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# *Paediatric HIV at the University of Port Harcourt Teaching Hospital, Port Harcourt*

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## Abstract

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**Background:** HIV/AIDS is a major cause of infant and childhood morbidity and mortality in Africa. It is also an escalating problem of frightening proportions in Nigeria.

**Objectives:** To determine the mode of transmission, clinical presentation, co-morbidity and the outcome among children with HIV/AIDS at the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt.

**Methods:** From January 2003 to December 2007, all children with HIV infection who registered in our clinic were followed up prospectively. Clinical and laboratory evaluation were performed at presentation, the children were managed according to standard treatment guidelines and the outcome noted.

**Results:** Of the 384 children with HIV infection, 190 (49.5 percent) were males and 194 (50.5 percent) females; a M: F ratio of 0.98:1. Their ages ranged from five months to 180 months. Two hundred and sixty three (68.5 percent) of the children were less than 18 months of age at presentation. Three hundred and forty six (90.1 percent) of the children acquired the infection vertically. The common symptoms at presentation in the 336 (87.5 percent) of the children who were symptomatic included fever in 75.3 percent, cough in 64.9 percent, weight loss in 41.1 percent and diarrhoea in 40.8 percent. The common signs were generalized lymphadenopathy in 44.1 percent, pallor in 39.3 percent and hepatomegaly in 38.1 percent. Common co-morbidities included tuberculosis in 23.7 percent and pneumonia in 15.4 percent. Majority (66.9 percent) presented in WHO stage 3 and 4. Twenty seven (7.0 percent) have died while 67 (17.4 percent) have been lost to follow up. Age specific mortality was highest among those aged below 18 months. The greatest contributors to case fatality were pneumonia (44.4 percent) and malnutrition (33.3 percent).

**Conclusion:** Paediatric HIV/AIDS is predominantly transmitted from mother to child and constitutes a significant cause of childhood morbidity and mortality at the UPTH. In view of a high rate of those lost to follow up, it is advocated that strategies such as support groups and expert patient training should be put in place to track down defaulters.


**Key words:** Paediatric HIV/AIDS, clinical presentation, co-morbidity, outcome, follow up.

## Introduction

SINCE mother-to-child-transmission of the Human Immunodeficiency Virus (HIV) is responsible for about 90 percent of the infections in children,[1,2] HIV infection has continued to spread at an alarming rate among children, matching the increase in infection rate in women of childbearing age. It was estimated that as at December 2005, 2.3 million children were living with HIV/AIDS with 700,000 new infections and 570,000 HIV related deaths among children worldwide, majority of them being in sub-Saharan Africa.[3] HIV/AIDS is a major issue of concern for children, young people and women in Nigeria with an estimated prevalence rate of 4.4 per cent in 2005. With an estimated 3.5 to 3.8 million Nigerians living with the virus, Nigeria is reputed to be the third worst affected country in the world.[4] About 4.4 per cent of women attending antenatal clinics are infected with HIV.[4] Similarly, an increasing number of children are infected with the virus, through mother-to-child-transmission. Yet, less than one percent of pregnant mothers have access to counseling and testing services

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for HIV in the country. According to UNAIDS latest estimates, about 240,000 children are living with HIV/AIDS in Nigeria.[4] In addition, 930,000 children are orphaned by AIDS.[4]

The diagnosis of this infection is a great challenge to paediatricians in resource-poor countries because the clinical presentations are similar to those of many other common childhood illnesses in developing countries. Such clinical presentations include prolonged fever, diarrhoea, generalized lymphadenopathy, persistent or chronic cough, weight loss, otitis media, oral thrush and dermatitis.[5-10] Facilities for laboratory diagnosis are also not readily available or affordable. In such situations, the clinician often has to wait for the full-blown development of clinical signs and symptoms of the disease before the diagnosis is made. Besides, the appropriate antiretroviral drugs are often not available or affordable. All these lead to delayed therapy and unfavorable outcome.

In the absence of reports of such a study from our centre, a prospective study was undertaken to determine the mode of transmission, clinical presentation, co-morbidity and the outcome of the illness among children with HIV/AIDS at the University of Port Harcourt Teaching Hospital (UPTH). It is hoped that the results will assist in adopting appropriate intervention strategies in clinical case management and preventive measures.

## Patients and Methods

A prospective study was undertaken of children with HIV/AIDS seen in the Paediatric Infectious Disease Unit of the University of Port Harcourt Teaching Hospital from January 2003 to December 2007. On enrolment, the biodata, presenting features, past medical history (including history of blood transfusion), family and social history, maternal and perinatal history, nutritional history, developmental history, immunization status, HIV status of parents and siblings and whether they were alive or dead and possible cause of death, among other data, were recorded in a pre-coded proforma. A complete physical examination and baseline investigations were carried out and the results were also entered into the pre-coded form. In children over 18 months of age, the diagnosis of HIV infection was confirmed by two positive ELISA (enzyme linked immunosorbent assay) tests using the WHO approved Immunocomb HIV 1&2 kits (Organics, Israel) – an immunochromatographic test for the qualitative and differential detection of antibodies to HIV 1& 2 and Genscreen HIV 1&2 ELISA kits (Bio Rad, France) – an in vitro qualitative enzyme immunoassay (EIA) test for the detection of antibodies to HIV 1& 2 in human serum, used according to the WHO protocol. Procedures adopted for all the tests and interpretation of the results were in accordance with the manufacturers' specifications. For children less than 18 months, a presumptive diagnosis was made if they were symptomatic and seropositive with evidence of immunonosuppression (low CD4 count for age namely: for children less than 12 months, a CD4 count of $< 1500$ cells/mm$^3$ or percentage CD4+ of $<25\%$ and for those between 12 months and 35 months, a CD4 count of $< 750$ cells/mm$^3$ or percentage CD4+ of $< 20$ percent).[11-13] It was not possible to assay for viral particles or antigens which is the gold standard of diagnosis in children less than 18 months in whom maternal antibodies may persist. The details of management and follow-up were also recorded. The presumed mode of transmission was arrived at on the basis of confidential interviews with the parents regarding high risk sexual behaviour in the parents and child, history of blood transfusion in parents and child and the HIV serology status of parents, if known. The mode of transmission was assumed to be vertical if the mother was HIV positive and there was no history of blood transfusion, sexual exposure in the child or any other high risk exposure such as tribal marks, scarification marks, patronage of quacks etc. The presumed mode of transmission was sexual intercourse, blood transfusion, or contaminated instrument if the mother was negative and the child had any of the high risk exposure.

All the children underwent the following investigations: complete blood counts, serum creatinine, urea, CD4 counts, hepatitis B surface antigen and hepatitis C antibodies. Chest radiograph was done when indicated and Mantoux test considered positive if the induration was e" 5mm.[14,15] The children were managed as per standard guidelines for children with HIV infection. Anti-retroviral therapy (ART) was given to all those meeting the WHO criteria for the initiation of therapy[16] (clinical stage 3 or 4 irrespective of CD4 count or clinical stage 1 and 2 with CD4 count showing moderate or severe immunosuppression). *Pneumocystis jiroveci* pneumonia (PJP) prophylaxis with cotrimoxazole and anti-tuberculous drugs for those with tuberculosis were administered according to the national guidelines.[16,17] They were followed up in the paediatric HIV clinic where new complaints, findings on physical examination, adherence to anti-retroviral (ARV) drugs, immunization and other issues were addressed. Nutritional counseling was provided to all the children.

The data obtained was analyzed using the statistical package EPI Info version 2000. Chi-square test was used for comparison of proportions and where figures were small, the Fisher's exact probability test was applied. The level of statistical significance was set at $p \geq 0.05$.

## Results

Between January 2003 and December 2007, 384 children comprising 190 (49.5 percent) males and 194 (50.5 percent) females were diagnosed with HIV infection, giving a male: female ratio of 0.98:1. The median age at presentation was nine months (range: five months - 180 months). Table 1 shows that 263 (68.5 percent) of the children were less than 18 months of age at presentation.

The predominant mode of transmission was through the vertical route (Table II). Analysis of the birth order of the patients indicates that 172 (44.8 percent) were the first borns of the respective families (Table III). Each of 21 had one sibling with HIV/AIDS, of which seven were dead. Three had two siblings each with HIV/AIDS of which two were dead, while one had three siblings with HIV/AIDS and one of them was dead. Of the 353 mothers that were screened, 315 (89.2 percent) were positive and 38 (10.8 percent) were negative. The remaining 31 mothers that were not screened were of unknown status (the babies of three mothers were adopted, 17 mothers were dead and the whereabouts of 11 mothers were unknown). Of the 231 fathers screened, 115 (49.8 percent) were positive. Ninety eight of the remaining 153 fathers were not tested because they refused testing, 39 were never seen in the hospital and 16 were dead. Of the screened parents, there were 74 serodiscordant results in which the fathers were negative while the mothers were positive for HIV. The fathers of 44 (11.4 percent) children and mothers of 54 (14 percent) had died of HIV/AIDS or HIV related illnesses. In five of the children, both parents had died from HIV related illnesses.

**Table I**

*Age Distribution in 384 Children with HIV/AIDS*

| *Age (months)* | *No of Cases* | *%* |
|---|---|---|
| < 18 | 263 | 68.5 |
| 18-59 | 60 | 15.6 |
| > 60 | 61 | 15.9 |
| Total | 384 | 100.0 |

**Table II**

*Mode of Transmission of HIV in 384 Children*

| *Mode* | *No of Cases* | *% of Total* |
|---|---|---|
| Vertical | 346 | 90.1 |
| Blood transfusion | 24 | 6.2 |
| Sexual | 6 | 1.6 |
| *Contaminated sharps | 5 | 1.3 |
| Not known | 3 | 0.8 |
| Total | 384 | 100.0 |

*Scarification marks 1, circumcision 1, hair clip 1, surgery 1, tooth brush 1.

**Table III**

*Birth Order of the 384 Children*

| *Birth Order* | *No of Cases* | *% of Total* |
|---|---|---|
| 1st | 172 | 44.8 |
| 2nd | 109 | 28.4 |
| 3rd | 54 | 14 |
| 4th | 46 | 12 |
| Not known (Adopted) | 3 | 0.8 |
| Total | 384 | 100.0 |

Three hundred and thirty six (87.5 percent) children were symptomatic at the time of presentation and 48 (12.5 percent) were asymptomatic. The common symptoms in the former were fever in 253 (75.3 percent), recurrent cough in 218 (64.9 percent), weight loss in 138 (41.1 percent) and diarrhoea in 137 (40.8 percent) (Table IV). Lymphadenopathy in 148 (44.0 percent), pallor in 132 (39.3 percent), hepatomegaly in 128 (38.1 percent), and oral thrush in 80 (23.8 percent) were the commonest clinical findings (Table IV). Table V shows the co-morbidities and their contributions to case fatality. Ninety one (23.7 percent) of the children had tuberculosis which was miliary or disseminated in 15 (16.5 percent); Mantoux test was positive (ee5 mm) in only 30 children. Fifty nine (15.4 percent) had pneumonia, while features of encephalopathy and severe malnutrition were present in 45 (11.7 percent), and 42 (10.9 percent), respectively. Pneumocystis jiroveci pneumonia (PJP) was suspected in 20 (5.2 percent) of the children. The greatest contributors to case fatalities were pneumonia in 12 (44.4 percent) cases, malnutrition in nine (33.3 percent), tuberculosis in eight (29.6 percent) and HIV encephalopathy in eight (29.6 percent) others.

Two hundred and fifty seven (66.9 percent) of the children had WHO stage 3 and 4 disease on presentation, 45 (11.7 percent) were in stage 2, and 82 (21.3 percent) in stage 1. Their CD4 counts on presentation ranged from 28 - 2800 lymphocytes/ μl. As regards immunological status at presentation, 276 (71.9 percent) were in category 3 (severe suppression), 69 (18 percent) in category 2 (moderate suppression), and 39 (10.2 percent) in category 1 (no suppression). Although all the 257 patients in clinical stages 3 and 4, and five patients in clinical stage 2 qualified for treatment, only 212 (80.9 percent of the 262 who qualified and 55.2 percent of the cohort of

the 384 children) were receiving highly active antiretroviral therapy; 10 of the remaining 50 died and the remaining 40 were lost to follow up before commencement of antiretroviral drugs.

With regard to the outcome, 278 (72.4 percent) of the children were still alive and being followed up, 67 (17.4 percent) were lost to follow up (LTFU), while 27 (7.0 percent) have died. Twelve (3.1 percent) seroconverted and have been discharged from the clinic. The greatest percentage of deaths (74.1 percent) occurred in those who were aged less than 18 months, three (11.1 percent) were in the 18-59 months age group, while four (14.8 percent) were aged 60 months and above. The age specific mortality was highest among the less than 18 months old although there were no significant differences among the different age groups (Fishers exact test p=0.35). Fifty (74.6 percent) of the 67 who were LTFU, were aged under 18 months, 10 (14.9 percent) in the 18- 59 months age bracket, and seven (10.4 percent) were aged 60 months and above. This difference was not statistically significant among the different age groups (x2 = 0.11, df 1, p= 0.744).

**Table IV**

*Symptoms and Signs in the 336 Symptomatic Children#*

| *Symptoms* | *No=336 (%)* | *Signs* | *No=336 (%)* |
|---|---|---|---|
| Fever | 253 (75.3) | Lymphadenopathy | 148 (44.0) |
| Cough | 218 (64.9) | Pallor | 132 (39.3) |
| Weight loss | 138 (41.1) | Hepatomegaly | 128 (38.1) |
| Diarrhoea | 137 (40.8) | Oral thrush | 80 (23.8) |
| Rashes | 118 (35.1) | Parotid swelling | 23 (6.8) |
| DDMS | 31 (9.2) | Splenomegaly | 16 (5) |
| CSOM | 29 (8.6) | Hypotonia | 15 (4.5) |
| Seizures | 20 (6) | Hypertonia | 10 (3) |
| RDMS | 14 (4.2) | Deep seated ulcers | 4 (1.2) |

Delayed developmental milestones
CSOM – Chronic suppurative otitis media
RDMS – Regression in developmental milestones
# Some patients had multiple symptoms/signs

**Table V**

**Co-Morbidity/Contributors to Case Fatality*

| *Cause* | *Morbidity n 384 (%)* | *Mortality n 27 (%)* |
|---|---|---|
| Tuberculosis | 91 (23.7) | 8 (29.6) |
| Pneumonia | 59 (15.4) | 12 (44.4) |
| Encephalopathy | 45 (11.7) | 8 (29.6) |
| Malnutrition | 42 (10.9) | 9 (33.3 ) |
| HIVAN | 8 (2.1) | 4 (14.8) |
| Septicaemia | 5 (1.3) | 5 (18.5) |
| PCP | 20 (5.2) | - |
| Hepatitis B | 4 (1) | - |
| Hepatitis C | 4 (1) | - |

* Some children had more than one co-morbidity
HIVAN = HIV-associated nephropathy
PCP = Pneumocystis carinii pneumonia

## Discussion

Paediatric HIV/AIDS is a significant cause of morbidity and mortality in UPTH. In the present study, there was no gender difference, a finding that is similar to observations in other parts of Nigeria, such as Nnewi[5] and Jos [10] but is at variance with results of studies carried out in Ife[18] where there was a female preponderance and findings in Zaria[8] and India [19] where male preponderance was reported. The predominant mode of transmission in this study was vertical. This is in agreement with other studies in Nigeria[5,8-10] and India.[19,20] It is an established fact that vertical transmission is the major mode of transmission of HIV in children. This means that in order to reduce HIV infection in children, emphasis should be on effective and readily available prevention of mother to child transmission of HIV (PMTCT) programme. Women represent the fastest growing

population of persons infected with HIV in this country, and heterosexual transmission has become a much bigger factor.

In this study, blood transfusion as the mode of transmission in 6.2 percent was comparable to 4.6 percent and 8.6 percent reported from Abuja[9] and Zaria,[8] respectively but very low when compared with 16.4 percent and 47.6 percent in Nnewi[5] and Enugu,[6] respectively . This may be explained by the fact that donation by paid donors is highly discouraged in our part of the country, hence most of the blood donated was provided by the fathers or relatives. The sexual mode of transmission of 1.6 percent though low, has also been reported by others in Nigeria,[5,18] while the sexual mode of transmission was not reported in studies from Zaria[8] and Abuja.[9] Sexual mode of transmission cannot be ignored in adolescents who are adventurous and engage in sexual exploration at this age. In addition, children may be exposed to HIV/AIDS from sexual activity through molestation (rape), sexual exploitation and child prostitution for survival.[21,22] Majority of the mothers were diagnosed following the primary diagnosis of the disease in their children. This is in accordance with previous observations that through the detection of children with HIV infection, their previously unsuspected parents could also be diagnosed.[23]

That 74 serodiscordant couples were identified in this study has enormous implication for the continuity of marriages, the continued care and support of the children as the men may abandon their families as occurred among some of our patients. The birth order showed that majority were the first and second born. This has an implication in our society where children are highly treasured, because these parents are likely to deliver more children thereby increasing the number of children exposed to HIV. This further highlights the need for effective and readily available PMTCT services.

The common clinical manifestations of HIV infection in this study were similar to those reported in other studies in Nigeria [5,6,8,10] and India.[19,20] Prolonged fever, weight loss and diarrhoea are major signs in the WHO case definition of AIDS in children.[24] These features also categorize patients into WHO clinical stage 3 and thus as severe disease. The majority of the children in the present series were symptomatic at presentation. Most of the children had advanced disease, as indicated by the clinical features and profound immunosuppression. This in turn, indicates delayed diagnosis, despite numerous previous contacts with the health-care system. Therefore, a high index of suspicion is necessary for early diagnosis.

Tuberculosis was diagnosed in as many as 91 patients (24 percent) in this study. Fifteen (16.5 percent) of the 91 had disseminated TB; a finding that is not surprising in view of the higher risk of TB in patients with HIV/AIDS.[5,8,19,25] In view of the difficulty in making a diagnosis of TB in children, a high index of suspicion is necessary to identify the disease in cases of paediatric AIDS. Other important co-morbidities in this study were pneumonia and encephalopathy. Pneumonia has been reported in several studies but encephalopathy (29.6 percent) was high compared to other studies[6,9] with fewer or no report of cases from some parts of the country.[5,8] The reason for this difference could lie in the fact that our study was prospective and neurological symptoms were actively sought for. HIV infection should be suspected in unexplained encephalopathy.

Antiretroviral (ARV) drugs initiated at an appropriate time have been shown to substantially reduce the risk of mortality and improve the survival and quality of life in children. Without antiretroviral therapy, a substantial proportion of infected children progresses rapidly to serious disease and death, and by the age of one year, only about 65 percent of infected children will still be alive.[26] While access to HAART in the developing world is improving, the costs of antiretroviral drugs and the need for monitoring continue to limit their use in these countries although WHO guidelines now propose clinical monitoring in situations where adequate laboratory support is lacking. Due to the difficulties in diagnosing HIV infection in children and related opportunistic infections, access to HAART is expected to continue to elude many children living with HIV in developing countries, even as ARV drugs become cheaper or free in most government hospitals.

The mortality of 7.7 percent is high compared to that reported from Nnewi,[5] but it is low compared to other studies.[8,9] The comparatively low mortality in the present series may not be correct because some of those lost to follow up might have died and such deaths were not reported to any health facility. Young children with HIV are at particularly high risk of death, and it is difficult to identify those at highest risk. With the difficulty of diagnosing HIV infection in the first year of life as a result of a lack of virological tests, many children die before they are recognized as HIV infected. The greatest contributors to case fatality in our study were pneumonia, malnutrition, tuberculosis and encephalopathy. Their roles in paediatric HIV should be further evaluated.

## Conclusion

The findings in this study indicate that paediatric HIV/AIDS occurs predominantly by mother to child transmission and constitutes a significant cause of childhood morbidity and mortality at the UPTH. Pneumonia, malnutrition, tuberculosis, encephalopathy

and HIVAN were found to be significant co-morbidities and contributors. The high rate of cases 'lost to follow up' indicates the need for strategies such as establishing support groups, while expert patient training should be put in place to track down defaulters for optimal care. We recommend intensification of efforts to implement the existing prevention of mother to child transmission programme and further evaluation of pneumonia in children. There is need for better understanding of the clinical presentations of these patients for early diagnosis and appropriate management. Emphasis should be on supportive care with good and regular follow-up of these patients. This may help in reducing morbidity and improve their quality of life.

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