

Original Research Article

Clinical and laboratory profile of ARV naïve HIV infected children in the era of highly active anti-retroviral therapy in Enugu, South-east Nigeria

Abstract:

Background: HIV/AIDS is one of the most dynamic epidemic infectious diseases. An estimated 1000 children are newly infected with HIV every day, most of them in sub-Saharan Africa. They often present with various clinical and laboratory manifestations that complicates their management.

Objectives: To determine the baseline clinical and laboratory features of HIV-infected children presenting at the University of Nigeria Teaching Hospital (UNTH) Ituku/Ozalla.

Methods: Clinical and laboratory data were collected from HIV infected children seen at the Pediatric HIV Clinic of UNTH between July 1st 2010 and June 30th 2012. Clinical and immunological staging of the patients were done using the WHO criteria and data analysis was with SPSS version19.

Results: Two hundred and ten children were enrolled into the study. The most common route of HIV infection was vertical transmission (95.2%). Common presenting clinical and laboratory data were: anaemia (92.9%), cough (76.2%), fever (63.3%), papular rash (62.9%) and poor weight gain (61.0%). Thirty-four children (16.2%) each had severe and moderate acute malnutrition while 92 children (43.8%) were stunted. Tuberculosis, hepatitis B and C co-infections were seen in 32.4%, 1.9% and 3.3% of the children respectively. Most of the patients had either a WHO clinical stage III (42.4%) or II (39.0%) disease. Severe immunosuppression based on CD4% or count was seen in more than half of the patients (59.1%).

Conclusions: Anemia was the most common clinical/laboratory finding; followed by cough. Although our patients were likely to present with WHO clinical 2 or stage 3 disease, severe immunological suppression was common.

Key words: Children, ARV naïve, clinical, laboratory

Introduction:

An estimated 23.5 million adults and children were living with HIV in sub-Saharan Africa (SSA) by the end of 2011.¹ Paediatric HIV/AIDS remains a significant public health issue in the sub-continent. More than 90% of the children who acquired HIV infection in 2011 live in the sub-region.¹ Most of these infections result from mother-to-child transmission.² Nigeria has the highest burden of paediatric HIV because of her large population, high rate of HIV infection among women of child bearing age and .high birth rate^{3, 4} . Recent UN report indicates that Nigeria tops the world in terms of number of under-five infected with HIV with about 60,000 new infections in 2012 ⁵

While concerted efforts are beginning to result in reduction in the incidence of paediatric HIV infection around the world, new infections are not uncommon in developing countries. HIV affects virtually all the systems in the body and present with varied clinical manifestations. Despite the significance of this disease in Nigeria, there are limited published data on clinical and laboratory characteristics of paediatric HIV in Nigeria. There may also be regional variation in the pattern of presentation. In the early years of the epidemic, HIV-infected children presented with severe and advanced forms of the disease. A previous study done in our center about a decade and half ago in the pre- highly active anti-retroviral therapy (HAART) era revealed that more than one-third of the HIV-infected children presented with features of AIDS.⁶ In this era of increased awareness and access to pediatric HIV services, we hypothesize that our population of HIV-infected children are more likely to present with mild to moderate HIV disease. It is therefore important, that the clinical and laboratory profiles of paediatric HIV in Enugu, south-east Nigeria is described. Such descriptions will highlight the prevailing clinical features of the disease in our environment, and will result in improved case detection.

Method:

This was a descriptive study of Paediatric HIV infected children seen at the Paediatric HIV clinic of the University of Nigeria Teaching Hospital (UNTH), Enugu, between July 1st 2010 to June 30th 2012. UNTH is a tertiary hospital situated in Enugu, South-eastern geopolitical zone of Nigeria, serving as a referral center for HIV care in Enugu state and neighboring states. The clinic provides care including antiretroviral therapy for infected children and is sponsored by the government of Nigeria and AIDS Prevention in Nigeria (APIN) program. Initial diagnosis of HIV among children 18 months and more was with Enzyme Linked Immunosorbent Assay (ELISA) and confirmed with Western blot. In children less than 18 months diagnosis was by DNA PCR using dried blood spot. All patients aged 0 – 10 years seen at the ART clinic were included in the study. Information on demographics, clinical manifestation and anthropometric parameters of the patients were extracted from our data base. Mode of HIV transmission was determined by establishing mothers' HIV status, evaluating for history of blood/blood product transfusion and sexual activity in the children. Children whose mothers' were HIV positive without other identified risk factors for HIV were assumed to be infected through vertical transmission. Children with antecedent history of blood/blood product transfusion and had HIV negative mothers were assumed to have acquired the infection through blood transfusion. Sexually active children without other identified risk factors for HIV infection were assumed to have acquired the infection through sexual route. If no risk factors were identified, the mode of transmission was classified as unknown.

Clinical and immunological staging were based on the WHO recommendations. The diagnosis of tuberculosis was based on the WHO guidelines for National TB program for children; cases were either smear positive or smear negative with clinical, radiological features and positive response to anti-TB drugs. Other baseline investigations that were obtained were viral load (HIV RNA level), complete blood count, HbSAg and HCV assays. CD4 lymphocyte estimation was done using Partec Cyflow machine. Severe immunosuppression was defined based on current WHO guidelines as a CD4 count <25% in children who are < 1 year, <20% in children aged 1 to 3

years, and <15% in children aged 3 to 5 years.⁷ Anemia was defined using the WHO criteria: 6-59 months, <11g/dl; 5-11 years, <11.5g/dl.⁸

Ethical approval was obtained from Health Research and Ethics Committee of UNTH. The data were analyzed using SPSS version 19. Chi-square and Fisher's Exact were used to test significant association of the categorical variables.

Results:

Two hundred and ten children were enrolled into the study. The mean and median ages of the children at HIV diagnosis were, 3.5 ± 2.2 years and 3 years (range, 3 months to 10 years) respectively. There were 110 (52.4%) males and 100 females (47.6%). Seventy-eight children (37.1%) were orphaned. Among the 78 orphans, 56 (71.8%) and 22 (28.2%) were single and double orphans respectively. The detailed demography of the patients is shown in Table 1.

The most common route of HIV infection was mother-to-child transmission (95.2%). Blood transfusion and sexual abuse contributed 1.9% and 0.5% respectively while the route of transmission was unknown in 2.4% of the children.

The most common presenting clinical/laboratory features were: anemia 92.9% (95% CI: 82.5 – 91.4), cough 76.2% (95% CI: 70.0 – 81.2), fever 63.3% (95% CI: 56.6–69.6), papular rash 62.9% (95% CI: 56.2–69.1), and weight loss/failure to gain weight 61.0% (95% CI: 54.2–67.3). The details of the clinical features seen are shown in Table 2. Thirty-four children (16.2%) each had severe and moderate acute malnutrition defined as weight for height z-score <-2 and -3 respectively. Ninety-two children (43.8%) had stunting defined as height for age z-score of <-2. Pulmonary tuberculosis was the most common co-infection (32.4%). Hepatitis B and C co-infections were seen in 1.9% and 3.3% of the children respectively.

Most of the children presented in either WHO clinical stage III (42.4%) or II (39.0%). The rest were either in WHO clinical stage I (13.8%) or IV (4.8%) disease. Two hundred and three of 210 children had baseline CD4 done. Among them, severe immunosuppression was present in 120 (59.1%). Baseline viral load assay was available in only 107 children. Among them, 63 (58.9%) had above 100,000 copies/ml while 12.1% and 39% had VL less than 10,000 and 10-100,000

copies/ml respectively. Fifty-five children (26.2%) had leukocytosis while 9.0% had thrombocytopenia.

Discussion:

The median age at HIV diagnosis among our patient population was 3 years. This is similar to the previously reported median ages of 3 and 4.5 years by Brown *et al*⁴ in Ibadan, Nigeria and Singh *et al*⁷ in India among their paediatric HIV-infected cohorts respectively. The continuing late presentation of HIV-infected children to health facilities in developing countries in spite of increased awareness and improved availability of testing may be a reflection of poorer health seeking behavior of Caregivers for these children. The predominant mode of HIV transmission in our study was MTCT in 95.2%. Blood transfusion and sexual abuse were less frequent in 1.9% and 0.5% of the subjects respectively. This is similar to the previously reported 88-92% rate of MTCT of HIV in the literature;^{4, 9-11} and a reduction in the role of blood transfusion that was noted in a previous study from the same centre.⁵ In that study, blood transfusion accounted for as much as 68% of the pediatric HIV infection. Our current study supports the new thinking that eliminating paediatric HIV will therefore require strengthening interventions that reduces MTCT of HIV.^{12, 13}

Cough (76.2%), fever (63.3%), rash (62.9%), and weight loss (61.0%) were the most common presenting symptoms in this study. In a previous study in our center, generalized lymphadenopathy, progressive weight loss and persistent fever were the top presenting features.⁵ In Ibadan, weight loss/failure to thrive, prolonged fever, generalized lymphadenopathy and chronic cough were the most common presenting features. Gomber and colleagues¹¹ in India noted that the most common clinical symptoms in their series were fever, cough and diarrhea. It does appear that the presenting features in HIV-infected children vary from locality to locality and over period of time even in same locality. However, fever remains a constant common presenting feature in the literature among HIV-infected children. This is likely due to the primary HIV infection and wide array of associated opportunistic infections especially in developing countries. Papular rash was present in 62.9% of our children. Shah *et al*¹⁴ also reported that skin manifestations were common among HIV-infected children in their center. However, skin manifestations were less common in studies by Brown *et al*⁴ and Gomber *et al*.¹¹

We report a 32.4% prevalence of pulmonary TB-HIV co-infection. High rate of TB-HIV co-infection has previously been reported among HIV-infected children in Nigeria.⁴ Lower rate of 27.5% was reported among Indian children in early 2000 by Rajasekaran.¹⁰ A more recent study done in India in 2011 reported a rate of 11%, although the study was limited by a small sample size of 100.¹¹ The varied reported rates of TB-HIV co-infections among children could be a reflection of existing TB burden in the adult population. Hepatitis B (1.9%) and C (3.3%) co-infections were less frequent in our study. Nwolisa *et al*¹⁵ and Aupibul *et al*¹⁶ in Nigeria and Thailand documented 5.8% and 3.3% rate of hepatitis B/HIV co-infection in children respectively. The reason for the low rate of hepatitis and HIV co-infection among children could be because most paediatric HIV are acquired perinatally; the latter being a less efficient mode of hepatitis B and C transmission compared to blood transfusion and sex.^{17,18}

Anaemia was very common among our patients (92.9%) although only 3.5% met the definition criteria for severe anaemia. Among HIV-infected ARV naïve children in Uganda, Ruhinda and co-authors¹⁹ reported that anemia was present in 57.6% of the children; and only 4.8% had severe anemia. It is unclear the criteria the authors used in defining anaemia. The aetiology of anaemia among ARV naïve HIV-infected children has been linked to iron deficiency, inflammation and deficiency of vitamin B12.²⁰

Most of our patients presented in either stage II or III clinical disease (over 80%) unlike in Ibadan where 70.6% presented with more advanced stages III and IV clinical diseases. Gomber *et al*¹¹ in 2011 reported that all their ARV naïve HIV-infected children presented in either WHO stage I or II clinical disease. Surprisingly, more than half of our patients (59.1%) presented with severe immunosuppression. This underscores the importance of evaluating HIV-infected children immunologically irrespective of their clinical stages.

Both acute and chronic malnutrition were common in our patients. HIV-related malnutrition is common and could result from reduced food intake, increased metabolism and poor absorption of nutrients.²¹ Among 42 symptomatic HIV-infected children, Shah *et al*¹⁴ reported 90% prevalence of protein-energy malnutrition. Among 37 HIV-infected but ARV naïve children in South Africa, Steenkamp *et al*²² reported that fifteen children (41%) were underweight, 30 (81%) were stunted and one (3%) was wasted. Conversely, a recent study in Kano, Nigeria, among

under-five malnourished children reported a high prevalence of HIV.²³ Thus, malnutrition remains a cardinal presenting feature of HIV in children.

Conclusions: Anemia, cough and fever were common presenting clinical features among our patients. Both acute and chronic malnutrition were relatively common. Although WHO clinical II or stage III disease were more likely, severe immunological suppression was common among our children.

Competing interest: The authors declare that they have no competing interests.

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240 Table 1: Socio-demographic characteristics of the HIV infected children

Age	Mean (SD)	3.5 ±2.2 years
	Median (range)	3.0 (0.25-10) years
Sex:		
	Male	110 (52.4)
	Female	100 (47.6)
Orphaned:		
	Yes	78 (37.1)
	No	132 (62.9)
	Primary Caregiver:	
	Mother	165 (78.6)
	Grandparents	18 (8.6)
	Father	13 (6.2)
	Maternal relative	12 (5.7)
	Paternal relative	2 (1.0)

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246 Table 2: Common presenting clinical features of the HIV infected children.

Clinical features	Yes (%)	Confidence Interval
Anemia	184 (92.9)	82.5 – 91.4
Cough	160 (76.2)	70.0 – 81.2
Fever	133 (63.3)	56.6 – 69.6
Papular rash	132 (62.9)	56.2 – 69.1
Weight loss	128 (61.0)	54.2 – 67.3
Diarrhea	55 (26.2)	20.7 – 32.5
Ear discharge	53 (25.2)	19.8 – 31.5
Parotid swelling	29 (13.8)	9.8 – 19.1
Delayed milestone	21 (10.0)	6.6 – 14.8
Oral thrush	14 (6.7)	4.0 – 10.9
Skin warts	11 (5.2)	3.0 – 9.1
Asymptomatic	6 (2.9)	1.3 – 6.5
abdominal swelling	6 (2.9)	1.3 – 6.5
Others	5 (2.4)	1.0 – 5.8

Others=Kaposi sarcoma, herpes zoster

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