rate of 4.7% reported in this study is lower compared to the 28.6% and 22.4% obtained from other Nigerian studies conducted before the scale up era. Studies conducted in both developing and developed countries have shown that HAART administration improves survival in HIV infected children. [15, 16] Furthermore, the present study further shows a statistically significant association between HAART and survival. Administration of HAART conferred a protective effect against death. The two major causes

of death in this study were infections and the complications of treatment namely, toxic epidermal necrolysis complicated by renal failure and immune reconstitution syndrome (IRS). It is interesting to note that the drugs implicated were antibiotics for treating opportunistic infections.

Studies on IRS and ADR in HIV infected children from developing countries are rare.[17,18] However, more studies are needed on IRS and ADR in other to determine the factors that predispose to them and how to avoid or manage these condition in order to avoid death. Mortality was also significantly associated with severe immunodeficiency in the present study. This finding is consistent with previous reports. [15,19,20]

CONCLUSION

Human Immunodeficiency Virus is an important cause of morbidity and mortality amongst paediatric admissions. The most common mode of transmission is vertical with fever, cough failure to thrive and chronic diarrhoea being the common manifestations. Secondary or opportunistic infections are the leading cause of death in among admitted HIV infected children. A significant association exists between death, severe immunosuppression and failure to use HAART. Prompt initiation of anti-retroviral therapy is recommended for protection against death.

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Table 1: Subject characteristics

Characteristics	Number (n=42)	Percentage
Mean age ± standard deviation; (range)	3.7±2.9 (2 months – 10 years)	
Sex		
Male	21	50
Female	21	50
Nutritional status		
Well nourished > 2S.D	9	21.4
Moderate malnutrition < 2 S.D	32	76.2
Severe malnutrition < 3 S.D	1	2.4
Mode of acquisition of HIV		
Vertical	41	97.6
Horizontal(from blood transfusion)	1	2.4
HAART		
Yes	12	28.6
No	30	71.4
Outcome		
Survived	33	78.6
Dead	9	21.4

Table 2: Clinical features

Clinical Features	Frequency n = 250	Percentage (%)
Fever	35	14.0
Hepatosplenomegaly	30	12.0
Generalized lymph node enlargement	23	9.2
Cough	21	8.4
Failure to thrive	20	8.0
Thrush	19	7.6
Diarrhoea	18	7.2
Wasting (weight loss)	17	6.8
Pallor	15	6.0
Dyspnoea	13	5.2
Microcephaly	10	4.0
Skin rashes	9	3.6
Dehydration	6	2.4
Parotid gland enlargement	4	1.6
Limb swelling	3	1.2
Developmental delays	2	0.8
Abdominal masses	2	0.8
Thrombocytopeania	1	0.4
Oliguria	1	0.4
Purulent ear discharge	1	0.4

Table 3: Diagnoses, complications andsequelaes of secondary infections.

Diagnoses	Frequency	Acute Complications	Frequency (%)	Chronic Sequelae	Frequency (%)
Pneumonia	10	pleural effusion febrile convulsion	1(10.0%) 1(100.0%)	Nil	0(0%)
Tuberculosis	10	pleural effusion	1(10.0%)	Nil	0(0%)
Septiceamia	10			Nil	0(0%)
Malaria	7	Severe anaemia	1(14.3%)	Nil	0(0%)
		Protracted vomits	1(14.3%)	Nil	0(0%)
		Cerebral malaria uncomplicated	1(14.3%)	*Hemiparesis & hearing loss	1(100.0%)
			4(57.1%)		
Septic arthritis	1	Nil	0(0%)	Ankylosis and limb shortening	1(100.0%)
Osteomyelitis of the right ring finger	1	Nil	0(0%)	Amputation of the terminal phalanx	1(100.0%)
Meningitis	1	Nil	0(0%)	Hemiparesis and facial palsy	1(100.0%)
Chronic otitis media	1	Nil	0(0%)	Hearing impair-ment	1(100.0%)
Pharyngotonsilitis	1	Nil	0(0%)	Nil	0(0%)