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Research Article

Prevalence of pulmonary tuberculosis in retroviral positive chest symptomatics in a tertiary care hospital, South India

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ABSTRACT

Background: Human immunodeficiency virus (HIV) associated tuberculosis (TB) remains a major global public health challenge. As this co-infection results in high mortality among retroviral positive patients, we undertook this study to find its prevalence in our region.
Methods: Sputum smears from all retroviral positive patients who attended the ART clinic from April 2015 to February 2016 were examined for the presence of *Mycobacterium tuberculosis* bacilli by fluorescent staining technique. CD4 lymphocyte counting was also done by using BD FACS count instrument.
Results: 65 patients were retroviral positive among the 180 patients who came to ART clinic. Of them 43 (66%) were males and 22 (34%) were females. 30 (46%) of retroviral positive patients were sputum positive indicating HIV-TB co-infection. 60% of co-infected patients belong to productive age group of 16-45 years. 93.4% of the co-infected patients had CD4 counts below 350 cells/µl. sputum negative retroviral positive patients had more than 250 CD4 cells/ µl.
Conclusions: Our study highlights the fact that HIV-TB co-infection is more prevalent in productive age group and has a positive correlation with lower CD4 counts.

Keywords: HIV, Mycobacterium tuberculosis, CD4 lymphocyte, HIV-TB co-infection

INTRODUCTION

TB may occur at any stage of HIV disease and is frequently the first recognized presentation of underlying HIV infection.[1,2] WHO recommends TB screening at the time that HIV infection is diagnosed, before the initiation of antiretroviral therapy and at regular intervals during follow up.

TB is the most common opportunistic infection (OI) among HIV-infected individuals, and co-infected individuals are at high risk of death.[3,4] HIV co- infection is the most powerful known risk factor for progression of *M. tuberculosis* infection to active disease, increasing the risk of latent TB reactivation to 20-fold.[5,6] In the host the two pathogens, *M. tuberculosis* and HIV, potentiate one another, accelerating the deterioration of immunological functions and resulting in premature death if untreated. TB is the largest single cause of death in the setting of AIDS 3, accounting for about 26% of AIDS-related deaths 5, 99% of which occur in developing countries.[7]

About a third of HIV infected individuals worldwide are co-infected with TB infection. The lifetime risk of developing active TB in immunocompetent adults is estimated to be 5%-10% during their lifetime, but in HIV-positive individuals this risk is increased to 5%-15% annually.[8] Around 14 million individuals worldwide are estimated to be dually infected and 0.38 million deaths among HIV-positive TB patients. Most TB cases were in the South-East Asia, Africa and Western Pacific regions.[9-11] This is especially important in India, where it is estimated that 40 per cent of the adult population is infected with M. tuberculosis. There were an estimated

5.134 million PLWHA at the end of 2004.[12] The incidence of TB is 1.8 million per year. With HIV pitching in, TB incidence levels could go up to 2.0 million or more per year, assuming HIV rates close to 1% and the incidence of TB remaining at 1990 levels.[13-15] It is estimated that 50-60 per cent of the HIV-infected persons in India will develop TB disease during their life-time.[16] Therefore, the task of controlling the dual epidemic of TB and HIV/AIDS remains a major challenge for the country.

In early 1990s, several institutional outbreaks of multidrug-resistant (MDR) TB among HIV-infected patients drew attention to the problem.[17-21] Unlike other opportunistic infections which occur at CD4+ counts below 200/mm3, active TB occurs throughout the course of HIV disease.[22]

Clinical presentation of TB in HIV-infected individuals depends on the level of immunosuppression resulting from HIV infection. In patients with relatively intact immune function (CD4+ count >200/mm3), pulmonary TB (PTB) is more frequently seen than extra pulmonary TB (EPTB).[23,24] In these patients, chest radiographic findings include upper lobe infiltrates and cavitation, similar to those in HIV- negative individuals with PTB.[25] Sputum smears are often positive for acid-fast bacilli (AFB) in these patients.

Diagnosis of pulmonary TB is based on simple techniques like sputum smear microscopy and chest radiography. Microscopy has the advantage of being inexpensive, relatively rapid to perform, and specific in most settings. However, to be considered smear positive a specimen needs to contain approximately 105 mycobacteria per millilitre. The sensitivity of sputum microscopy in HIV infection ranges from 43 to 51%, and in many resource-limited settings with high rates of co-infection, the sensitivity may be much lower.[26]

Methods that improve speed or sensitivity include fluorescence microscopy.[27] The advantages of fluorescence over light microscopy for the detection of pulmonary TB have been confirmed in a systematic review of 45 studies comparing the 2 methods, which found that fluorescence microscopy yielded an average increase in sensitivity of 10% with no loss of specificity.[27]

METHODS

This is a prospective study conducted in the Department of Microbiology and ART, Government Thiruvarur Medical College and hospital, Thiruvarur, India. The institutional ethical committee approval was obtained. The study period is from April 2013 to February 2014. About 180 patients who had attended the ICTC clinic were chosen. Of them, only 65 were retroviral positive and they were included in the study.

CD4+ counting

Whole blood sample was collected from the patients in K 3 EDTA liquid vacutainer tube. Samples were processed on the day of collection itself. First, control run was done. Controls supplied with the kit were prepared by adding normal blood and fixative solution to the CD4 reagent tube. Before running the reagent tubes on the instrument control beads were added.

A set of three reagent tubes were used and labelled as low, medium and high. Tubes were vortexed, cored, 50 micro litres of normal blood added and vortexed, incubated at room temperature for 30 minutes. Fixative solution was added and vortexed. Control beads added and tubes were run on BD FACS count instrument within 2 hours. Control results are printed and reported as Passed or Failed.

Patient samples were prepared by adding blood, fixative solution to the CD4 tube. A reagent tube is taken, labelled, vortexed. Then tubes were cored and 50 micro litre of patient blood added and vortexed again and incubated. Fixative solution added and vortexed. Samples were run in instrument and results recorded.

Sputum microscopy

Patients were asked to collect 2 sputum samples (1 early morning and 1 spot). Samples were labelled. Smears were prepared from purulent part of sputum and heat fixed. Staining was done using fluorescent stains. 0.1% Auramine O was added and let stand for 7-10 minutes. Washed with water, decolourised with 0.5% acid alcohol for 2 minutes washed with water.

Counterstained with 0.5% potassium permanganate for 30 seconds. Washed and air dried. Examined with LED fluorescence microscopy under 20 or 25 X objectives and 10X eyepiece lenses. Using LED fluorescence microscopy slides can be examined at lower magnifications 250X and 400X. Thus larger area per unit of time can be examined; 6% more sensitive than light microscopy.

RESULTS

A total of 180 patients were screened for HIV. Of them 65 were retroviral positive. All the patients, irrespective of whether they had signs and symptoms of chest infection, were screened for pulmonary TB by repeated microscopic examination of sputum for acid fast bacillus (AFB) using standard technique and subsequently by chest X-ray.

Of the total 65 retroviral positive cases, 43 (66%) were males and 22 (34%) were females (Table1). Among them, 30 were infected with both HIV and sputum positive TB and 35 (54%) were only retroviral positive.

Thus 46% of retroviral positive patients were co-infected with TB (Table 2). Among the 30 HIV/TB co-infected patients, 20 (67%) males and 10 (33%) were females.18 (60%) belong to productive age group of 16-45 years, one person was below 16 years and 11 (37%) were above (Table 3).

Table 1: Gender distribution in HIV-TB co infection.

Gender	HIV-reactive sputum negative		HIV-reactive sputum positive		Total	
	No	%	No	%	No	%
Male	23	66.0	20	67.0	43	66.0
Female	12	34.0	10	33.0	22	34.0
Total	35	100.0	30	100.0	65	100.0

Table 2: HIV-TB co infection and CD4 count.

CD4 count	HIV/TB co-infection	HIV alone	Total
< 50	13 (43.3%)	2 (5.7%)	15
50-150	11 (36.6%)	9 (25.7%)	20
151-250	2 (6.6%)	8 (22.8%)	10
251 - 350	2 (6.6%)	2 (5.7%)	4
>350	2 (6.6%)	14 (40.0%)	16
TOTAL	30 (100.0%)	35 (100.0%)	65

P<0.0001 for HIV/TB co-infection and CD4.

Table 3: Age wise distribution of HIV-TB co infection.

Age	Male	Female	Total
1-15	1	0	1 (3.3%)
16-30	4	3	7 (23.3%)
31-45	7	4	11 (36.6%)
46-60	5	3	8 (26.6%)
61-75	3	0	3 (10.0%)
Total	20	10	30 (100.0%)

DISCUSSION

In this study, out of the total 65 HIV positive patients, who attended ART clinic and received treatment, 30 (46%) had HIV/TB co- infection and the remaining 35 (54%) were HIV positive alone. An estimate shows that globally around 5.1 million people are infected with HIV and about half of these cases are co-infected with tuberculosis. This is similar to the study done by Narain et al in a tertiary care hospital in New Delhi.

His study shows, in developing countries TB is the most common life-threatening opportunistic infection (OI) in patients with HIV/AIDS with about 25 to 65 per cent patients with HIV/AIDS having tuberculosis of any organ. This prevalence of HIV/TB co-infection is different from the national figure (60.30%).[28]

Incidence of HIV/TB co-infection was reported to be very high (50%) in sub-Saharan Africa compared to that in Asia.[29] The rates of HIV/TB co-infection have been reported to vary in different regions of India. It was found to be between 0.4% and 20.1% in north India.[30] However, the incidence was 3.2% in 1991, which increased to 20.1% in 1996 in south India.[31] The increase in prevalence may be due to improvement in diagnostic methods to detect TB.

In the present study the incidence of HIV/TB co-infection was higher in the productive age group of 16-45 years. About 60% of the co-infected belong to this age group. Similarly a study conducted by Sameer Singhal et al in HIV/TB co-infection in patients attending Department of Pulmonary medicine, Wardha showed incidence of HIV/TB co-infection was higher 55 (84%) in the productive age group of 16-45 years.

Unlike Cryptococcal meningitis or toxoplasmosis, which occur at very low CD4 counts, TB is unique in that it can occur over a wide range of CD4 counts, although it is more frequent at CD4 counts <300 cells/µl. In our study we found that of the 30 HIV/TB co-infected patients 13 (43.3%) had CD4 counts <50 cells/ µl, 11 (36.6%) had CD4 counts 50-150 cells/µl, 2 (6.6%) with 151-250 cells/

µl, 2 (6.6%) with 251 - 350 cells/ µl and only 2 (6.6%) had >350 cells/ µl. This shows that out of 30 HIV/TB co-infected patients 93.4% had CD4 counts below 350 cells/ µl. On the contrary, in retroviral patients who are sputum negative, their CD4 counts were >250 cells/ µl.

Thus sputum negativity has positive correlation with high CD4 counts. This is similar to the study done by Purushottam et al., in Prevalence of Pulmonary Tuberculosis among HIV Positive Patients Attending Antiretroviral Therapy Clinic.[32] Thus sputum smear examination with fluorescent microscopy helps in increased detection of pulmonary TB in HIV patients.

CONCLUSION

This study wants to highlight the fact that the prevalence of pulmonary tuberculosis in HIV positive patients in our area is similar to the incidence elsewhere in the world. The HIV-TB co infection is more prevalent in the productive age group of 16-45 years which is highly significant in developing country like India. Thus early diagnosis and proper treatment is mandatory to reduce the mortality rate.

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