Prevalence of Human Immunodeficiency Virus Infection in Children with Tuberculosis

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This prospective study was carried out in the pediatric ward and outpatient department of a tertiary care centre to estimate the prevalence of HIV seropositivity in children with tuberculosis. Two hundred and fifty consecutive children below 12 years of age with (pulmonary and extrapulmonary) tuberculosis diagnosed between March 1999 and July 2000 were screened for HIV infection. A patient was labeled as HIV positive if two consecutive ELISA tests were found positive using different antigen/principle. Supplemental western blot test was also done. Parents of seropositive children were also screened for HIV infection and tuberculosis. Total 5 cases were HIV positive giving a seroprevalence of 2%. All the five patients had disseminated tuberculosis. We suggest regular screening of children with disseminated/miliary tuberculosis for HIV co-infection.

Key words: *Co-infection, HIV, Tuberculosis.*

The scale of the AIDS crisis now outstrips even the worst case scenarios of a decade ago as dozens of countries are in the grip of the HIV/AIDS epidemic. Of the 14000 new HIV infections per day in 2002, 95% occurred in developing countries and 2000 of these were children(1). About a third of the 40 million people living with HIV/AIDS worldwide at the end of 2001 were co-infected with Mycobacterium tuberculosis, majority of these in resource constrained countries. Tuberculosis accounts for up to a third of AIDS deaths worldwide(2). Escalating tuberculosis case rates over the past decade in many countries in sub-Saharan Africa and in parts of South-east Asia are largely attributable to the HIV epidemic.

The risk of active tuberculosis in children with HIV is 5-10 times higher than those without HIV(3). Not much data is available on the prevalence and association of HIV with tuberculosis in children in India. The present study was undertaken to estimate the prevalence of HIV infection in children with tuberculosis.

Subjects and Methods

This study was carried out between March 1999 and July 2000 after being cleared by the Institutional Ethics Committee. Consecutive cases of tuberculosis up to 12 year old both hospitalized as well as those attending the outdoor clinics were studied. For the diagnosis of tuberculosis, suggestive clinical, radiological, cytological and histopathological criteria were taken into consideration(4). Asymptomatic Mantoux test positive cases were excluded.

Pre-test and post-test counselling was given to the parents/guardians. After written consent from parents, detailed history, physical examination, relevant investigations

and HIV screening of the children were done. About 4 mL venous blood was collected, serum separated and stored at –20º C. Samples were tested for HIV-1 and HIV-2 antibodies by INNOELISA (INNOGENETICS NV, Belgium). If tested negative, the child was labeled as HIV negative; positive result was confirmed by a second ELISA using a different antigen/principle. If the first ELISA was equivocal then a second ELISA was performed. If the second ELISA was also equivocal, then ELISA was repeated 2 weeks later. If this ELISA tested negative, then the child was labeled as HIV negative. A supplemental western blot test was also done in all ELISA positive/equivocal cases at National Institute of Communicable Diseases, New Delhi. Parents of all children with positive ELISA were also screened for HIV infection and tuberculosis.

Results

Only five of 250 patients with tuberculosis were HIV positive giving a prevalence of 2%; most patients were in the 1-9 year age group (72.4%) and belonged to lower and middle socio-economic class (65% and 34% respectively). The male to female ratio was 2.3:1. Mean weight for age in the study population was 67.2% and height for age 87.6%. History of contact with tuberculosis was present in 47% of the total cases and in two-thirds of those in 0-1 year age group. Both the parents were illiterate in 61.5% cases, with illiteracy amongst the mothers in 203 (81.2%) cases.

Fever was the most frequent complaint (87.6%) followed by anorexia (48.5%), cough (41.2%), altered sensorium (33.2%), failure to thrive (32.4%), abnormal movement (28%) and lymphnode enlargement (23.6%). Pallor (82.4%) and lymphadenopathy (28.4%) were the most frequent general examination findings. Systemic examination revealed central nervous system involvement in 29% cases, while respiratory system findings and hepatosplenomegaly were present in 26.5% and 11.5% cases respectively. About 53.6% of the cases had tuberculosis involving one or more extrapulmonary sites (*Table I*). Nearly 78% of those with extra pulmonary involvement had coexisting pulmonary tuberculosis. Chest *X*-ray revealed pleuropulmonary lesions in 69.5% cases with miliary findings in 10.8% cases. BCG vaccination as assessed by the presence of BCG scar was seen in only 21% cases; 90% of those with tubercular meningitis and 77.3% of those with disseminated tuberculosis were unvaccinated. Overall Mantoux test positivity was 29% while BCG test was positive in 59.8% cases.

TABLE I– *Extrapulmonary Tuberculosis in Different Age Groups.*

Sites involved	0-1 yr N = 34	1-4 yr N = 97	4-9 yr N = 84	9-12 yr N = 35	Total N = 250
Meningoencephalitis	18(52.9%)	38(39.2%)	14(16.7%)	6(17.1%)	76(30.4%)
Lymph node	1(2.9%)	16(16.4%)	19(22.6%)	6(17.1%)	42(16.8%)
Disseminated	6(17.6%)	16(16.4%)	3(3.6%)	2(5.7%)	27(10.8%)
Tuberculoma	0	0	3(3.6%)	1(2.9%)	4(1.6%)
Abdominal	0	0	1(1.2%)	3(8.6%)	4(1.6%)
Osteoarticular	0	0	3(3.6%)	0	3(1.2%)

All the five HIV positive cases had disseminated/miliary tuberculosis, were males, and were HIV-1 positive. The clinical and radiological profile of the HIV positive cases is summarized in *Table II*. There was only one seropositive case of 9 months (in whom PCR could not be done) where ELISA repeated on follow up at 18 months of age was also found to be positive for HIV. HIV-seropositive parents were asymptomatic. None of the parents of seropositive cases had active tuberculosis.

Discussion

HIV seroprevalence in the tubercular patients below 12 years of age in this study was 2%, which is much more than the prevalence of 0.7% reported among adults with tuberculosis from Delhi(5). This is also more than the prevalence of less than 1% reported in hospitalized children with high likelihood of HIV from this center(6). The

TABLE II–*Clinical and Radiological Profile of HIV Seropositive Cases.*

Characteristic§	Case 1	Case 2	Case 3	Case 4	Case 5
Age* (yr)	0.75	3	2	10	5
BCG vaccination	+	+	–	–	–
History of blood transfusion	–	–	–	+	–
Clinical features					
Weight loss/Abnormally slow growth	+	+	+	+	+
Cough >1 month	+	+	–	+	+
Diarrhea >1 month	+	–	–	–	–
Fever >1 month	–	+	+	+	+
Candidiasis	–	–	+	+	+
Lymhadenopathy	+	+	+	+	+
Hepatosplenomegaly	+	+	+	Hepatomegaly only	+
Generalized dermatitis	+	–	+	–	–
Nutritional status					
Weight for age (%)*	72	74	50	45	46
Height for age (%)*	79	90	94	90	87
Neurotuberculosis	–	–	+	+	+
Mantoux test	Negative	Negative	Negative	Negative	Negative
Chest *X*-ray	Infiltration in right upper zone	Middle zone consolidation	Miliary	Miliary	Miliary
HIV status of parents					
Mother	+	+	–	–	+
Father	+	–	–	–	Na†

§ ± means present/absent, * based on NCHS standard, † Not available for screening

Key Messages

- HIV seroprevalence in patients with tuberculosis below 12 years of age was 2%.
- Disseminated/miliary tuberculosis is more commonly associated with HIV infection in children.

high HIV seropositivity observed in tubercular adults in Mumbai (5.89%), and Pune (20.1%) is probably a reflection of the higher prevalence of HIV infection in general population in these regions(7,8). A prevalence rate of 18% is reported in children with miliary or neurotuberculosis(9). High seropositivity has been reported in both children and adults with tuberculosis in several regions in the grip of HIV epidemic in Central and East African countries(10-12). In contrast, we observed HIV positivity in 5/107 (4.7%) cases of disseminated and neurotuberculosis. If cases of disseminated tuberculosis alone are considered, then the seroprevalence increases to 18.50%, which is very high for a relatively low prevalence region.

In our study, none of the HIV positive cases were Mantoux positive which is in agreement with the observations of Dhurat, *et al.*(13). This makes it difficult to establish the diagnosis of tuberculosis in these HIV infected children. The clinical features of HIV infection in the seropositive cases were similar to the observations of other studies(13-16). We did not find any notable difference in clinical and radiological manifestations between HIV seropositive and negative tubercular patients confirming the observation of previous report(11); detailed clinico-radiological comparison was not possible due to the small number of seropositive children. Like other reports from children with HIV infection in India(9,15), we noted possible perinatal transmission in 3 of the 5 cases, in the other two cases the probable route of infection was parenteral. However, no conclusions can be drawn regarding the predominant route of transmission in pediatric HIV from such small number of seropositive cases.

HIV and tuberculosis are intersecting epidemics. While it is clear that HIV infection increases the risk of tuberculosis, immunologic and virologic evidence indicate that the reverse is also true(3,17). Moreover, both these infections have overlapping symptomatology. Tuberculosis, which is common in this part of the world, may itself satisfy clinical criteria similar to those for AIDS. Hence, tuberculosis and HIV/AIDS programmes will need to collaborate to deliver a more effective response to TB/HIV. Recently a study from Mumbai has suggested clinically-directed selective HIV screening in the face of increasing HIV prevalence and limited financial resources in India(18). Based on our observations, it can be concluded that in areas where HIV infection is still not very high but prevalence of tuberculosis is much higher, regular screening of cases of disseminated and miliary tuberculosis in children may reduce the number of patients with undiagnosed HIV. However, larger and preferably multi-centric data on prevalence of HIV in disseminated/miliary tuberculosis is required to confirm this observation. Whether the prevalence, pattern and progression of tuberculosis in HIV infected children has any relation to CD4 counts also needs to be evaluated.

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AM performed the ELISA test for HIV. KA and TS drafted the article; KA will act as the guarantor.

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REFERENCES

1. HIV-AIDS: Facts and Figures - AIDS epidemic update 2002, WHO. Available from URL: http://www.who.int/hiv/facts/plwha.
2. Joint HIV/Tuberculosis interventions. WHO; Available from URL: http://www. who. int/ hiv/topics/tb/tuberculosis/en.
3. Cherian T, Verghese PV. Tuberculosis and human immunodeficiency virus infection. Indian J Pediatr 2000; 67: S47-S52.
4. Seth V. Diagnosis-I: Clinical aspects, tuberculin test and radiology. *In:* Seth V. Essentials of Tuberculosis in Children. New Delhi, Jaypee; 1997, pp 206-209.
5. Jain SK, Aggarwal JK, Rajpal S, Bareja V. Prevalence of HIV infection among tuberculosis patients in Delhi-A sentinel surveillance study. Indian J Tub 2000; 47:21.
6. Lahiri S, Shahab T, Malik A, Alam S. HIV seropositivity in hospitalized children with high likelihood of AIDS. Indian Pediatr 2002; 39: 372-375.
7. Mohanty KC. Changing trend of HIV infection in patients with respiratory diseases in Bombay since 1988. Indian J Tub 1994; 41: 147.
8. Paranjape RS, Tripathy SP, Menon PA, Mehendale SM, Khatavkar P, Joshi DR, *et al*. Increasing trend of HIV seroprevalence among pulmonary tuberculosis patients in Pune. Indian J Med Res 1997; 106: 207-211.
9. Merchant RH , Shroff RC. HIV seroprevalence in disseminated tuberculosis and chronic diarrhea. Indian Pediatr 1998; 35: 883-887.
10. Luo C, Chintu C, Bhat G, Raviglione M, Diwan V, DuPont HL, *et al*. Human immunodeficiency virus type 1 infection in Zambian children with tuberculosis: changing seroprevalence and evaluation of a thiaceta-zone free regimen. Tuber Lung Dis 1994; 75: 110-115.
11. Mukadi YD, Witkor SZ, Coulibaly IM, Coulibaly D, Mbengue A, Folquet AM, *et al.* Impact of HIV infection on the development, clinical presentation and outcome of tuberculosis among children of Abidjan, Cote d' Ivoire. AIDS 1997; 11: 1151-1158.
12. Batungwanayo J, Taelman H, Dhote R, Bogaerts J, Allen S, Van de Perre P. Pulmonary tuberculosis in Kigali, Rwanda. Impact of human immunodeficiency virus infection on clinical and radiographic presentation. Am Rev Respir Dis, 1992; 146: 53-65.
13. Dhurat R, Manglani M, Sharma R, Shah NK. Clinical spectrum of HIV infection. Indian Pediatr 2000; 37: 831-836.
14. Verghese VP, Cherian T, Cherian AJ, Babu PG, John T J, Kirubakaran C, *et al*. Clinical ranifestation of HIV-1 infection. Indian Pediatr 2002; 39: 57-63.
15. Merchant RH, Oswal JS, Bhagwat RV, Karkare J. Clinical profile of HIV infection. Indian Pediatr 2001; 38: 239-246.
16. Daga SR, Verma B, Gosavi DV. HIV infection in children: Indian experience. Indian Pediatr 1999; 36: 1250-1253.
17. Nakata K, Rom WN, Honda Y, Condos R, Kanegasaki S, Cao Y, *et al*. Mycobacterium tuberculosis enhances human immunodeficiency virus-1replication in the lung. Am J Respir Crit Care Med 1997; 155: 996-1003.
18. Karande S, Bhalke S, Kelkar A, Ahuja S, Kulkarni M, Mathur M. Utility of clinically-directed selective screening to diagnose HIV infection in hospitalized children in Bombay, India. J Trop Pediatr 2002; 48: 149-155.