Original Article

Proportion and determinants of tuberculosis among human immunodeficiency virus-positive patients attending the antiretroviral therapy center attached to a Medical College in South India

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ABSTRACT

Background: The human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) pandemic has caused a re-emergence of tuberculosis (TB). In persons infected with both HIV and TB, the lifetime risk of developing TB disease is 50–70% compared to 10% in HIV-negative individuals. India has world's 3rd highest HIV burden and is also one of the countries endemic for TB, so the country faces a dual epidemic of HIV and TB. **Objectives:** To find out the proportion and determinants of TB in HIV-positive subjects. **Subjects and Methods:** This study was undertaken at the ART center from June 01, 2012, to May 31, 2013. HIV-positive subjects aged above 15 years who had been on antiretroviral therapy (ART) for more than 6 months were included in the study. Nonprobability purposive sampling was adopted. A predesigned semi-structured questionnaire was used to obtain data. **Results:** A total of 536 HIV-positive people were interviewed, 58.8% of whom were males, 79.1% were Hindu, 61.0% had up to high school education, and 57% were unskilled laborers. About 63% were married, 40% were from the upper lower class, and 60% were from urban areas. For the majority (89.1%), the probable mode of transmission of HIV was by the heterosexual route. TB co-infection was present in 38.4% subjects. The most common form of TB was extra-pulmonary in subjects on antituberculous treatment (47.3%) and among old cases (57.6%). On bivariate analysis, 136 (42.4%) married subjects and those from rural areas were more commonly affected by TB compared to subjects who were unmarried and from urban areas with odds ratio (OR): 1.555, confidence interval (CI): 1.077–2.246 and OR: 1.523, CI: 1.061–2.185, respectively. The proportion of TB was high among subjects who lived in overcrowded houses 130 (44.2%), and who had a habit of alcohol use compared to others with OR: 1.731, CI: 1.734–2.179 and OR: 1.524, CI: 1.045–2.223, respectively. Logistic regression analysis showed that TB among people living with HIV/AIDS was highest in persons living in overcrowded houses (OR: 1.706, CI: 1.185–2.458) and those who consumed alcohol (OR: 1.605, CI: 1.090–2.362). **Conclusions:** Demographic factors like male gender, middle age, living in the rural areas, consumption of alcohol, and living in overcrowded houses were found with a higher proportion of TB. The use of highly active ART appeared to progressively decrease but did not completely eliminate the risk of TB.

Key words: Antiretroviral therapy, co-infection, human immunodeficiency virus, tuberculosis

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INTRODUCTION

Tuberculosis (TB), one of the oldest diseases known to mankind, has many risk factors such as malnutrition, smoking/indoor air pollution, alcohol, diabetes, and human immunodeficiency virus (HIV). Infection with HIV carries the greatest risk of all known risk factors. TB is the most common treatable HIV-related disease and a leading killer of people with HIV/acquired immunodeficiency syndrome (AIDS).[1] An interaction between HIV and TB in a co-infected person is bidirectional and synergistic; each accelerating the progression of the other.[2]

In persons infected with both HIV and TB, the lifetime risk of developing TB disease is 50–70% compared to a 10% risk in HIV-negative individuals.[3] The newly acquired tuberculous infection can rapidly progress to active disease or a reactivation of a latent infection. HIV epidemic can facilitate the emergence of multidrug-resistant strains of *Mycobacterium tuberculosis* which has a deleterious effect on the overall health care system.

Worldwide, HIV/AIDS pandemic has led to a re-emergence of TB, and in India, although the HIV epidemic appears to have stabilized, HIV-associated TB continues to be an important challenge.[4] Globally, one-third of the people living with HIV/AIDS are co-infected with *M. tuberculosis*.[5] As India is one of the countries endemic for TB, the co-infection rates tend to be higher than the global rate. India is facing a dual epidemic of HIV and TB.

To combat this problem of HIV-TB co-infection, Revised National Tuberculosis Control Programme and National Aids Control Programme have developed a joint action plan for TB-HIV coordination. The objective is to reduce TB-associated morbidity and mortality in people living with HIV/AIDS.[2] With this in mind, we started our study to find out the proportion and determinants of TB among HIV-positive patients attending the antiretroviral therapy (ART) center attached to a Medical College in South India.

SUBJECTS AND METHODS

The study was undertaken at the ART center from June 01, 2012, to May 31, 2013, after approval and clearance by Ethical Review Committee of the Institute. All ethical requirements such as written informed consent and assurance of confidentiality of responses were strictly adhered to throughout the study.

A nonprobability purposive sampling was adopted to select study subjects. HIV-positive subjects aged above 15 years and on ART for more than 6 months were included in the study. HIV-positive subjects not willing to participate or who were seriously ill were excluded from the study.

A predesigned semi-structured questionnaire was used to obtain data after explaining the purpose of the study and obtaining written informed consent. A relevant primary data on the sociodemographic profile, clinical profile was collected by interviewing the patient. Secondary data regarding the history and diagnosis of TB was taken from the ART register, which followed the joint action plan for TB-HIV coordination.[2] A total of 536 subjects were interviewed.

A database was created in MS Excel and after appropriate cleaning, analysis was done using SPSS Version 20, IBM, New York, USA. Appropriate descriptive statistics like proportion and percentage were used to analyze the findings and to draw the inferences. Chi-square was used to test for statistical significance; a $P < 0.05$ was considered as statistically significant. Bivariate analysis were performed, and variables found to be statistically significant on bivariate analysis were included in multiple logistic regression analysis.

RESULTS

A total of 536 HIV-positive persons constituted our study subjects, 58.8% of whom were male, 42.9% were from the 25 to 34 years age group, and 32.8% were between 35 and 44 years [Table 1]. The majority of the study subjects (79.1%) were Hindu; 62.7% were married, 60% had high school education, and 57.1% were unskilled laborers. More than one-third of the study subjects were from upper lower class (39.6%) followed by 31.0% from the lower middle class. A higher proportion of the study subjects (59.9%) lived in urban areas while 40.1% were from rural areas [Table 1].

For the majority of the study subjects, the probable mode of transmission of HIV was by the heterosexual route (89.1%) followed by unsafe injections (5.2%). The most common means of access to the ART center was through Voluntary Counselling and Testing Centre (89.2%) followed by 3.5% who had come through the outpatient department, 2.1% by PPTCT and 2.1% through private practitioners.

TB co-infection was present among 38.45 of the study subjects. Of the 206 subjects with HIV-TB co-infection, 6.7% were currently on antituberculous treatment (ATT) while 31.7% had completed the treatment and were declared as cured [Table 2]. The proportion of TB came down to only 6.1% after initiation of ART. The most

Table 1: Association between sociodemographic profile of study subjects and tuberculosis co-infection status

Sociodemographic profile	Tuberculosis co-infection		Total *N* (%)	*p*-value
	Present *N* (%)	Absent *N* (%)		
Age in years				
15-24	002 (05.3)	36 (94.7)	038 (07.1)	0.001
25-34	096 (41.7)	134 (58.3)	230 (42.9)	
35-44	074 (42.0)	102 (58.0)	176 (32.9)	
45-54	030 (41.7)	42 (58.3)	072 (13.4)	
≥55	004 (20.0)	16 (80.0)	020 (03.7)	
Gender				
Male	134 (42.5)	181 (57.6)	315 (58.8)	0.026
Female	068 (31.8)	146 (68.2)	214 (39.9)	
Transgender	004 (57.1)	003 (42.9)	7 (1.3)	
Religion				
Hindu	161 (38.0)	263 (62.0)	424 (79.1)	0.707
Muslim	033 (38.4)	53 (61.6)	86 (16.0)	
Others	012 (42.2)	14 (53.8)	26 (4.9)	
Education				
Illiterate	012 (30.8)	27 (69.2)	39 (7.3)	0.160
Primary school	026 (38.8)	41 (61.2)	67 (12.5)	
High school	121 (37.0)	206 (63.0)	327 (61.0)	
PUC/diploma	045 (48.4)	48 (51.6)	91 (16.9)	
Graduate	002 (20.0)	008 (80.0)	12 (2.3)	
Occupation				
Unemployed	050 (33.3)	100 (66.7)	150 (28.0)	0.269
Unskilled	129 (42.2)	177 (57.8)	306 (57.1)	
Semi-skilled	020 (31.2)	44 (68.8)	64 (11.9)	
Skilled	003 (50.0)	3 (50.0)	6 (1.1)	
Professional	004 (40.0)	6 (60.6)	10 (1.9)	
Socioeconomic class*				
Upper	004 (33.3)	08 (66.7)	12 (2.2)	0.292
Upper middle	040 (36.4)	70 (63.6)	110 (20.5)	
Lower middle	055 (33.1)	111 (66.9)	166 (31.0)	
Upper lower	093 (43.8)	119 (56.2)	212 (39.6)	
Lower	014 (38.8)	22 (61.2)	36 (6.7)	
Marital status				
Married	142 (42.3)	194 (57.7)	336 (62.7)	0.061
Single	020 (31.2)	044 (68.8)	64 (11.9)	
Widowed/separated	044 (33.8)	092 (66.2)	136 (25.4)	
Area of residence				
Rural	136 (42.4)	185 (57.6)	321 (59.9)	0.022
Urban	070 (32.6)	145 (67.4)	215 (40.1)	

*Modified B. G. Prasad classification was adopted

common form of TB was extrapulmonary in both groups of subjects on ATT (47.3%) and among old cases (57.6%).

The proportion of TB was found to be significantly high in the 25–34 years age group (41.7%), those aged 35–44 years (42.0%) and those aged 45–54 years (41.7%) compared to other age groups ($P = 0.001$). Transgender subjects (57.1%) and males (42.5%) were more commonly affected by TB than females (31.8%), and this was statistically significant ($P = 0.026$). Subjects from the rural areas were more commonly affected by TB (42.4%) than those from urban areas (32.6%), and this difference was statistically significant ($P = 0.002$) [Table 1].

Table 2: Human immunodeficiency virus-tuberculosis co-infection profile of study subjects

Profile of HIV-TB co-infection	Frequency	Percentage
HIV-TB co-infection (*n*=536)		
Present	206	38.4
Absent	330	61.6
Status of antitubercular treatment (*n*=206)		
Currently on treatment	36	6.7
Old and cured cases	170	31.7

HIV-TB: Human immunodeficiency virus-tuberculosis

On bivariate analysis, married subjects (42.3%) and subjects who were from the rural areas (42.4%) were more commonly affected by TB compared to subjects who were unmarried and came from urban areas with odds ratio (OR): 1.555, confidence interval (CI): 1.077–2.246 and OR: 1.523, CI: 1.061–2.185, respectively [Table 3]. The proportion of TB was high among subjects living in overcrowded houses: (44.2%) and those who had the habit of alcohol use: (45.6%) compared to others with OR: 1.731, CI: 1.734–2.179 and OR: 1.524, CI: 1.045–2.223, respectively [Table 3].

After logistic regression, the determining factors for the occurrence of TB in people living with HIV/AIDS were overcrowding (OR: 1.706, CI: 1.185–2.458) and alcohol consumption (OR: 1.605, CI: 1.090–2.362) [Table 4].

DISCUSSION

In this study, the mean duration since HIV diagnosis was 3.95 ± 2.24 years and the mean duration of ART was 3.67 ± 1.99 years. About 38.4% had a history of TB; of the subjects who had a history of TB, 6.7% were on ATT at the time of the interview, and 31.7% had completed their treatment and been declared cured. Similar percentages of TB were observed in some of the studies done in our country[6-9] and also in studies conducted in Pakistan[10] and Nigeria.[11] However, a higher proportion of TB was seen in some other studies, probably because of geographical variation of TB and HIV in different areas or different study settings and the methodology adopted. The higher proportions observed by Chakraborty *et al*.[12] (57%), Ghiya *et al*.[13] (49.2%) were mainly because of the methodology they used, since in these studies, apart from

Table 3: Association between sociodemographic, environmental factors, and tuberculosis among people living with human immunodeficiency virus/acquired immunodeficiency syndrome by bivariate analysis

Variables	Tuberculosis co-infection		*p*-value	OR	95% CI
	Present *N* (%)	Absent *N* (%)			
Age (years)					
<45	98 (36.4)	171 (63.6)	0.339	0.844	0.596-1.195
≥45	108 (40.4)	159 (59.6)			
Gender					
Males	134 (42.5)	181 (57.5)	0.581	0.905	0.636-1.288
Females and transgender	68 (31.8)	146 (68.2)			
Religion					
Hindus	161 (38.0)	263 (62.0)	0.669	0.911	0.596-1.401
Others	45 (40.2)	67 (59.8)			
Education					
Illiterate	12 (30.8)	27 (69.2)	0.309	0.694	0.344-1.403
Literate	194 (39.0)	303 (61.0)			
Occupation					
Unemployed	50 (33.3)	100 (66.7)	0.13	0.737	0.494-1.094
Employed	156 (40.4)	230 (59.6)			
Marital status					
Married	142 (42.3)	194 (57.7)	0.019	1.555	1.077-2.246
Others	64 (32.0)	136 (68.0)			
Monthly income in rupees					
<5000	108 (36.7)	186 (63.6)	0.373	0.853	0.602-1.210
≥5000	98 (40.5)	144 (59.5)			
Area of residence					
Rural	136 (42.4)	185 (57.6)	0.022	1.523	1.061-2.185
Urban	70 (32.6)	145 (67.4)			
Type of house					
Kutcha	32 (36.4)	56 (63.6)	0.663	0.9	0.560-1.446
Others	174 (38.8)	274 (61.2)			
Ventilation					
Adequate	70 (38.5)	112 (61.5)	0.992	1.002	0.694-1.447
Inadequate	136 (38.4)	218 (61.6)			
Overcrowding					
Present	130 (44.2)	164 (55.8)	0.004	1.731	1.734-2.179
Absent	76 (31.4)	166 (68.6)			
Tobacco					
Users	94 (41.0)	135 (59.0)	0.283	1.212	0.853-1.722
Nonusers	112 (36.5)	195 (63.5)			
Alcohol					
Users	72 (45.6)	86 (54.4)	0.029	1.524	1.045-2.223
Nonusers	134 (35.4)	244 (64.6)			

HIV: Human immunodeficiency virus; OR: Odds ratio; CI: Confidence interval; TB: Tuberculosis

standard clinical and microbiological criteria, sputum culture and serology tests were done to detect TB. The extensive investigations carried out increased the chances of diagnosing TB. In the study by Bhagyabati Devi *et al*.,[14] the high proportion (55%) noted may have been due to the inclusion of only admitted HIV patients. The proportion of TB in HIV also depends on the type of diagnostic test applied, which was observed in a study done by Olaniran *et al*.[15] in Nigeria, in which the proportion of TB diagnosed by acid-fast *Bacillus* positive sputum smear was 13.8%, whereas when the same subjects were examined by radiological investigations, the prevalence was 60.5%.

It was evident in this study that extremes of age were less affected by TB and that the proportion of co-infection was high among those aged between 25 and 44 years (41% to 42%) compared to those aged 15–24 years (5.3%) and >55 years (20%). Similar results were observed by Affusim *et al*.,[11] Ngowi *et al*.,[16] Olaniran *et al*.,[15] and Onipede *et al*.[17] The middle-aged group, working class are mainly prone to TB probably

Table 4: Determining factors of tuberculosis among people living with human immunodeficiency virus/ acquired immunodeficiency syndrome by multiple logistic regression

Variables	Tuberculosis co-infection		*p*-value	Adjusted OR	95% CI
	Present *N* (%)	Absent *N* (%)			
Marital status					
Married	142 (42.3)	194 (57.7)	0.075	1.409	0.966-2.053
Others	64 (32.0)	136 (68.0)			
Area of domicile					
Rural	136 (42.4)	185 (57.6)	0.061	1.423	0.984-2.058
Urban	70 (32.6)	145 (67.4)			
Overcrowding					
Present	130 (44.2)	164 (55.8)	0.004	1.706	1.185-2.458
Absent	76 (31.4)	166 (68.6)			
Alcohol					
Users	72 (45.6)	86 (54.4)	0.016	1.605	1.090-2.362
Nonusers	134 (35.4)	244 (64.6)			

HIV: Human immunodeficiency virus; OR: Odds ratio; CI: Confidence interval; TB: Tuberculosis

because of exposure outside of their homes as they go to and from work, etc. This can have a serious negative effect on the socioeconomic status of a country since the reproductive and economically productive age groups are mostly affected.

In our study, males were most commonly affected by TB (42.5%). Similar findings were noted by Olaniran *et al*.[15] (58.3%), Corbett *et al*.,[18] Abeld,[5] and Holmes *et al*.[19] Therefore, middle age and male gender were the predominant risk factors for TB, which could reflect a combination of behavioral, socioeconomic, and biological/genetic factors.

In a study done by Taha *et al*.,[20] illiterate individuals had a higher proportion of active TB compared to literate individuals. In our study, however, illiterates and subjects who had studied up to graduate level or higher were less commonly affected. This could be attributed to the sampling method adopted (nonprobability purposive), which may not have revealed an overall picture of HIV-positive people. Occupation was not associated with TB in our study. A similar finding was observed by Kibret *et al*.,[21] however, in a study by Corbett *et al*.,[18] manual labor was associated with TB.

In our study, married subjects were more commonly affected by TB (42.3%) compared to single and widowed/separated subjects. This is in contrast to Taha *et al*.[20] and Lienhardt *et al*.[22] who reported a higher proportion of single subjects and divorced or widowed to be affected by TB. This may be the result of the differences in sociocultural factors among countries.

Smoking makes the HIV-positive subjects more susceptible to TB either by causing local epithelial damage or by lowering the immunity. In this study, a higher proportion of HIV-TB co-infected subjects used tobacco, but it was statistically not significant. However, an association between smoking and TB has been reported by Corbett *et al*.,[1] Taha *et al*.,[20] and Kibret *et al*.[21] Another common habit, alcohol consumption was associated with TB; Kibret *et al*. made a similar observation.[21]

Overcrowding is an important social factor which indirectly contributes to the causation of TB. In our study, living in overcrowded conditions was associated with TB. This finding is consistent with studies done by Hill *et al*.,[23] Hermans *et al*.,[24] and Lönnroth *et al*.[25] Other living conditions investigated in various other studies found an association between TB and living in a house with mud walls,[20] using gas (kerosene) as the source of energy, and not having a separate kitchen in the house.[21] Our study also showed that subjects living in "Pucca" houses were less commonly affected by TB, but this was statistically not significant.

One of the important determinants in HIV-positive people regarding the development of opportunistic infections like TB is the maintenance of CD4 count, which in turn depends on ART and the nutritional status. Therefore, a lower proportion of TB was seen in HIV-positive people after initiation of ART. This was 6.1% in our study and 5.1% in the study by Rajasekaran *et al*.[26] However, the higher proportion of 17% was found by Giri *et al*.[27] which may be because of the inclusion of HIV subjects with a CD4 count of <350.

Some other factors associated with TB such as (1) nutritional factors (weight, Hb) (2) immuno-clinical factors (CD4 count, WHO stage), and (3) past history or

exposure to TB in the home or at the workplace have been not looked in this study. Nonprobability sampling method was adopted in this study, which may not have provided an equal chance of selection of study subjects.

Greater attention should be paid to male and middle-aged HIV-positive subjects during regular checkups to detect TB. HIV subjects should be counseled on the hazards of alcohol use. Importance should be given to ART, the cornerstone in the prevention of opportunistic infections like TB.

CONCLUSION

In our study, the proportion of TB was 38.4% among HIV-positive subjects and comparatively more in males. Some demographic factors like male gender, middle age, living in rural areas, habits like the consumption of alcohol, and living in overcrowded homes revealed a higher proportion of TB. The use of ART appears to progressively decrease but does not completely eliminate the risk of TB.

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Conflicts of interest
There are no conflicts of interest.

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