ORIGINAL ARTICLE

The Clinical Features of Paediatric HIV/AIDS at Presentation at the University of Abuja Teaching Hospital, Gwagwalada

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Abstract

***Background**: The reported geographical differences in the HIV-1 sub-type across the continent and the entire world makes it necessary to investigate whether the clinical presentation and outcome of such presentation can demonstrate differences in the multiple sub- type of HIV-1 infection. To determine whether the clinical presentations and outcome of HIV/AIDS in children in Abuja, Nigeria conforms with reports from elsewhere both within and outside the country.*

***Method:** A one- year prospective study of HIV infected children attending the University of Abuja Teaching Hospital (UATH), Gwagwalada, from November 2006 to October 2007,was carried out to determine the clinical presentation and outcome of such presentation in the area.*

***Results**: A total of 173 patients were diagnosed with signs and symptoms of HIV/AIDS and on antiretroviral therapy (ARVT). There were 90 (52.0%) males and 83 (48.0%) females giving a male to female ratio of 1.1:1. Less than 5 years constituted 81.5% of paediatric patients seen, with less than 2 years responsible for 52.0% of cases, and 11.8% being those between the ages of 10-15 years. The commonest presenting complains were that of recurrent fever (80.3%), progressive weight loss (77.5%), and persistent diarrhoea (69.1%). Chronic cough (62.2%) and skin rashes (52.7%) were equally common. While persistent diarrhoea, oral thrush, discharging ear, and failure to thrive were commoner in children less than two years, generalised lymphadenopathy, skin rashes and parotid swelling were commoner in older children. Mortality rate was found to be 3.5%, while WHO case definition for paediatric HIV/AIDS in African setting was found to be sensitive with low specificity and positive predictive value (PPV).*

***Conclusion:** Clinical presentation of paediatric HIV/AIDS appears similar with reports from other centers in spite of the wide variation in HIV-1 sub-types. Mortality was also found to be low. This was attributed largely to the availability of free antiretroviral drugs (ARVD), potent antibiotics and anti-fungal agents which were made freely available to HIV infected patients. The findings underscore the need for government to extend such services to HIV/AIDS patients across the country as a major way of reducing the sufferings of this scourge in children..*

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Introduction

Sub-Sahara Africa (SSA) has continued to bear the greatest burden of paediatric HIV/AIDS epidermic in the whole world.[1] The magnitude of the problem has continued to increase in the sub-region since the first case was reported two decades ago.[2] The World Health Organization (WHO) in 2006 has estimated that over 90% of 2.3million children living with HIV in the world over resides in SSA.[2,3] While there is a reduction in the number of new cases in the developed world due to advances in the medical management of the disease, a vast majority of new case still occur in the developing countries. [4] In Nigeria for example, HIV infection has continued to record an exponential increase with only a slight drop recently. According to recent reports, in 1992 the sero-prevalence rate was 1.8%, this steadily increased to 3.8% by 1994, 5.4% and 5.8% in 1999 and 2003, and then to 4.4% in the year 2005.[5] It has been projected that the annual deaths due to HIV/AIDS in children may increase from 31,000 in 2000 to about 56,000 by 2010.[5]

The clinical features of HIV/AIDS appears to varies from one part of the world to another. While some studies observed weight loss, recurrent fever, skin rashes as their main clinical presentation, others reported chronic cough, generalized lymphadenopathy, parotid swelling as their own main clinical features.[6-9] In Africa for example, there are many sub-types of HIV-1 virus,

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ranging from A to D.[2] While A and D is common in East and Central Africa, C is commoner in the South Africa, while A recombinant is predominant in West Africa.[2] The sub-type C which is responsible for over 90% of infection in South Africa is more virulent than other sub-types. It has a higher transcription rates, is associated with faster disease progression and has a higher motherto-child transcription than sub-types A and D which are more prevalent in West Africa.[2] It therefore became questionable whether the consequences of HIV-1 infection observed in studies from different countries can be generalized across the multiple sub-types found in Africa in general, and Nigeria in particular.

Centre for Disease Control (CDC) in the United States of America (USA) has established strict criteria for the diagnosis of Paediatric HIV/AIDS,[2] this involves use of expensive diagnostic technology out of reach of most developing countries, especially in Africa setting. The World Health Organization (WHO) now proposed a much simpler protocol for diagnosis of paediatric HIV/AIDS in Africa setting.[10] However, some reports have demonstrate lack of sensitive and specificity of the protocol with poor positive predictive value (PPV),[7,9,11,12] others have shown high sensitivity, but suggested pneumonia to be included in the major classifying features.[7,11,12]. Going by the WHO protocol of HIV/AIDS diagnosis in children in African setting, the aim of the present study is to document the clinical signs and symptoms of this disease at presentation in children in the Federal Capital Territory (FCT), Abuja and to compare the findings with reports from other centers. It is also aimed to determining the outcome of such presentations as well as the sensitivity and specificity of WHO case definition for HIV/AIDS in African setting .

Patients and Methods

The study was a prospective one, conducted at paediatric outpatient special treatment clinic (POSTC) for HIV/AIDS children at the UATH, Gwagwalada, over a one year period, from November 2006 to October 2007. University of Abuja Teaching Hospital is a 350 bed capacity referral hospital, sub-serving FCT and neighbouring states including Nasarrawa, Kogi, Benue, Niger and part of Kaduna. It one of the first centers to start offering free HIV/AIDS services in the country, through Presidential Emergency Programme for AIDs Relief (PEPFAR), courtesy of United State of America (USA) government.

The subjects were paediatric patients aged 2 months to 15 years who were attending POSTC and were positive for HIV infection either by serological method or by deoxy-ribonucleic acid (DNA) polymerase chain reaction (PCR) test. For children from 18 months and above, sera was screened for the presence of HIV 1 or 2 antibodies using commercially available recombinant antigen based double ELIZA test (STATPAK by Chemsio Diagnostic System New York) with sensitivity and specificity of 100%. For those less than 18 months of age, double ELIZA and DNA PCR test was used for the diagnosis of HIV. DNA PCR test amplifies and detects the HIV pro-viral DNA sequences within the mono nuclear cells in the blood, it is the gold standard test for diagnosis HIV infection in infancy in the developed countries [20]. The test is 100% sensitive by 4 to 6 weeks of postnatal life. [2,13]

On recruitment of patients, a thorough history and physical examination was carried out. This included history of presenting complain, duration of such complains, age, sex of the patient, possible mode of transmission of HIV infection, general physical examination, as well system by system examination. The WHO[10] clinical case definition for Paediatric HIV/AIDS was applied for all subjects at recruitment. The major features were weight loss or failure to thrive, chronic diarrhoea (> one month), prolong fever (> one month), while the minor features were generalized lymphadenopathy of 0.5cm present in two or more areas, with bilateral lymph modes counting at one site, repeated common infections (otitis, oropharyitis, sinusitis etc), orophargnyeal candidiasis, generalized dermatitis, and confirmed HIV status of the mother. [10] Under this classification, paediatric HIV/AIDs was suspected when there are at least two major features with two minor ones in the absence of known cause of immuno suppression. Baseline full blood count with differentials and CD4 count were done to determine the CD4 count as well as its percentage in the peripheral blood.

WHO clinical and immunological staging[3] was equally carried out for all positive subjects to determine those to benefit from highly active antiretroviral therapy (HAART).[3] Those who met the clinical and immunological criteria as pointed out in paediatric HIV/AIDS National guideline[3] were commenced on antiretroviral therapy. Those who did not meet the criteria for commencement of HAART were followed up and monitored with quarterly CD4 cell count/percentage at POSTC. Patients who requires admission were admitted and opportunistic infections treated accordingly before continuation or commencement on HAART at POSTC.

Ethical approval was obtained from the ethic committee of the hospital, as well as signed or thumb printed

informed written down consent from the mothers of the subjects. The research data will be coded, and privacy of the study subject will be protected and confidentiality maintained at all times. Data analysis was conducted using SPSS program version 7.5 which provided standard deviation, test of significance and frequency tables. The chi-squared was used were appropriate and test of significance when p-value was less than 0.05.

Results

A total of 173 patients with signs and symptoms of HIV/AIDS were studied, there were 90 (52.0%) males and 83 (48.0%) females given a male to female ratio of 1:1:1. Fifty two percent of the recruited patients were children less than 2 years, while under five years constituted 81.5% of the entire patients. Only 11.8% were children between the ages of 10-15 years. HIV infection in the two categories of paediatric age group, i.e < 5 year and > 10 years was statistically significant, X^2=8.347 df=3, <0.05, (table 1).

Table 11 shows the signs/symptoms of patients at presentation, as well as WHO clinical staging system for HIV infection in infants, children and adolescent. The commonest presenting complaints at presentation were recurrent fever (80.3%), weight loss (77.5%), chronic diarrhoea (69.1%), chronic cough (62.2%), and skin rashes (52.7%). Non-Hodgkin lymphoma (0.6%), muco-cutaneous Kaposi sarcoma (1.7%), and severe jaundice (2.3%) were rare finding in HIV positive children especially those with severe immune suppression. While chronic diarrhea, discharging ear, oral thrush and failure to thrive were commoner in younger age group of less than 2 years, (69.7%, 73.4%, 65.3% and 78.8% respectively), skin manifestation and parotid swelling were commoner in older children between the ages of 5-15 years (79.7% and 48.3%). Two cases of muco-cutaneous Kaposi sarcoma (KS) were diagnosed histological during the one study period. First case was a 13 years HIV naive male patient with 4 month history of subcutaneous painless nodular swelling on the right check extending to the right eye. The second case was a 15 year old boy with multiple painless nodular swellings on the inner aspect of the right forearm and a patchy licheniod lesions from below the knee of left leg with bilateral lymph-oedma of both lower limbs. Of the 108 that presented with chronic cough 31(19.2%) were diagnosed as having tuberculosis (TB), while 75 (69.4%) had clinical and radiological features of pneumonia. No bronchial lavage was performed for the diagnosis of pneumocystis carinnii pneumonia.

Using HIV serology as a standard for HIV diagnosis, the sensitivity/ specificity and positive predictive value (PPV) for WHO case definition for paediatric case, and clinical features at presentation were tested. The WHO criteria gave a sensitivity of value of 73.6%, specificity and PPV of 43.2% and 48.5% respectively. The following clinical manifestations had significant PPV as follows; chronic diarrhoea 55.0%, recurrent fever 58%, persistent cough 50%, severe weight loss 52.0%, herpes zoster 100.0%, generalized lymphadenopathy 92.0%, skin and manifestation of 69.0%.

Of the 134 patients that had progressive weight loss with features of protein energy malnutrition (PEM), 121 (90.2%) had marasmus, 11(8.2%) were under weight, while 2(1.5%) had marasmic-kwashiorkor, non presented with kwashiorkor using World Health Organization (WHO) 1970 classification of PEM. Generalized lymphadenopathy was recorded in 90 (40.9%) while hepatosplenomegaly was identified in 77 (44.4%) of patients. Though discharging ear was a common findings in 33(19.2%) of cases, 29 (87.9%) of such cases was seen in children less than one years. Neurological manifestation ranged from delayed milestone 18/30 (60%), to loss of acquired milestone in 10/30 (33.3%), and cryptococcal meningitis 2(6.7%).

Table III represents the out come of 173 patients seen and managed at the POSTC over a one year period. One hundred and fifty two (88.0%) of the patients were alive and healthy and on first line drug treatment. Three (1.7%) were on second line medication following clinical, immunological and virological evidence of failure of first line drug treatment. Thirty (17.3%) of patients on first line drug were transferred to other HIV/AIDS treatment centers on request. Ten (5.7%) were lost to follow up and 6 (3.5%) died. Two patients (1.1%) discontinued ARVD, as a result of adherence failure following several serious counseling sessions. Of the six patients that died, 2 (33.3%) was as a result of severe pneumonia, another 2 (33.3%) from severe jaundice with positive antibody to hepatitis B surface antigen, the remaining two, 1 (16.7%) from HIV encephalopathy and another 1 (16.7%) from severe anaemia with septicaemia.

Table I: Age and Sex distribution of HIV positive patients

Age (years)	Male	Female	Total	% of Total
0 1.99	49	41	90	52.0
2 4.99	28	23	51	29.5
5 9.99	5	7	12	6.7
10 15	8	12	20	11.8
Total	**90**	**83**	**173**	**100.0**

Table II: Clinical manifestation and WHO Clinical staging of HIV positive infants, children and adolescents at presentation.

Clinical Features at Presentation	Total No.	% age of Total	WHO Clinical Stage
Recurrent fever	139	80.3	3
Progressive weight less	134	77.5	4
Persistent Diarrhoea	120	69.1	4
Chronic cough	108	62.2	4
Pallor	112	64.7	3
Skin rashes	91	52.7	2
Generalized lymphadenopathy	90	52.6	2
Hepatosplenomegly	77	44.4	2
Oral thrush	70	40.4	2
Ear discharge	33	19.2	2
Neurological manifestation	30	17.3	4
Parotid swelling	15	8.4	2
Refusal to feed	13	7.5	4
Herpes zoster	6	3.5	2
Jaundice	4	2.3	4
Kaposi Sarcoma	3	1.7	4
Lymphoma	1	0.6	4

Table III: Outcome of HIV positive patients

Variables	Total No	Percentages
Alife and on 1st line drug	152	88.0
,, ,, ,, 2nd line drug	3	1.7
Lost to follow up	10	5.7
Discontinue ART	2	1.1
Dead	6	3.5
Total	**173**	**100.0**

ART anti-retroviral therapy

Discussion

The clinical features of HIV infection in the present study is keeping with both WHO case definition for Paediatric HIV in Africa[8] and findings from elsewhere both within,[15-19] and outside[9-14] the country. The presenting clinical features that were highly sensitive and specific with high PPV of HIV infection in children were progressive weight loss, persistent diarrhoea, chronic cough, recurrent fever, generalized lymphadenopathy, herpes zoster, and skin rash. These were in conformity with result elsewhere,[7-10,15] and supports the WHO major and minor clinical manifestation of peadiatric HIV/AIDS in African setting. However, the case definition for paediatric AIDS by WHO with pneumonia not inclusive as a major clinical manifestation as observe by many workers,[7,11-12] appears a bit uncontroversial. The present study was very much in support of earlier suggestions made by Ojukwu,[7] Beyene,[6] and Schneider[12] whom were of the opinion that pneumonia should be considered a major classifying features of paediatric HIV/AIDS in the developing countries, considering the fact that it contributed significantly in morbidity as well as mortality in their various studies as well as in the present one. The higher incidence of pneumonia in paediatric HIV patients as demonstrated in many studies was however not observed in a ten year review study by Fetuga and co-workers,[14] who instead noticed a very low cases of pneumonia in their study population.

Other uncommon clinical features associated with severe immune suppression in this study were muco-cutaneous KS, non-hodgkin's lymphoma, and severe jaundice. Reports of KS co-existing with HIV infection in children are rare in this country.[7,14-18] This is in contrast to some other African countries like Uganda where KS co-existing with HIV infection in children is common.[19,20] Pulmonary KS which usually presents with cough, progressive dyspnoea and radiological features of bilateral interstitial infilterate with mediastinal lymphadenopathy[2] could be mistaken for pulmonary tuberculosis (PTB) or lympoid interstitial pneumonitis (LIP) especially when there is minimal muco-cutaneous manifestation,[2,19] and may be responsible for the low cases seen in this environment..

Another rare clinical manifestation in association with severe immune suppression in HIV infection in this study was severe jaundice seen in four patients, two of whom were positive for hepatitis B surface antigen. Most reports on clinical features of HIV infection in children in the country were also very silent on its co-existent with jaundice.[7,14-19] Reports from elsewhere have highlighted increased risk of chronicity of HIV infection with exposure to hepatitis B virus (HBV).[21,22] Suggestions were made on a direct putative effect of some HBV factors on HIV transcription which favors an enhanced HIV replication with resultant faster CD4 T-cell decline in HIV/HBV co-infector.[24] In support of increased risk of chronicity and poor prognosis of HIV infection co-existing with HBV is the liver histological findings showing progressive and rapid deterioration with shortened time frame of HBV related complications and death.[2122]

Pallor was not documented as a common manifestation of HIV infection in children in most reports in the country.[7,14,15,17,18] However the present study reported 64.7% cases of pallor which was a bit lower than 73.7% earlier reported in Jos in 1996.[16] It appeared surprising why many researchers from different parts of the country[7,14,15,17,18] did not demonstrates pallor as a major

manifestation of HIV infection in children, considering the fact that anaemia of chronic infections associated with chronic HIV disease will be expected to worsen the nutritional anaemia, anaemia of malaria, sick cell disease, helminthiasis and micro-nutrient deficiencies which are prevalent in children in the country.[23,24]

It is widely believed that HIV infection predisposes an individual to TB infection. In children, the prevalence ranges from 10% to 60%, with the highest prevalence occurring in South Africa, and the lowest cases reported in West Africa.[2] The TB prevalence rate of 19.6% obtained from the present study appeared similar to 15.6% reported at Nnewi,[18] but much lower than 48.0% from South Africa study.[26] Apart from geographical locations and disease burden in adults, culture proven diagnosis of TB used in South African studies appeared more realist and probably responsible for the high prevalence of TB features obtained in their study.[26]

The age distribution of paediatric HIV/AIDS patients in this study does not differ much from what was obtained in the previous studies.[2,3,7,12-18] In conformity with earlier reports, more than 80% of children manifesting with features of HIV/AIDS were less than five year, with under two responsible for over 50% of the patients. This reflects the magnitude and influence of maternal HIV infection in their children which needs an urgent intervention to address this menace.

The mortality rate of 3.5% observed in the present study was in keeping with 4.7% from Nnewi.[18] The two centers offer free ARV treatment to HIV victim courtesy of U S government. In addition to free ARV treatment made available to patients, potent antibiotic, antifungal, antiviral, anti-TB, laboratory and supporting services were also made freely available to patients in this study. This was in contrast to high mortality in areas with little or no availability of free ARV interventions.[6,7,14-17,27] While Uganda[9] and Abakiliki[7] studies reported 23.5% and 38.7% mortality, Ile-Ife[15] observed 46.3% and Shagamu[14] noted 33% mortality. High mortality rates were recorded in centers where free ARV treatment were not available to patients. This brought to focus the havoc HIV/AIDS is wrecking among African population were ARV treatment were not readily available to patients either free of charge or at a cost they can afford.

Conclusion

Clinical presentation of HIV/AIDS in this study appears similar to the WHO case definition of Paediatric HIV/AIDS in Africa as well as findings from other centers both within and outside the country. WHO case definition however lack some degree of specificity and sensitivity with low PPV. Mortality was also found to be low and this was largely attributed to availability of free ARVD, with free potent antibiotics, antifungal, antiviral and anti-TB agents made available to patients. The findings underscores the need for government to extend this laudable gesture to infected individuals in remote areas across the country either free of charge or at a cost they can afford.

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