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Paediatric HIV/AIDS in Abakaliki

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Summary

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Background: The increasing prevalence of HIV infection in Nigeria makes it desirable to document the clinical features of the disease in environments where there are often limited financial resources for HIV testing.
Objectives: The study was aimed at determining the mode of transmission, clinical presentation, and outcome of HIV infection in children admitted with clinical manifestations suspicious of HIV infection. It was also to examine whether the WHO clinical case definition for paediatric AIDS in Africa could help predict the infection in the local community.
Method: A retrospective review of 342 patients aged between one month and 15 years, who were admitted and screened for suspected HIV infection between January 2000 and September 2001, was carried out.
Results: Forty-six (13.7 percent) of the 342 patients were confirmed positive. However, adequate clinical data was obtained in only 31 patients. Vertical transmission was a significant source of infection in these children ($p<0.05$) having been documented in 21 (67.7 percent) of the 31 patients, while four (12.9 percent) were probably infected through blood transfusion. The main clinical features in HIV positive children at presentation were persistent and/or recurrent fever (90.3 percent), progressive weight loss (83.9 percent), chronic diarrhoea (67.7 percent), persistent cough (64.5 percent), generalized lymphadenopathy (51.6 percent), dermatitis (48.4 percent), and oral candidiasis (41.9 percent). Only 54.8 percent of the HIV positive patients presented with features corresponding to the WHO case definition of paediatric AIDS in Africa. Seven patients died (22.6 percent) and 19 patients were lost to follow up. Pneumonia constituted a significant morbidity (64.5 percent) as well as the commonest (57.1 percent) cause of death.
Conclusion: The WHO clinical case definition for paediatric AIDS in Africa was poorly sensitive and poorly specific in this study. In view of this, HIV screening is of vital importance in the diagnosis of AIDS. Prevention of vertical transmission through the prophylactic use of anti-retroviral therapy in pregnancy may be the most powerful tool against HIV infection in the community.

Key words: HIV/AIDS, paediatric age group

Introduction

SINCE the first cases of paediatric acquired immunodeficiency syndrome (AIDS) were described elsewhere in 1983[1] and in Nigeria in 1986,[2] the HIV pandemic has continued to evolve in both magnitude and diversity with a profound impact on the health and survival of children. While there has been a reduction in the number of new AIDS cases in the United States and Western Europe due to advances in treatment, a vast majority of new infections still occur in developing countries and currently, Africa remains in the eye of the storm.[3] HIV infection in Nigeria continues to record an alarming exponential increase from 1.8 percent sero-prevalence in 1992, through 3.8 percent in 1994, 4.7 percent in 1997, to 5.4 percent in 1999[4] among sexually active population of 15 years and above. Current projections on annual child deaths due to AIDS in Nigeria, show that the number of deaths may increase from around 37,000 in the year 2000 to about 56,000 in 2010.[4] Earlier reports on HIV infection in children were in those who received transfusion of blood or its products. However, African women of child-bearing age are becoming increasingly vulnerable to HIV infection, and this has led to an

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increase in the number of paediatric HIV infections due to mother to child transmission (MTCT) during pregnancy, delivery and breastfeeding.[5] Locally, HIV sero-positivity has been reported to be as high as 11.1 percent in pregnant women who register for antenatal care.[4]

The Centers for Disease Control (CDC) in the USA has established strict criteria for the definition of paediatric AIDS. These criteria are of limited use in developing countries because of the unavailability of expensive diagnostic technology. As a result, the World Health Organization (WHO) proposed a much simpler case definition of Paediatric AIDS for Africa.[6] However, there are doubts about the sensitivity and specificity of this definition due to the overlap that exist with common childhood diseases on the continent. Various clinical aspects of paediatric AIDS have been reported in many countries in Africa.[5,7,8] However, the true magnitude, prevalence and mode of transmission of paediatric AIDS in Nigeria remain largely unknown as a result of under-reporting and the paucity of reports on its clinical manifestations.[9-11]

The objective of this study was to determine the mode of transmission, clinical presentation, the sero-positivity and the outcome of HIV infection in children admitted to the Ebonyi State University Teaching Hospital (EBSUTH), Abakaliki. It was also aimed at evaluating the sensitivity and specificity of the WHO clinical case definition for paediatric AIDS in Africa in predicting HIV infection in the locality.

Patients and Methods

The present retrospective study was carried out at the EBSUTH, Abakaliki, Ebonyi State. The hospital is a major referral centre serving an estimated population of over two million people and a sentinel site used for the 1999 national HIV sero-prevalence survey on antenatal clinic attendees. The state was designated a *'hot-spot'* state for HIV infection among the states in the south-east zone of the country because of its recorded high sero-prevalence rate of 11.1 percent in the 1999 national survey.[4] It is home to a thriving national/international rice industry/market, while the majority of the inhabitants are peasant farmers. The area is replete with long distance lorry drivers both on temporary and permanent basis.

The study involved children who were suspected to be HIV positive, and were admitted to the hospital between January 1, 2000 and September 30, 2001. The usual practice in the hospital was to routinely screen admitted children for HIV if they had clinical evidence of immunodeficiency, or were to undergo surgery; others were infants of HIV positive mothers, and those with past history of blood transfusion, rape or sexual abuse. The cases included in this study were children aged one month to 15 years who had clinical features suspicious of HIV infection, who were either HIV negative or HIV positive by ELISA and confirmatory test. In children less than 18 months of age, the diagnosis of HIV infection was made if they and their mothers were ELISA positive and also fulfilled the clinical criteria as recommended by WHO clinical case definition for paediatric AIDS in Africa. Those excluded in this age group were neonates, routine pre-operative patients and other asymptomatic patients. The WHO clinical case definition for paediatric AIDS in Africa[6] was applied in every case during data collection. The major features of this are weight loss or failure to thrive; chronic diarrhoea (>one month); prolonged fever (>one month), while the minor features are generalized lymphadenopathy measuring at least, 0.5cm and present in two or more sites, with bilateral lymph nodes counting as one site; oropharyngeal candidiasis; repeated common infections (otitis, pharyngitis, etc); persistent cough (>one month); generalized dermatitis, and confirmed maternal HIV. Under this definition, Paediatric AIDS is suspected when there are at least, two major features associated with at least, two minor ones, in the absence of a known cause of immunosuppression.

Sera were initially screened for the presence of HIV-1 or HIV-2 antibodies using commercially available recombinant antigen-based ELISA (*Immunocomb* from *ORGENICS, Israel*) supplied by the Petroleum Trust Fund (PTF). The test had a sensitivity of 100 percent and a specificity of 98 percent and detects antibodies to either or both viruses at the same time. Sera found to be positive at this stage were confirmed using *Immunocomb II HIV 1& 2 Combfirm* (developed by *ORGENICS, Israel*) also supplied by PTF. The test had a sensitivity of more than 99 percent and a specificity of 100 percent. A sample was considered HIV antibody positive if the serum was reactive in both tests. The test kits were used in strict compliance with the manufacturer's instructions.

Data extracted from the records of the subjects included age, sex, date of admission, presenting symptoms, physical findings, history of previous blood transfusion, use of non-sterilized body piercing instruments and the HIV status of the mother in order to establish the likely source of infection. The outcome of hospitalization was also noted for each patient. The data was analyzed using EPI info version 6. The chi-squared test was used where appropriate and P values less than 0.05 were considered significant. Sensitivity and specificity tests were also applied where appropriate.

Ethical approval

Approval for the study was obtained from the Ethics Committee of the ESUTH.

Results

Three hundred and forty two children were admitted with clinical manifestations suspicious of HIV infection during the period of study, but only 46 (13.7 percent) of these tested positive for HIV. Of the 46, only 31 case files were available for study; this was in addition to the 251 case files of the 296 who tested negative.

Table I

Age and Sex Distribution of HIV Positive Patients

Age (years)	*M*	*F*	*Total*	*% of Total*
< 3	10	10	20	64.5
3 - 6	1	1	2	6.4
7 - 10	4	2	6	19.4
11 - 14	-	-	-	-
>14	0	3	3	9.7
Total	15	16	31	100.0

$X^2 = 3.64$, $df = 3$, $p = 0.3033$

Table I shows the age and sex distribution of the HIV positive patients. The majority of the patients (64.5 percent) were less than three years old, while the male to female ratio was 1: 1.1. There was no significant variation of sero-prevalence with sex and age. Table II shows the age distribution of all the 282 subjects grouped into four categories. The first two groups were the 31 who were HIV positive; the first of these groups consisted of 17 (54.8 percent) confirmed HIV positive patients, who also satisfied the WHO clinical case definition of paediatric AIDS in Africa (true positive); the second consisted of 14 patients (45.2 percent) who were confirmed HIV positive, but did not have sufficient symptoms and signs to be classified as AIDS by the WHO case definition of paediatric AIDS in Africa (false negative). The remaining two groups were made up of the 251 patients who were seronegative for HIV; they were subdivided further into one group of 167 patients (66.5 percent) who satisfied the WHO clinical case definition of paediatric AIDS in Africa but were sero-negative (false positive), and the other group of 84 patients (33.5 percent) who were sero-negative and did not meet the WHO clinical case definition of paediatric AIDS in Africa (true negative). Sensitivity and specificity tests were applied using HIV serology as the gold standard for HIV diagnosis. The WHO criteria gave a low sensitivity of 54.8 percent and a low specificity of 33.5 percent. Thirteen (76.5 percent) of the 17 in the AIDS group and seven (50.0 percent) of the 14 in the false negative group, were aged below three years.

Table III summarizes the probable modes of transmission in relation to age. In 21 (67.7 percent) cases, it was most probably vertical, as both mother and child had HIV infections at the time of diagnosis. Seventeen (80.9 percent) of the 21 were less than three years; 13 (76.5 percent) of these 17 had full-blown AIDS on presentation. The oldest patient who probably acquired the infection vertically was 10 years old on presentation. This patient did not receive blood transfusion in the past, but the mother had died of AIDS four months prior to the patient's presentation,

Table II

Ages of Patients with Symptomatic HIV infection, AIDS, and HIV Negative Test

	HIV positive			*HIV negative*		
Age	*Symptomatic*	*AIDS*	*Total*	*Satisfied WHO Criteria*	*Did not satisfy WHO Criteria*	*Total*
<3	7	13	20	63	42	105
3-6	0	2	2	41	20	61
7-10	5	1	6	37	18	55
11-14	-	-	-	19	3	22
>14	2	1	3	7	1	8
Total	14	17	31	167	84	251

Table III

Probable Modes of HIV Infection

Age (years)	*Vertical Transmission*	*Blood Transfusion*	*Not established*	*Total*
<3	17	1	2	20
3-6	1	-	1	2
7-10	3	2	1	6
11-14	-	-	-	-
>14	-	1	2	3
Total	21	4	6	31

$X^2 = 9.044$; $df = 3$; $p < 0.05$

while the two-year old sibling was also HIV positive. Four children (12.9 percent) received blood transfusion in hospitals where HIV screening of donor blood was lacking. Three of the four were transfused during surgical procedures and the fourth was a nine-month old child who received blood transfusion following severe anaemia from complicated malaria infection at the age of six months. As their mothers' HIV serology was negative, it was presumed that these patients got infected through the transfusion of contaminated blood. Overall, the HIV infection transmission through the vertical route was statistically more significant than via blood transmission ($X^2 = 9.044$, df=3, $p<0.05$).

Table IV shows the initial symptoms and signs on admission in the 31 cases of HIV infection. The patients were grouped into those who satisfied the WHO clinical case definition for paediatric AIDS in Africa and those who had symptomatic HIV infection, but failed to satisfy the definition.

HIV positive children

The number of children with AIDS who presented with progressive weight loss, chronic diarrhoea, persistent cough, generalized lymphadenopathy, dermatitis and oral candidiasis was more than twice that in the symptomatic group. These features often occurred in combinations. Pneumonia occurred in 20 (64.5 percent) of the 31 patients. Of the 20, 19 had bronchopneumonia while one had lobar pneumonia. None had bronchial lavage performed for the diagnosis of *Pneumocystis carinii* pneumonia. Three of the five children admitted for possible septicaemia had blood cultures taken; the only positive culture grew *Staphylococcus aureus*. Blood films were examined for

Table IV

Clinical Features in 31 Children with HIV Infection

Features	*Symptomatic HIV infection*	*AIDS*	*Total*	*% of Total*
Persistent/recurrent fever	11	17	28	90.3
Progressive weight loss	9	17	26	83.9
Chronic diarrhoea	6	15	21	67.7
Persistent cough	6	14	20	64.5
Generalized lymphadenopathy	4	12	16	51.6
Dermatitis	3	12	15	48.4
Oral candidiasis	3	10	13	41.9
Hepatosplenomegaly	2	6	8	25.8
Otitis media	2	6	8	25.8
Neurological manifestation	1	5	6	19.4
Parotid swelling	2	1	3	9.7

malaria parasites in all the 28 patients who presented with persistent/recurrent fever, and this was positive in 21 who subsequently received appropriate anti-malarial drugs. Ten children had protein energy malnutrition; six (60.0 percent) of these were either severely underweight or marasmic, three had kwashiorkor and one marasmic-kwashiorkor. Chronic parotitis was also present in three of the 16 children with generalised lymphadenopathy. Of the two patients with tuberculosis, one had multiple cavitatory lesions on chest x-ray and the other had miliary tuberculosis. Six children, five with AIDS and the other one in the symptomatic group had neurological abnormalities. These were in the form of delayed milestones in five, and loss of previously acquired milestones in one. The dermatitis present in 15 cases consisted mainly of impetigo contagiosum, recurrent eczema and scabies. Eight children (25.8 percent) had suppurative otitis media, which persisted despite appropriate treatment.

HIV negative children

The diseases present in the HIV negative children included severe malaria in 221 (88.0 percent) of 251, gastroenteritis in 205 (81.7 percent) and pneumonia in 196 (78.8 percent). Others were septicaemia in 119 (47.4 percent), septic dermatoses in 65 (25.9 percent), sickle cell disease in 55 (21.9 percent), protein energy malnutrition in 51 (20.3 percent), tuberculosis in 39 (15.5 percent) and malignancy in 36 (14.3 percent); these conditions occurred singly or in combinations.

Outcome

Seven children (22.6 percent) in the HIV positive group died during the admission. Four (57.1 percent) of the seven died of pneumonia, two (28.2 percent) of pulmonary tuberculosis with septicaemia, while the remaining one (14.3 percent) died of chronic diarrhoea with severe anaemia and septicaemia. Nineteen patients were lost to follow up. Only five patients still attended the outpatient clinic for follow up and all had full-blown AIDS. From available records, none of the HIV positive children received anti-retroviral drugs. The patients still attending the outpatient clinic were placed on multivitamins, ferrous sulphate and trimethoprim-sulfamethoxazole prophylaxis.

Discussion

It is obvious from the present study that HIV infection in children is increasingly becoming a major problem in the area where this study was undertaken. Paediatric HIV/AIDS is now threatening much of the progress that has been made in child survival during the past 20 years. The high prevalence rate of 13.7 percent obtained in the present study is likely to represent the tip of the iceberg. This is partly due to the characteristics of the population, an underreporting of cases, and the fact that many children with HIV infection/AIDS die without reaching a health facility and thus, the diagnosis is never made.

The age distribution of patients in our study does not differ much from those in previous studies.[10,11] In keeping with other studies from Nigeria[9-11] and elsewhere in sub-Saharan Africa,[7,8] over half of these children manifested with features of AIDS by three years of age. Only a few infants have signs of HIV infection at birth but by one year, between 80-90 percent manifest features of AIDS,[8] reflecting the magnitude and influence of maternal HIV infection on our children. Vertical or mother-to-child transmission was the commonest mode of HIV infection in the present study, being responsible for 67.7 percent of the cases. This is similar to the 69.6 percent reported from Jos[11] but differs from the 30 percent in 63 HIV-positive children in Enugu.[10] Even though vertical transmission is believed to be the commonest route of HIV infection in children, accounting for about 75-80 percent of all paediatric AIDS,[1,7,12] there seems to be a considerable variation in the proportion of paediatric HIV infection attributable to such transmission in Nigeria. While there are major differences in study designs and areas, the time interval between the Enugu study (1989-1996)[10] and the present one (2000-2001) suggests a changing pattern in the mode of transmission. Furthermore, the Enugu study[10] was carried out when HIV screening of donor blood had not become widely available resulting in equal incidence of vertical transmission and blood transmission. Transmission by blood transfusion appears to be on a downward trend in our hospital, probably due to the scrupulous screening of donor blood before transfusion and the widespread practice of HIV screening of donor blood in the community.

The present study has shown that the WHO clinical definition of paediatric AIDS in Africa lacks optimal sensitivity and specificity in our locality. This is due to the presence of other prevalent childhood diseases such as malaria, gastroenteritis, pneumonia, malnutrition, non-specific dermatitis and failure to thrive which can mimic HIV infection. This is in conformity with previous studies in Nigeria[10,11] and elsewhere in Africa,[7,8] and suggests that clinical syndromes associated with HIV infection in African children are, without the aid of HIV serology, difficult to distinguish from those not so associated. Therefore, the diagnosis of paediatric AIDS requires a high index of suspicion. It is important that all children presenting with these

features, especially when recurrent or persistent, be suspected and screened for HIV infection.

The clinical manifestations of HIV infection observed in the present study were similar to previous reports from other nations.[1,7-12] However, pneumonia, which was identified as a significant cause of morbidity and mortality in our study was not included as a major classifying feature in the WHO case definition of paediatric AIDS in Africa. The present finding is similar to that reported by Schneider in 1999[13] who reported that pneumonia was significantly more common in persons who were HIV-infected especially with advanced HIV disease and immunosuppression than in the general population. Pneumonia may therefore be considered a major classifying feature for AIDS in developing countries. The incidence of tuberculosis was very low in the present study contrary to the widely held belief that HIV infection predisposes infected individuals to tuberculosis. Unfortunately, both patients diagnosed with tuberculosis died despite appropriate and adequate therapy. Neurological manifestation was seen in very few children in our study although it has been reported as being common in paediatric AIDS.[14] However, delayed attainment of normal milestones reported in the present study is similar to the findings in other series.[10] Similarly, otitis media was recorded in a small number of children in the present study; this is contrary to reports of its being a very common otological manifestation of HIV infection in children.[15] The reason could be that this being a retrospective study, there was incomplete documentation of subtle physical signs. However, as congenital HIV infection becomes more common, children may present initially with recurrent acute otitis media during the first year of life, since primary immune deficiency does predispose to otitis media.[15] Likewise, generalized lymphadenopathy has been classified as a minor finding in the WHO classification for paediatric AIDS in Africa. The present study as well as previous studies in Nigeria[10,11] and in other parts of Africa[16] have documented generalized lymphadenopathy in at least, 50.0 percent of patients with HIV infection. Inclusion of this physical sign as a major feature of AIDS is warranted considering its incidence in these studies.

Majority of the children were lost to follow up. This is not unexpected in an environment where the infection has continued unabated without availability of affordable anti-retroviral drugs. The children probably had died or their mothers might be too ill to bring them to hospital or the mothers themselves were also dead.

One important limitation of our study is that it provides a 'snapshot' of the situation at the time the study was carried out. Asymptomatic HIV positive children who are still in good health and do not require hospitalization are not identified. Again, patients attending teaching hospitals in particular are highly selected and may not reflect the true disease burden in the community. Despite these limitations however, hospital records of diseases serve as a pointer to what exists in the population at large. They remain useful in situations where population-based routine disease surveillance systems fall short of the optimum, and provide a baseline against which future surveys can be compared. Thus, it is our view that the findings are a true reflection of the problems in the community. As far as can be established, this is the first major study carried out to determine the magnitude of HIV infection in children in the state.

Finally, our results have shown the overlap of WHO clinical case definition of paediatric AIDS in Africa with commonly prevalent illnesses that require admission in public hospitals in Ebonyi State. They provide data which will facilitate early suspicion, recognition and diagnosis of HIV infection in hospitalized children. This is very crucial in providing preventive services, effective medical diagnosis and treatment, and improving the quality of life. Prevention of vertical transmission can be achieved through the prophylactic use of anti-retroviral therapy according to ACTG079 regimen[12] in both breastfeeding and non-breastfeeding mothers, and in their babies up to six weeks of age. This may be the most powerful tool against paediatric HIV infection in the community.

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