

Original Research Article

A study on clinical profile of tuberculosis in HIV children

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Received: 30 April 2019

Accepted: 08 May 2019

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ABSTRACT

Background: Children born to Human immunodeficiency virus (HIV) positive parents who are not infected with tuberculosis (TB) themselves, are also at higher risk of acquiring TB because of exposure. The source of transmission of TB to a child is usually an adult with sputum-smear positive PTB. To evaluate the clinical, bacteriological and radiological pattern of TB in HIV seropositive children in correlation with CD4 count.

Methods: This study was conducted over a period of 12 months from May 2008- April 2009 at GMKMCH Salem. 100 children screened positive for HIV at voluntary counselling and testing centers (VCTC) in Antiretroviral therapy (ART) center and diagnosed to have TB infection as per Revised national tuberculosis control programme (RNTCP) guidelines.

Results: Out of the 100 children with HIV and TB infection 62 were males and 38 were females. The ratio was 1.63:1. The sputum positivity in our study shows that only 9% of the children are sputum positive. Sputum culture for *M. Tuberculosis* remains the gold standard for the diagnosis of Pulmonary TB. In resource-poor countries, the diagnosis is heavily dependent on the sputum AFB smear. In our study CD4 cell count, less than 300 was observed in 33 children. In these children the predominant X-ray lesions were Hilar adenopathy, lower lobe infiltrations, diffuse infiltrates and miliary mottling. Upper lobe infiltrates was common with higher CD4 count mean 350.

Conclusions: With the conventional sputum positivity and Tuberculin test not providing an adequate diagnostic help, familiarity with clinical radiological spectrum of TB and HIV co-infection will help in early diagnosis and improve survival among HIV seropositive children.

Keywords: CD4 count, Chest x-ray, Human immunodeficiency virus, Pulmonary tuberculosis

INTRODUCTION

HIV is driving TB epidemic in many countries, especially in sub-Saharan Africa and increasingly, in Asia and South America.¹ TB in populations with high HIV prevalence is a leading cause of morbidity and mortality. Children who are HIV infected have a higher risk of progression after primary infection. Children born to HIV positive parents who are not infected with TB themselves are also at higher risk of acquiring TB because of exposure.² The source of transmission of TB to a child is usually an adult with sputum-smear positive PTB. While only 10% of TB infection progresses to TB disease, if

untreated the death rate is 51%. The primary complex of tuberculosis includes local infection at the portal of entry and the regional lymph nodes.³ TB infection begins when the MTB bacilli reach the pulmonary alveoli, infecting alveolar macrophages where the mycobacteria replicate. The primary site of infection in the lungs is called the Ghonfocus, which is the combination of a parenchymal pulmonary lesion and a corresponding lymph node site.⁴ The tubercle bacilli are carried to most tissues of the body through the blood and lymphatic vessels to the more distant tissues and organs where TB disease could potentially develop: lung apices, peripheral lymph nodes, kidneys, brain, and bone Tuberculosis is classified as one

of the granulomatous inflammatory conditions. Macrophages, T lymphocytes, B lymphocytes, and fibroblasts are among the cells that aggregate to form a granuloma, with lymphocytes surrounding infected macrophages.⁵ The granuloma functions not only to prevent dissemination of mycobacteria but also provides a local environment for the communication of cells of the immune system.⁶ Within the granuloma, T lymphocytes (CD4+) secrete a cytokine such as an interferon gamma, which activates macrophages to destroy the bacteria with which they are infected, making them better able to fight infection.⁷ T lymphocytes (CD8+) can also directly kill infected cells by secreting perforin and granzyme. Importantly, bacteria are not eliminated within the granuloma but can become dormant resulting in a latent infection.⁸ Latent infection can be diagnosed by tuberculin skin test, which yields a delayed hypersensitivity type response to purified protein derivatives of *M. tuberculosis* in an infected person.⁹ Another feature of the granulomas of human tuberculosis is the development of cell death, also called necrosis, in the center of tubercles. To the naked eye, this has the texture of soft white cheese and was termed caseous necrosis. Cases of TB in children represent between 10% to 20% of all TB cases. Extrapulmonary TB manifestations are Lymphadenopathy, Pleural effusion, Miliary TB, TB meningitis, TB Abdomen, Disseminated TB, Potts Spine.¹⁰

METHODS

This study was conducted over a period of 12 months from May 2008- April 2009 at GMKMCH Salem. 100 children screened positive for HIV at VCTC in ART center and diagnosed to have TB infection as per RNTCP guidelines.

Inclusion criteria

Children who are seropositive in the age group of 18 months to 12 years registered in the ART center. Children with stigmata for TB like fever, cough with expectoration lasting for more than three weeks, loss of appetite and loss of weight. Children who are suffering from Extrapulmonary TB infection like TB pericarditis, TB Meningitis, TB Abdomen, Isolated TB Potts spine, Disseminated TB.

Exclusion Criteria

Children <18 months were not taken into consideration, as the facility for making a diagnosis of HIV by PCR was not available in our center. Informed consent was obtained from the parent/ guardian for registering the required data.

Statistical analysis

Data were entered using Microsoft Excel and analyzed using STATA software. A continuous variable was

analyzed using the student 't' test which was used to determine the significant difference.

RESULTS

The study population was derived from the persons attending the outpatient department at GMKMCH, Salem. Out of 512 confirmed cases of HIV infection, 100 were found to be suffering from Tuberculosis, they formed the study population.

Table 1 shows Out of 100 seropositive children with TB co-infection, 62% were males and 38% were females. This indicates that the male: female ratio is 1.6:1. The prevalence of HIV-TB co-infection is 70% in the age group of 6-12 years. 92 Children were delivered by normal vaginal delivery out of which 13 were delivered at home, rest 79 were delivered in hospital. 8 Children were delivered by emergency LSCS.

Table 1: Age group distribution

Age group	Male	Female
1 ½ to 5 Years	19	11
6-12 Years	43	27
Total	62	38

Table 2 shows the sputum positivity in our study shows that only 9% of the children are sputum positive. Sputum culture for Tuberculosis remains the gold standard for the diagnosis of Pulmonary TB. In resource-poor countries, the diagnosis is heavily dependent on the sputum AFB smear. The clinical presentations was Lymphadenopathy mostly cervical (11%) and axillary in 1%. In respiratory system signs of pneumonia was present in 60%, 2 children had pleural effusion, 2 had bronchiectasis, 2 children had consolidation/collapse. Thus, respiratory system was involved in 66% of children.

Table 2: Sputum positivity

Sputum for AFB	Number
Sputum Positive	9
Sputum Negative	91

Table 3: The CD4 count correlation with who clinical staging was as follows

WHO STAGE		
CD4 Count	STAGE III	STAGE IV
0-100	9	5
101-200	6	2
201-300	12	2
>300	59	5
Total	86	14

Table 3 shows the sputum positivity in our study shows that only 9% of the children are sputum positive. Sputum culture for *M. Tuberculosis* remains the gold standard for

the diagnosis of Pulmonary TB. In resource-poor countries, the diagnosis is heavily dependent on the sputum AFB smear. In our study CD4 cell count, less than 300 was observed in 33 children.

Table 4 shows CD4 cell count less than 300 was observed in 33 children. In these children the predominant X-ray lesions were Hilar adenopathy, lower lobe infiltrations, diffuse infiltrates and miliary mottling. Upper lobe

infiltrates was common with higher CD4 count mean 350. Shows. In these children the predominant X-ray lesions were Hilar adenopathy, lower lobe infiltrations, diffuse infiltrates and miliary mottling. Upper lobe infiltrates was common with higher CD4 count mean 350.

Table 4: The correlation of CXR findings with CD4 count.

CD4 Count	Segmental /Lobar infiltrates	Diffuse infiltrates	Miliary TB	Pleural effusion	Bronchiectasis	Hilar adenopathy	Normal
0-100	3	5	2	-	1	-	2
101-200	-	1	1	-	-	-	2
201-300	7	3	-	2	-	1	1
>300	31	16	2	2	2	3	13
Total	41	25	5	4	3	4	18

DISCUSSION

Tuberculosis (TB) is a global health problem with India contributing more than 40% of the total infected population. The burden of childhood tuberculosis is unclear but 10% of the total tuberculosis load is found in children. In children, due to difficulties in obtaining microbiological confirmation, timely management of patients is affected, which leads to increased morbidity and mortality.¹¹ An incidence rate of 2.85 cases per 100,000 children per year is reported in the United States while in India, an incidence rate of 100-299 per 100,000 people per year has been reported in different districts. Pulmonary TB is more commonly seen in children less than 5 years of age.¹² Diagnosis of TB in children usually follows the discovery of a case in an adult and needs to be confirmed by tuberculin skin testing, chest radiograph, and clinical signs and symptoms. In our study, Pulmonary TB was more commonly found in children less than 5 years of age. This is similar to a study done by Johnson JL et al.¹³ We found that primary complex was more common in children <years of age whereas cavitary TB was more common in children above 5 years of age. However, no such differentiation has been reported in the literature. Our study showed a male predominance. A similar study by Lederman MM et al showed more males being more affected. The male predominance in the study may be due to their ambulatory nature, which makes them more exposed to the TB infected cases. It could also be due to a referral bias due to better care seeking for males due to a preference for boys in Indian families.¹⁴ The protective efficacy of BCG vaccination is known but in the present study pulmonary TB was seen in children who had received BCG immunization. This indicates that there is still a significant chance of developing pulmonary

TB even in the presence of BCG vaccination. A positive Mantoux test also supports the diagnosis of TB and has been used for circumstantial evidence for the diagnosis of TB. However, a negative Mantoux test does not rule out the diagnosis of TB. Mantoux test was found to be positive in more than half the patients in our study.¹⁵ One of the main reasons for children developing tuberculosis is through contacts but in our study, only 35.5% of patients gave a history of TB contact. This may be because of the family members not giving true history due to the social stigma attached to this disease and also the adult source case may not be identified in the areas endemic for TB. Diagnosis of tuberculosis is difficult in children and hematological parameters usually aid in the diagnosis. Raised ESR was seen in most types of TB in our patients, which is similar to a study done by Misra SN et al who found a high ESR in most patients with pulmonary Tuberculosis.¹⁶ Children acquired infection by perinatal transmission, one child has infected following blood transfusion. In two children the actual mode of transmission could not be identified. Moore M, et al study reported that perinatal transmission was the predominant root of transmission (87%) followed by blood transfusion (10%) and the mode of transmission could not be ascertained in rest 3%. Blood and blood products remain an important source of infection in 10-30% of the total cases in developing countries.¹⁷ The children in stage IV were severely malnourished and belonged to Grade III and Grade IV PEM. All children in our study population were on regular Cotrimoxazole prophylaxis.¹⁸ The most important finding of this study is the impact of HIV related immunosuppression among children with TB. 8 children with CD4% of less than 10% died during 6 months of therapy.^{18,19}

CONCLUSION

This study documents the importance of HIV infection as an independent risk factor for the development of TB in children and also demonstrate that HIV related immunosuppression as a critical risk factor for mortality in this population. With the conventional sputum positivity and Tuberculin test not providing an adequate diagnostic help, familiarity with clinical radiological spectrum of TB and HIV co-infection will help in early diagnosis and improve survival among HIV seropositive children.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Nirmala M, Narmadha V. A study on clinical profile of tuberculosis in HIV children. *Int J Contemp Pediatr* 2019;6:1506-9.