Original Research Article

Prevalence of HIV infection among children with TB and correlation of CD4 cell count level with types of TB

Sivabalan T., Rajkumar G.*

Department of Paediatrics, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamil Nadu, India

*Correspondence:
Dr. Rajkumar G.,
E-mail: grkmedico@outlook.com

ABSTRACT

Background: Tuberculosis (TB) is the second most common cause of death from infectious diseases at the global level, being second only to HIV/AIDS. The present study has been undertaken to find out the prevalence of HIV infection among children with TB and correlation of CD4 cell count level with different types of TB.

Methods: This cross-sectional study was carried out in children below 12 years who were diagnosed as having TB, using the modified Kenneth Jones criteria (742 TB infected children) between 2008 and 2010. Descriptive statistics were used to calculate the frequency, mean, median and standard deviation. The linear trend of proportions and trend of chi-square was used to find out the test of association.

Results: The HIV prevalence rate among children with Tuberculosis was 9.7%. In TB/HIV coinfection, Pulmonary TB was 44 (61.1%), lymph node TB was 22 (30.6%), Central Nervous System TB was 4 (5.6%), abdominal TB was 1 (1.4%) and spine TB was (1.4%). Pulmonary TB was the most common type is the not significant, mild and advanced grade of immune suppression. CNS tuberculosis was the most common type in the severe grade of immune suppression. CNS TB occurred more commonly in children more than 60 months of age. Lymph node TB is the commonest type of tuberculosis in children with HIV coinfection less than 35 months of age.

Conclusions: The prevalence of HIV among tuberculosis children was 9.7%. This prevalence rate indicates the need for routine screening of all newly diagnosed tuberculous children for HIV coinfection.

Keywords: Coinfection, HIV, Prevalence, Screening, Tuberculosis

INTRODUCTION

As per the Global TB report 2017, the estimated prevalence of TB in India was approximately 28, 00,000 accounting for about a quarter of the world's TB cases. The incidence of TB is 211 per lakh population, with a mortality rate of 32 per lakh population. The incidence of HIV-TB co-infection was 6.6 per lack and mortality due to HIV-TB co-infection was 0.92 per LAKH population. When translated to absolute numbers, TB contributed to 4,23,000 deaths and TB-HIV co-infection contributed to close to 12,000 deaths across the country in the year 2017.[1] Tuberculosis in children is an important problem especially in countries like India where adult tuberculosis is very common. Children can present with tuberculosis at any age, but the majority of cases present between 1 and 4 years. The disease usually develops within one year of infection in younger individuals and the disease progression is earlier and more disseminated. Pulmonary tuberculosis is usually smear-negative. Pulmonary tuberculosis (PTB) to extrapulmonary tuberculosis (EPTB) ratio is usually around 3:1. In infants, the period between infection and disease can be as little as 6 to 8 weeks.[2,3]

Worldwide, tuberculosis is the most common cause of death among patients with AIDS, killing one in every three patients.[4] CD4 cut-offs predict the risk of clinical

disease progression and mortality. CD4 percentage and CD4 counts are higher in infants compared to that of adult values by age 5 years. Also, the counts vary due to diurnal change, undercurrent illnesses, steroid treatment, splenectomy, etc. Hence repeated measurements are more informative than one single value. The absolute CD4 counts change with the age of the child. CD4 percentage does not vary as much with age, and hence this is used in the determination of the level of immunosuppression. The decision to start antiretroviral therapy is based on clinical indicators supplemented with the CD4 counts. It also helps to monitor disease progression. When the CD4 count is more severely affected than the clinical stage, one should consider CD4 cut-off for initiation of antiretroviral therapy.[5,6]

The present study was undertaken to find the out prevalence of HIV infection among children with tuberculosis and correlation of CD4 cell count level with the types of tuberculosis.

METHODS

This cross-sectional study was carried out in the Department of Paediatrics after obtaining approval from the Institutional Ethical Committee.

Inclusion criteria

- Children of both genders below 12 years who were diagnosed as having tuberculosis using the modified Kenneth Jones criteria were included in this study.

Consent was obtained from parents of each child enrolled in the study. Children were subjected to tests like ELISA or PCR as per their age for the diagnosis of HIV following the WHO/NACO/UNAIDS strategy. In this study, strategy 2 (symptomatic individuals, the i.e.

sample was considered negative if the first report was negative. If positive the children were subjected to second ELISA antibody test and reported positive if the second test was also positive) and strategy 3 (asymptomatic individuals, i.e. additional to strategy 2, this included a third ELISA confirmation before reporting as HIV positive) were used for the diagnosis of HIV. Those children who were HIV positive were subjected to further tests. The CD4 count is done for all children who turned out to be HIV positive at the ART centre and results were collected and analysed. The CD4 grading was done according to the WHO revised the classification of immunosuppression in children.[7]

Statistical analysis

Descriptive statistics were used to calculate the frequency, mean, median and standard deviation. To examine the linear trend of proportions, trend chi-square was used and to find out the test of association chi-square was computed. All the statistical analysis was performed using SPSS, version 16.0.

RESULTS

A total of 742 children infected with various forms of TB were included in the study. Of these, 72 (9.7%) TB infected children showed HIV coinfection of which male children (63.9%) were more affected than female children (36.1%).

Table 1 shows the grading of the immune status of the children based on WHO revised the classification of immunosuppression in children. Absolute CD4 counts are more reliable than % in children more than 5 years of age. Hence both parameters are used for that age group. Age-wise distribution of TB co-infected with HIV was shown in Table 2.

Table 1: Grading of the immune status of the children based on WHO revised the classification of immunosuppression.

Grade of immunosuppression	Frequency (%)	CD4 values			
		< 11Mo (%)	12-35Mo (%)	36-59Mo (%)	>59Mo (cells/mm^3 or %)
Not significant	6 (8.3)	>35	>30	>25	>500
Mild	34 (47.2)	30-35	25-30	20-25	350-499
Advanced	30 (41.7)	25-30	20-25	15-20	200-349
Severe	2 (2.8)	<25	<20	<15	<200 or <15%

Table 2: Age-wise distribution and type of TB co-infected with HIV.

Age	Type of TB, number (percentage)					
	Pulmonary TB	Lymph node TB	Abdominal TB	CNS TB	Spine TB	Total
12-35 months	3 (42.9)	4 (57.1)	-	-	-	7 (100)
36-59 months	11 (52.4)	9 (42.9)	-	-	1 (4.7)	21 (100)
>59 months	30 (68.2)	9 (20.5)	1 (2.3)	4 (9.1)	-	44 (100)
Total	44 (61.1)	22 (30.6)	1 (1.4)	4 (5.6)	1 (1.4)	72 (100)

Table 3: Correlation of CD4 with the type of TB.

Grade of immunosuppression	Pulmonary TB	Lymph node TB	Abdominal TB	CNS TB	Spine TB	Total
	Number (percentage)					
Not significant	3 (60)	2 (40)	-	-	-	5 (100)
Mild	20 (64.5)	11(35.5)	-	-	-	31 (100)
Advanced	19 (63.03)	9 (30)	1 (3.3)	1 (3.3)	-	30 (100)
Severe	2 (33.3)	-	-	3 (50)	1 (16.7)	6 (100)
Total	44 (61)	22 (30)	1 (1.75)	4 (5.5)	1 (1.75)	72 (100)

Distribution of type of TB and its co-infection with HIV among the study population is shown in Table 2. Commonest type of TB was pulmonary TB followed by Lymph node TB in all age groups. CNS and abdominal TB are seen in children more than 5 years of age.

Table 3 shows the correlation of the type of TB with the CD4 count. A severe grade of immune suppression is seen only with CNS and Spine TB, while a mild and advanced grade of immune suppression is seen in pulmonary and lymph node TB. This linear trend of association is done using Chi-Square test which showed a significant association (p=0.04).

DISCUSSION

In this study, out of 742 children, 72 children were HIV positive. This implies that 9.7% of children with tuberculosis were co-infected with HIV which can have a great impact on the morbidity and mortality and treatment outcome of these children. This was very low when compared to studies in South Africa where it was 45%.[8] But higher than the 5.12% in an another India study.[9] This difference could be because of the variations in prevalence (higher burden) of HIV in the respective areas. However, this was very similar to the study done in Agra, India which showed a seroprevalence rate of 8.51%.[10]

The major chunk was in the age group of more than 5 yrs (44%) in present study. This is different from other study[9], which showed an increased prevalence in the age group of 1-5 yrs of age. In the study by the highest prevalence was seen in the age group of 2-5 years.[10] In the study by Parthasarathy P et al, most participants belonged to the age group of 4-7 years.[11]

In this study male children (63.9%) were more affected than female children (36.1%) and the findings were similar to the Agra study, which also showed a high distribution in male (85.61%) than a female child (17.39%).[10] This may be due to the parental bias to care more for a male child than a female child in the lower socioeconomic groups who are the major people getting health care in this hospital. Parthasarathy P et al in their study also showed 65.1% were males and 3.8% were females in their study which was also in accordance with the current study.[11]

In this study pulmonary TB was the most common tuberculosis type (61.1%) followed by lymphatic TB (30.6%). CNS tuberculosis was next (5.6%), and abdominal and spinal TB had a share of 1.4% each. Overall 39.9% of HIV/TB co-infected children had extrapulmonary TB. Most participants were more than 5 years old. In the Agra study, a similar pattern of distribution with more pulmonary (86.75%) than extrapulmonary TB (13.4%) was found.[10] whereas, the overall extrapulmonary TB was 46.1% in the study by Jain SK et al which was more compared to the current study.[12]

In this study, authors have classified HIV/ TB coinfected children into four groups according to WHO classification. In this study, 47.2% of the co-infected children had a mild grade of immunosuppression, and 41.7% had an advanced grade of immune suppression. Only 8.3% of the coinfected children had a CD4 count level which was not significant. The pulmonary TB was more common in the mild grade of immune suppression (45.5%) than in advanced grade (43.2%) of immune suppression.

Lymphatic TB was more common in the mild grade of immune suppression (50%) followed by advanced (40.9%) grade of immune suppression. CNS TB was seen in the advanced grade of immune suppression. In the study by Antonucci G et al, it was seen that there is an increasing risk of tuberculosis as CD4 declines.[13] The CD4 count distribution among HIV-infected patients was markedly skewed, with a majority of cases having CD4 cell counts <200 cells/μL in the study by Gupta RK et al.[14]

HIV coinfection and lower CD4 cell counts were associated with lower rates of laboratory-confirmed disease, a higher proportion of EPTB and lower sputum smear grades even among those with the highest CD4 cell counts. However, decreasing CD4 cell counts were not associated with a linear decline in the proportion of pulmonary cases testing sputum smear-positive.

Limitations: This study was done in a tertiary care centre hence the same prevalence needs not to be true at the community level. The CD4 count was not done for all tuberculosis patients. Outcome of these HIV/TB co-infected individuals was not studied.

CONCLUSION

The HIV prevalence rate among tuberculous children in this study was 9.7%. Hence screening of all newly diagnosed tuberculous children for HIV coinfection can be undertaken as a routine. Pulmonary TB is the most common type of TB in HIV/TB coinfection in this study. Pulmonary TB was the most common type in the not significant, mild and advanced grade of immune suppression. CNS tuberculosis was the most common type in the severe grade of immune suppression. CNS TB occurred more commonly in children more than 60 months of age. Lymph node TB was the commonest type of tuberculosis in children with HIV co-infection less than 35 months of age.

REFERENCES

1. India TB Report 2018. New Delhi: Directorate General of Health Services, Ministry of Health and Family Welfare; 2018:7-11. Available at: http://file:///C:/Users/Archana/Downloads/62503114 44TB%20India%20Report%202018.pdf. 2018.
2. Newton SM, Brent AJ, Anderson S, Whittaker E, Kampmann B. Paediatric tuberculosis. Lancet Infect Dis. 2008;8(8):498-510.
3. Marais BJ, Schaaf HS. Tuberculosis in children. Cold Spring Harb Perspect Med. 2014;4(9):a017855.
4. Sandhu GK. Tuberculosis: current situation, challenges and overview of its control programs in India. J Glob Infect Dis. 2011;3(2):143-50.
5. Yin DE, Warshaw MG, Miller WC, Castro H, Fiscus SA, Harper LM, et al. Using CD4 percentage and age to optimize pediatric antiretroviral therapy initiation. Pediatr. 2014;134(4):e1104-e16.
6. Guideliness for HIV care and treatment in infants and children by IAP and NACO Nov 2006. Available at: http://www.iapsmgc.org/userfiles/4Guidelines_for_ HIV_care_and_treatment_in_Infants_and_children. pdf.
7. WHO. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Progress report. 2007. Available at: http://www.who.int/hiv/mediacentre/universal_acce ss_progress_report_en.pdf.
8. Flick RJ, Kim MH, Simon K, Munthali A, Hosseinipour MC, Rosenberg NE, et al. Burden of disease and risk factors for death among children treated for tuberculosis in Malawi. Int J Tuberc Lung Dis. 2016;20(8):1046-54.
9. Ramzan M, Ali SM, Malik A, Zaka-ur-Rab Z, Shahab T. Frequency of HIV infection amongst children with disseminated tuberculosis and tuberculous meningitis in Aligarh (North India)-a low HIV prevalence area. J Coll Physicians Surg Pak. 2009;19:566-9.
10. Hussain T, Sinha S, Kulshreshtha KK, Yadav VS, Sharma P, Sengupta U, et al. Seroprevalence of HIV infection among tuberculosis patients in Agra, India--a hospital-based study. Tuberculosis (Edinb). 2006;86(1):54-9.
11. Parthasarathy P, Mittal SK, Sharma VK. Prevalence of pediatric HIV in New Delhi. Indian J Pediatr 2006;73(3):205-7.
12. Jain SK, Ordonez A, Kinikar A, Gupte N, Thakar M, Mave V, et al. Pediatric tuberculosis in young children in India: a prospective study. Biomed Res Int. 2013;2013:783698.
13. Antonucci G, Girardi E, Raviglione MC, Ippolito G. Risk factors for tuberculosis in HIV-infected persons. A prospective cohort study. The Gruppo Italiano di Studio Tubercolosi e AIDS (GISTA). JAMA. 1995;274(2):143-8.
14. Gupta RK, Lawn SD, Bekker LG, Caldwell J, Kaplan R, Wood R. Impact of human immunodeficiency virus and CD4 count on tuberculosis diagnosis: analysis of city-wide data from Cape Town, South Africa. Int J Tuberc Lung Dis. 2013;17(8):1014-22.