Clinical spectrum of paediatric HIV in Nnewi, Nigeria

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Summary

Background: **HIV/AIDS is increasingly becoming a predominant cause of childhood morbidity and mortality in this part of the world.**

Study Design: **A descriptive, prospective study was carried out at the Nnamdi Azikiwe University Teaching Hospital, Nnewi, Southeast Nigeria, to ascertain the clinical features and probable modes of transmission of HIV infection in Children.**

Results: **Out of 128 HIV -infected children, 53.1 % were males and 46.9 % females, giving a male: female ratio 1.1:1. They were aged from 3 months to 16years, with a mean of 4.78 (± 3.97) years. Those in the 1-5 year age bracket made up 47.7%. The presumed route of infection was mother-to-child in 79.7% and blood transfusion in 16.4%. Majority(82.0%) presented with WHO clinical stage 3 disease and 55.7% were severely immunosuppressed. The most frequent clinical features were recurrent/persistent fever, persistent cough,weight loss/failure to thrive and generalised lymphadenopathy. There was co-infection with tuberculosis in 15.6% of patients. Eighteen patients (14.0%) were lost to follow up. Six children (4.7%) died during the period under review. They all presented in WHO stage 3 and 4. A hundred percent of the dead children had severe weight loss, 83.3% had generalized lymphadenopathy and recurrent or persistent fever respectively. Fifty percent presented with diarrhea and oral thrush. There was no gender difference in mortality. Mortality was highest among infants.**

Conclusion: **The high rate of vertical transmission of HIV reinforces the need for effective PMTCT interventions in reducing the incidence of HIV in children. A high index of suspicion and awareness of modes of presentation of HIV infection in children is needed for early diagnosis of those infected with HIV.**

Key-words: ***HIV, AIDS, Childhood, Nigeria.***

Résumé

Introduction: VIH/SIDA est de plus en plus devenu une cause prédominante de la morbidité et mortalité d'enfance chez nous.

Pland'etude: Une étude descriptive en perspective a été effectuée au centre hospitalier universitaire de Nnamdi Azikiwe, Nnewi, sud-est Nigéria, afin de déterminer les traits cliniques et des façons probables de la transmission d'infection de VIH chez des enfants.

Résultats: Parmi un numbre total de 128 enfants infectés de VIH, 53,1% étaient du sexe masculin et 46,9% du sexe féminin; c'est-à-dire une proportion sexe masculin: sexe feminin de 1,1:1. Ils étaient dans la tranche d'âge de 3 mois au 16 ans, avec moyen de 4,78 (± 3,97) ans. Ceux dans la tranche d'âge de 1-5 ans constitue 47,7%. La cause présumée de l'infection était mère-à-enfant en 79,7%, et transfusion sanguine en 16,4%. La majorité (82,0%) se sont présentés avec l'OMS 3 étape de la maladie clinique et 55,7% étaient gravement d'immunodépression. Les traits cliniques les plus ordinaire étaient la fièvre chronique, la toux chronique, perte du poids/impuissance de se bien porter et lymphadénopathie générale. Il y avait eu un co-infection avec la tuberculose chez 15,6% des patients. Dix huit patients soit 14,0% étadient perdu sans soins post-hospitaliers. Six enfants soit 4,7% étaient mort au cours de la période en cours de révision. Ils se sont tous présentés dans le cadre de OM3 étapes et 4. Cent pourcent des enfants qui sont mort avaient eu la perte du poids 83,3% avaient eu la lymphadénopathie générale et la fièvre chronique respectivement. Cinquante pourcent se sont présentes atteints de la diarrhée et le muquet buccal. Il n' y avait aucune différence du genre en ce qui concerne la mortalité. Mortalité était la plus élevée chez des enfants.

Conclusion: Le taux élevé de la transmission verticale de VIH vient de renforcer le besoin de l'intervention PMTCT efficace afin de reduire la fréquence du VIH chez des enfants. Un taux élevé d'indice de soupçon et la prise de conscience des moyens de présentation de l'infection du VIH chez des enfants est nécessaire pour un diagnostique précoce de ceux révélés infectés du VIH.

Introduction

HIV/AIDS is a major cause of infant and childhood mortality and morbidity in Sub-Saharan Africa, and is a threat to recent gains in infant and child survival and health [1]. This is a sad situation, considering the fact that HIV infection in children is preventable. In most of Sub-Saharan Africa (Nigeria inclusive) there are limited paediatric HIV diagnostic facilities and most HIV-infected children are diagnosed very late in the course of illness, or not at all.[1] Until January 2004, when Ranbaxy pharmaceuticals commenced local production of antiretroviral (ARV) drugs in Nigeria, paediatric formulations had been inaccessible to the masses of children ravaged by HIV. This study was, therefore, embarked on to determine the clinical features and modes of transmission of HIV infection in children presenting to the Nnamdi Azikiwe

Correspondence

University Teaching Hospital, (NAUTH) Nnewi since commencement of an organized paediatric HIV Care. N.A.U.T.H. is supported by the U.S. Centers for Disease Control and Prevention (CDC) and is one of the Federal Government primary ARV (Antiretroviral Therapy) Centers.

Subjects and methods

A prospective twenty-eight month review spanning from May 1 2003 to August 31 2005, yielded 128 HIV-infected children seen in the paediatric HIV clinic. These children were recruited from four sources:

- Patients presenting to the Children's out-patient clinics and Children Emergency room of NAUTH, who were screened on suspicion by the attending physicians;
- Referrals of HIV- positive children from private clinics, primary and secondary level health facilities, and HIV/AIDS Support groups and Non-Governmental Organisations within Anambra state and beyond;
- Referrals of HIV- positive progeny of patients attending the Adult HIV clinic of NAUTH;
- Symptomatic babies of HIV-positive mothers on follow-up in the PMTCT (Prevention of Mother to Child Transmission of HIV) programme in NAUTH.

On enrolment, a pre-coded proforma was completed. Presenting features, demographic data, family history, maternal perinatal history, HIV status of parents and siblings and immunization status of each child, among other data were filled in. A complete physical examination and base line laboratory investigations were carried out. These included an HIV screening test, Confirmatory test (Western Blot or Double Elisa), CD4 lymphocyte count, complete blood count, liver function tests, urine analysis and chest x-ray when indicated. Child-Parent/guardian pairs had post-test counselling (since they usually came with a positive test result). All referred patients had a repeat HIV screening test done after an informed consent was obtained from the parent/guardian. At follow-up visits, new complaints, findings on physical examination, adherence issues to ARV and other drugs were addressed. Searching for opportunistic infections were also made. In the absence of definitive virologic diagnosis, seropositive children below 18 months of age were assumed infected when they became symptomatic (World Health Organisation (WHO) criteria for symptomatic HIV infection) and showed evidence of immunosuppression (low CD4 count for age). Age is an important determinant of the rate of disease progression in HIV, the disease progressing much faster in infants and children than in adults,therefore there is a provision for diagnosis of probable HIV infection in those with clinical features and positive antibody results where virologic tests are not available.[1,2] The result should be confirmed by repeat antibody testing after the child is more than 18months of age.[1] The WHO clinical case definition for paediatric AIDS[3] and the U.S. Centers for Disease Control and Prevention (CDC) immunological classification[4] were applied for all patients.

Initial Screening was done with Genscreen Plus (Bio-Rad laboratories) for antibodies to HIV I and II. Confirmation was done initially with New- Lav Blot I (Bio-Rad lab) until September 2004, when the U.S PEPFAR (Presidential Emergency Program For AIDS Relief) program supplied rapid test screening kits (Capillus and Genie II) for confirmation. A sample was considered HIV antibody-positive if the serum was reactive in both tests. Where discordance occurred Determine test kit was used as a tie breaker. CD4 lymphocyte counts were carried out with the Dynal CD4 kit, Manual Culter counter CD 4 kit (in March 2005), and from April 2005, Partec Cyflow machine. Strict compliance with manufacturer's instructions on usage and storage of reagents was adhered to.The presenting features were categorized as recurrent or chronic diarrhea (> 1 month), chronic or recurrent otitis media, recurrent or persistent fever (>1 month), persistent cough, weight loss or failure to thrive, oral thrush (beyond the neonatal period), persistent generalised lymph node enlargement, hepatosplenomegaly, parotid enlargement, anemia (unexplained and especially recurrent), papillomata and dermatitis of varying types.

The presumed mode of transmission of HIV was arrived at after obtaining a history of blood transfusion in the child and serology status of the parents. The transmission was attributed to blood transfusion in those children who had a history of transfusion more than three months prior to presentation and whose parents were HIV negative. Plausible reasons for arriving at such conclusions include:

a) A screened HIV- seronegative donor may possibly be recently infected and be in the 'window period' with a high viral load undetectable by antibody serological screening tests[5]
b) Insensitive and unstandardized, poor quality screening reagents may give false negative results.These could occur in the numerous privately operated laboratories in the country, since there is at present no strict monitoring of blood transfusion services.
c) Some blood transfusion carried in private hospitals with blood donated by parents were hitherto unscreened.

The mode of transmission was assumed vertical, if the mother was HIV-positive and there was no

Table 1 Age distribution of patients

Age of patients	Number of patients	Percent of total patients
< 12 months	20	15.6
1-5years	61	47.7
5.1-12 years	39	30.4
>12 years	8	6.3
Total	128	100.00

Table 2 Presenting clinical features of the HIV-infected children

Feature	Frequency	Percent
Persistent fever	89	69.5
Persistent cough	75	58.6
Persistent generalized lymph node enlargement	72	56.3
Weight loss /failure to thrive	72	56.3
Dermatitis	49	38.3
Recurrent or chronic diarrhea	38	29.7
Hepatosplenomegaly	37	28.9
Oral thrush	25	19.5
Chronic otitis media	14	10.9
parotid gland enlargement	13	10.2
Anaemia (unexplained)	5	3.9
Papillomata	2	1.6

history of blood transfusion or other high risk exposure in the child. When there was no obvious route of infection the mode of transmission was termed indeterminate.
Data was analyzed with the SPSS statistical package.

Results

Out of the 128 HIV-infected children, 68 (53.1%) were males and 60 (46.9%) females giving a male: female ratio of 1.1:1. Their ages ranged from 3 months to 16 years with a mean of 4.78 (± 3.97) years.
The age distribution is given in Table 1. Infants made up 15.6%. Those between 1 and 5 years were 47.7%. The paediatric age group spans up to 16 years, including adolescents. Adolescents and older children may have similar presenting features as adults as the CD4 count approximates the adult count from above 6 years of age (according to the CDC Immunological classification[4]). One hundred and two children (79.7%) were infected by vertical transmission. Another twenty-one (16.4%) were infected via blood transfusion. In four children (3.1%) the mode of transmission could not be ascertained. One teenager (0.8%) got infected by engaging by unprotected sex with multiple partners. Fifty-two children (40.6%) were on ARV drugs and 76 (59.4%) were not. The drugs used were a combination of 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and 1 non Nucleoside reverse Transcriptase Inhibitor (NNRTI)- the Highly Active Anti-Retroviral Therapy (HAART) regimen. The NRTIs included Zidovudine 240 mg/m^2 body surface area twice daily; Lamivudine 4mg/kg body weight twice daily; Stavudine 1mg/kg body weight twice daily. In the NNRTI group were Nevirapine commenced once daily for the first 14 days, then maintained on 7mg/kg twice daily for age <8 years, and 4mg/kg twice daily for age ≥ 8 years; Efavirenz for age > 3 years (especially for those on concomitant anti- tuberculosis therapy) as a single daily dose as follows: 10-< 15kg 200mg, 15-< 20kg 250mg, 20-<25kg 300mg, 25 - <33kg 350mg and 33 - <40kg 400mg. Stavudine and Zidovudine were not used together. The number of children receiving ARV drugs have increased since late June and early July 2005 with the supply of free ARVs from the PEPFAR and Government of Nigeria (GON) programs.

Majority (102, 82.0%) presented in WHO stage 3 disease[3], 16 (11.0%) in stage 2,6 (4 .7%) in stage 1, and 1 (0.8%) in stage 4. All the patients in stage 1 were asymptomatic {in immune categories 1 [66.7%] and 2 [33.3%]} and were screened following a diagnosed symptomatic family member. Their CD4 counts on presentation ranged from 20-2447 lymphocytes/µl. As regards the immunological status, 55.7% were in category 3 (severe immunosuppression), 22.8% in category 2 (moderate immunosuppression) and 21.5% in category 1 (no immunosuppression). The common presenting features are outlined in Table 2. The most frequent clinical features were fever, cough, weight loss/failure to thrive and generalized lymphadenopathy. Twenty children (15.6%) were co-infected with tuberculosis. Outcome was cataloged into 'alive and being followed up' (81.3%), 'lost to follow up' (14.0%), and 'dead' (4.7%). With progressive immunosuppression clinical symptomatology increased (p=0.5259). Even though the finding was not statistically significant (p=0.9917) those children infected vertically were more symptomatic. There was no gender difference in the presenting features (p=0.9958). Children aged one to five years had more symptoms than their younger and older counterparts (p=0.2177). All the children who died had WHO[3] stages 3 (83.3%) and 4 (16.7%) diseases. Death was from pneumonia and diarrheal disease. A hundred percent of the dead children had severe weight loss, 83.3% had generalized lymphadenopathy and recurrent or persistent fever respectively. Fifty percent presented with diarrhea and oral thrush. There was no gender difference in mortality (p=0.9717). Mortality was highest among infants (p=0.5212).

Discussion

This study serves as an initial audit of clinical cases presenting to the paediatric HIV clinic of NAUTH, Nnewi since its formal inception in May 2003.There was an equal affectation of male and female children in this study. The same was observed by workers in Jos, Northern Nigeria. [6] In Ife, Southwest Nigeria,[7]there were more females than males, while in India [2,8] there was a male preponderance. No reason could be advanced for this. The mean age of 4.78 years is at par with the 4.5year average age observed in India. [8] The predominant mode of transmission of HIV in this cohort of children was vertical. This concurs with studies in ife [7] in southwest Nigeria, Jos [6] in Northern Nigeria, and else where in India [2,8,9,10] and Barbados. [11] However, Emodi and Okafor [12] in a review in Enugu, Southeast Nigeria, found blood transfusion a major route of infection in children. This was probably in the pre-

PMTCT (Prevention of Mother- to- Child Transmission of HIV) era when few mothers were screened for HIV. Blood transfusion was second to vertical transfusion. In this study, a significant proportion of the blood transfused to the children was donated by their fathers and given unscreened on trust in private health facilities. This practice is common in this part of the country and is at variance with the observation by Adejuyigbe et al [13] of HIV transmission occuring more from blood donated by paid donors. Transfusion of unscreened parent's blood should be discouraged. There was a case of transfusion of screened 'HIV negative' blood subsequently resulting in infection of the recipient. This has been reported in literature as infection during the 'window period'. [5] Reduction in the prevalence of blood transfusions by good nutrition and micronutrient supplementation is advocated. A National Blood Transfusion Service that regulates blood donation and transfusion and has facilities for viral antigenic testing would obviate transfusion of infected antibody-negative blood. Even though transmission by sexual intercourse was low among the children, it has also been reported in Ife [7] and cannot be neglected among teenagers in our primary and secondary schools who experiment with sex. Paediatric age group may be exposed to HIV/AIDS from sexual activity through molestation (rape), sexual exploitation and child prostitution for survival. [1,14,15] In this study, as in others,[6,8,12] prolonged fever, persistent cough, failure to thrive, and generalized lymphadenopathy rank the most frequent presenting features. Prolonged fever and failure to thrive are major signs in the WHO case definition of AIDS in children [16], and both features appear to be the most consistent in symptomatic HIV in children in the developing world. These features also categorize patients into the WHO clinical stage 3 and hence are late symptoms[3]. Clinical suspicion-based screening even though important provides a relatively under-utilized opportunity for detection of new cases and detects mainly advanced cases. Approximately 16% of patients were co-infected with tuberculosis. Higher figures were recorded in other studies [2,8,9,10,17] with proportions ranging from 29.47% to 67.5%. HIV infection predisposes to tuberculosis because of the underlying immunosuppression. [18,19] A mortality of 4.7% is low compared to findings elsewhere. [2,7,20] This was probably because of the availability of antiretroviral therapy in this study. The high mortality among infants in this review was corroborated in North eastern Nigeria [20] and in Barbados.[11] This is as a result of an immature immune response to HIV mounted by infants in comparison to adolescents and adults. The clinical progression to AIDS and death is more rapid the younger the patient. Another noteworthy observation was a high loss to follow up. This was consistent in various reviews. [6,9,12,20,21] All the losses to follow up in this study occured when patients had to buy their antiretroviral drugs.

Conclusion

The high rate of vertical transmission of HIV reinforces the need for effective PMTCT interventions in reducing the incidence of HIV in children. A high index of suspicion and awareness of modes of presentation of HIV infection in children is needed for early diagnosis of those infected with HIV.

References

1. Tindyebwa D, Kayita J, Musoke P, et al (Editors). Epidemiology, pathogenesis and Natural History of HIV: In Handbook on paediatric AIDS in Africa, First Edition, Africa Network for the Care of Children Affected by AIDS (ANECCA), 2004; 11-31.

2. Madhivanan P, Mothi SN, Kumarasamy N, Yepthomi T, Venkatesan C, Lambert JS, Solomon S.: Clinical manifestations of HIV infected children. Indian J Pediatr 2003; 70: 615-620.

3. World Health Organisation: Guidelines for the clinical Management of HIV infection in children. WHO, Geneva, 1993; 1.2–1.3.

4. Centers for Disease Control and Prevention: Revised Classification system for human immunodeficiency virus infection in children less than 13 years of age. Morbidity and Mortality Weekly Reports 1994; 43 (RR - 12): 1-10.

5. Ward JW, Holmerg SD., Allen JR, et al: Transmission of human immunodeficiency virus (HIV) by blood transfusion, screened as negative for HIV antibody. N Engl J Med 1988; 318: 973-978.

6. Angyo IA, Okpeh ES, Onah J.: Paediatric AIDS in Jos, Nigeria. West Afr J Med 1998; 17: 268-272.

7. Adejuyigbe EA, Oyelami O, Onayemi O, Durosimi MA.: Paediatric HIV/AIDS in Ile-Ife, Nigeria. Cent Afr J Med 2003; 49: 74 - 78.

8. Lodha R, Singhal T, Jain Y, Kabra SK, Seth P, Seth V.: Paediatric HIV infection in a Tertiary Care Center in North India: Early Impressions. Indian Paediatrics 2000; 37: 982-986.

9. Merchant RH, Oswal JS, Bhagwat RV, Karkare J.: Clinical profile of HIV infection. Indian Paediatr 2001; 38: 239.

10. Dhurat R, Manglani M, Sharma R, Shah NK.: Clinical spectrum of HIV infection. Indian Pediatrics 2000; 37: 831-836.

11. Kumar A, St John MA.: HIV infection among children in Barbados. West Indian Med J 2000; 49: 43–46.

12. Emodi IJ, Okafor GO: Clinical manifestations of HIV infection in children at Enugu, Nigeria. J Trop Pediatr 1998; 44: 73-76.

13. Adejuyigbe EA, Durosimi MA, Onyia FN, Adeodu OO. Blood transfusion related paediatric HIV/AIDS in Ile-Ife, Nigeria. AIDS care 2003; 15: 329-335.

14. Ladnęr J, Cartoux M, Dauchet L, Van de Perre P, Czernichow P.: Teenage African Women and HIV-1 infection. Lancet 2002; 360: 1889.

15. Willis BM, Levy BS.: Child prostitution: global health burden, research needs, and interventions. Lancet 2002; 359: 1417-1422.

16. World Health Organisation: Acquired Immunodeficiency Syndrome (AIDS): provisional WHO clinical case definition for AIDS. Wkly Epidemiol Rec 1986; 61: 72-73.

17. Hashim MS, Salih MA, El Hag AA, Karrar ZA, Osman EM, el-Shiekh FS, el Tilib IA, Attala NE.: AIDS and HIV infection in Sudanese children: a clinical and epidemiological study. AIDS patient care STDS 1997; 11: 331 - 337.

18. Murray JF.: Tuberculosis and HIV infection: global perspctives. Respirology 1997; 2: 209- 213.

19. Zumla A, Malon P, Henderson J, Grange JM.: Impact of HIV infection on tuberculosis. Postgrad Med J 2000; 76: 259-268.

20. Akpede GO, Ambe JP, Rabasa AI, Akuhwa TR, Ajayi BB, Akoma MA, Bukbuk DN, Harry TO.: Presentation and outcome of HIV-1 infection in hospitalized infants and other children in North-eastern Nigeria. East Afr Med J 1997; 74: 21-27.

21. Evans-Gilbert T, Hambleton I, McKenzie CA, SammsVaughan M.: Paediatric HIV/AIDS in Jamaica.A hospital -based description.West Indian Med J 2002; 51: 74 -79.