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HIV and Tuberculosis Co-infection in Children: Presentation and Treatment Outcome

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Summary

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Background: The association between tuberculosis (TB) and human immune deficiency virus (HIV) in adults has been well described. There is however, paucity of information on the association, if any, in Nigerian children.

Objectives: The objective of the present study was to determine the prevalence of HIV among children diagnosed with TB and their treatment outcome.

Design: This was a retrospective study of children diagnosed with TB between January 2000 and December 2004 in Sagamu.

Method: Clinical records of children diagnosed with TB were reviewed. The number of HIV seropositive cases among them was also determined. Their demographic characteristics, clinical presentation and treatment outcomes were noted and comparisons made between those who were HIV positive and others who were HIV negative.

Results: Seventy six children comprising 46 males and 30 females (M:F ratio, 1.5:1) were diagnosed with TB. Eight (10.5 percent) of these were HIV-infected. HIV sero-prevalence increased over the years although this was not statistically significant ($X^2 = 8.02$; $p = 0.09$). The major routes of transmission were mother-to-child (4/8) and blood transfusion (3/8). Only one case of sexually transmitted HIV was observed. HIV-infected children were significantly older than non-infected children (8.5 ± 4.4 v 5.5 ± 3.9 years; $p = 0.04$), and more likely to have a negative Mantoux test. Mortality was significantly higher among children with TB and HIV co-infection than in those who were HIV negative (3/8 vs 2/68; $p = 0.01$).

Conclusions: The study showed a higher HIV sero-prevalence among children with TB than the national average. HIV and TB co-infection was associated with higher mortality. Effective strategies to prevent mother-to-child-transmission of HIV and to improve safe blood transfusion services should be vigorously pursued to stem the tide of HIV infection in children.

Key words: Childhood TB, HIV Sero-prevalence, Treatment outcome

Introduction

THE HIV/AIDS epidemic continues unabated with little or no decline globally. About 40 million people are infected worldwide, with children below the age of 15 years numbering about 2.5 million.[1] In 2004 alone, about five million people including 700,000 children were newly infected with the virus. Ninety-nine percent of these individuals live in sub-Saharan Africa where access to treatment and care is still limited.[1] Also in the same year, a 4.4 percent national HIV sero-prevalence rate was reported in Nigeria.[2] This is enormous considering the estimated population of over 120 million people. An increasing HIV prevalence among adult patients diagnosed with TB has also been reported in our centre, where the prevalence rose from 4.7 percent in 1998 to 12.8 percent in 2001 and 15 percent in 2002.[3,4] There is however, a paucity of published data on the association of TB and HIV among children in Nigeria. Some studies conducted in Africa and other developing countries to estimate the prevalence of HIV among children diagnosed with tuberculosis have

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shown varying results ranging from 2-46 percent.[5-7] The present studywas embarked upon to determine the HIV sero-prevalence among children presenting with TB and to compare the treatment outcome of TB/HIV positive and TB/HIV negative children at the Tuberculosis and Leprosy (TBL) Control Centre, Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu.

Subjects and Methods

This was a retrospective study of children diagnosed with TB and referred to the TBL Control Centre at the department of Community Medicine and Primary Care, OOUTH, Sagamu. The children were referred from the Paediatrics department of the OOUTH and from private and public hospitals in and around Sagamu. The clinical records of patients being followed up in the clinic between January 2000 and December 2004 were reviewed. Diagnosis of TB was made on clinical (history of cough > three weeks with or without weight loss or no weight gain, history of contact with a suspected or diagnosed case of active TB within the last two years), microbiological (sputum smear examination; Mantoux test) and radiological (chest X-ray changes suggestive of TB) grounds. Children who were smear-positive for acid fast bacilli were started on anti-TB medications while those who were smear-negative underwent a one to two weeks' course of antibiotics and those who did not improve were considered for anti-TB treatment using a score chart as advocated in the National Tuberculosis and Leprosy Control guidelines; a score of 7 or more was considered diagnostic for TB.[8] Only those who improved on the anti-TB treatment were considered as cases of tuberculosis in this study.

The patients were classified into three diagnostic groups based on the clinical, microbiological and radiological findings as reported in a study in Abidjan.[5]

1. Pulmonary tuberculosis was diagnosed in children with pulmonary symptoms and signs, radiological abnormalities on chest X-ray and acid-fast bacilli in the sputum.

2. Extra-pulmonary tuberculosis was diagnosed in the absence of acid-fast bacilli in sputum but with appropriate clinical or radiological signs, microbiological or histological proof of extra-pulmonary TB.

3. Children were considered to have clinical tuberculosis when radiological abnormalities were noted on chest X-ray suggestive of tuberculosis including primary disease but acid-fast bacilli were not detected in the sputum.

The Centre for Special Studies (CSS) New York commenced anti-retroviral treatment programme in Sagamu in 1999.[6] The services included pre and post-test counselling for HIV; these services were extended to all patients diagnosed with TB. HIV screening, which was carried out on all children after informed consent was obtained from their parents/guardian, was carried out using two methods namely, the immunocombs II HIV 1&2 Bispot test kit (*Orgenics, France*) and the Capillus HIV-1/HIV-2 kit (*Cambridge Diagnostics, Ireland*). A positive test was considered only when the blood sample was positive with the two test kits. The Western Blot confirmatory test was not done because the test was not available at the centre during the period covered in this study. Living parents of all the children with positive HIV test were also screened for HIV. The treatment outcome categories were defined as "Died": death during TB treatment, "Treatment completed": patient completed prescribed treatment, and "Defaulted": patient failed to collect medication for more than two consecutive months after the date of the last attendance during the course of treatment.

Statistical analysis was performed using standard statistical methods by means of computer software for epidemiological studies (Epi info 6.04). The difference between TB/HIV positive and TB/HIV negative children were compared using Fisher's exact statistical methods to account for the small number of children. Differences between groups were considered significant where P d" 0.05.

Results

Seventy six patients (46 males and 30 females; a M:F ratio of 1.5:1) aged between one and 14 years presented at the TBL control centre during the study period. The mean age (SD) in the males was 5.3 ($\pm$3.8) years and 6.5 ($\pm$4.3) years for females, a difference that was not significant ($p=0.2$). Children aged four years and below, accounted for 51.3 percent of the cohort, 21.1 percent were aged between 5-9 years and 27.6 percent were aged 10-14 years (Table I). Of the 76 children, 60 (78.9 percent) had clinical tuberculosis, as defined above, 10 (13.2 percent) had pulmonary tuberculosis, and six (7.9 percent) had extra-pulmonary tuberculosis (TableI). Overall, clinical tuberculosis was more frequent in younger children while pulmonary tuberculosis was commoner in older children.

Eight (10.5 percent) of the 76 children tested HIV positive. HIV sero-prevalence increased over the years of the study but this increase was not statistically significant ($X^2=8.02$; $p=0.09$). HIV positive children were significantly older than HIV negative children

Table I

Ages and Categories of Tuberculosis in 76 Children

	Clinical TB		*Extra pulmonary TB*		*Pulmonary TB*	
Age (yrs)	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*
0-4	25	12	1	1	0	0
5-9	8	5	0	1	0	2
10-14	8	2	1	2	3	5
Total	41	19	2	4	3	7
HIV positive		4/60 (6.7%)		3/6 (50%)		1/10(10%)

Table II

Characteristics of Children with TB ± HIV

Characteristics	*HIV positive N=8*	*HIV negative N=68*	*Pvalue*
Age (years)			
0-4	3	36	
5-9	1	15	0.32
10-14	4	17	
Sex			
Male	4	42	
Female	4	26	0.55
Mean (years) ±SD	8.5±4.4	5.5±3.9	0.04
Mantoux positive	0	45*	0.00001

*Mantoux test results in nine patients were not documented

(8.5±4.4 v 5.5±3.9 years; p=0.04). The age range of HIV positive children was between 3-13 years. The age-specific HIV infection rate was 19.1 percent for children aged 10-14 years, 7.7 percent for those aged 0-4 years and 6.25 percent for those aged 5-9 years (Table II). The HIV sero-prevalence was 3/6 (50 percent) in children with extra-pulmonary tuberculosis, 1/10 (10 percent) in children diagnosed with pulmonary tuberculosis and 4/60 (6.7 percent) in children with clinical tuberculosis. The probable routes of transmission in the children that tested positive for HIV infection were perinatal transmission in four, blood transfusion in three and sexual transmission in one case.

Table III indicates that only one (12.5 percent) of the eight HIV positive children completed treatment

Table III

Treatment Outcome in Children with TB±HIV

Treatment Outcome	*HIV positive N=8*	*HIV negative N=68*	*Pvalue (Fishers exact)*
Treatment completed	1	46	0.004
Defaulted	4	20	0.19
Died	3	2	0.01

successfully compared to 46 (67.7 percent) of the 68 HIV negative children, a difference that was significant (p=0.004). Similarly, mortality was significantly higher among TB/HIV positive compared to TB/HIV negative children (3/8 vs 2/68; p=0.01). The default rate was however, similar in both groups of patients (4/8 vs 20/68; p=0.21).

Discussion

The HIV prevalence among children in the present study was 10.5 percent. This is comparable to that reported by workers from other countries such as Cote d'Ivoire,[5] India,[7] and Jamaica[9] where the rates range between 2-46 percent. It is however higher than the Nigerian national average of 4.4 percent obtained from a sentinel survey among pregnant women.[2] As far as we are aware, there is thus far, no data available on the HIV prevalence rate among children in this country.

None of the children with HIV had a positive Mantoux reaction. Furthermore, most of the children with HIV and TB co-infection presented mainly with clinical TB and extra-pulmonary TB. This development poses a major diagnostic challenge in resource poor settings where access to modern diagnostic methods for TB in children are lacking. This may eventually lead to a situation where many HIV positive children who have active TB are missed or sometimes result in the mistaken diagnosis of TB in children without the disease. There is therefore a need for clinicians to maintain a high index of suspicion for active TB among HIV positive children at all times. The use of a validated and standardized scoring system or improved diagnostic procedures for TB in the presence of HIV infection may be the solution to the likely diagnostic dilemma in such resource poor settings.[10]

Among those infected with HIV, the major routes of transmission were vertical and via blood transfusion. In view of this finding, pregnant women should be encouraged to undertake voluntary counseling and testing to identify those who are HIV infected so that they can benefit from effective low cost interventions available for the prevention of mother-to-child transmission of HIV. In addition, the Government should actively encourage the integration of counseling and testing services within existing antenatal care services in the country. The need for an operational blood safety policy cannot be overemphasized. The government needs to set up functional blood transfusion services adequately equipped with highly sensitive HIV diagnostic tests such as HIV polymerase chain reaction (PCR) which can detect HIV infection during the window period.

We observed a poor TB treatment outcome among HIV positive compared with HIV negative children. HIV positive children were significantly less likely to complete treatment and are more likely to die during TB treatment. This is consistent with findings in other studies in Africa which reported a higher mortality rate among HIV and TB co-infected children compared with those without HIV.[11-15] However, HIV/TB co-infected children commenced on anti-retroviral treatment during TB treatment have been shown to have a better outcome.[10] There is therefore a need to make antiretroviral drugs available, accessible and affordable to HIV infected children that need them, particularly those with HIV/TB co-infection as a child survival strategy. Close integration of HIV/AIDS and TB control programmes is essential in combating the dual epidemic.

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