A STUDY ON DETERMINANTS OF TB–HIV CO–INFECTION AMONG PATIENTS ENROLLED AT DISTRICT TUBERCULOSIS CENTRES

B. Pavani[1], S. Prasanth Kumar[2] & B. KiranMai*[3]

[1] Department of Community Medicine, Osmania Medical College, Hyderabad, Telangana

[2]Department of Community Medicine, Government Medical College, Rajamahendravaram,

Corresponding author: andasukiranmai@gmail.com

ABSTRACT

Introduction: Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) co-infection remains a major public health challenge in India, the country with the highest TB burden globally. India's TB Report 2022 notified 1.93 million cases. People living with HIV are about 18 times more likely to develop active TB. However, not all HIV-infected individuals develop TB, suggesting the role of additional determinants. This study assessed the socio-demographic profile and factors associated with TB–HIV co-infection. **Methods:** A retrospective record-based case–control study was conducted among 242 adult subjects (121 cases and 121 controls) enrolled at designated district TB centers and 19 affiliated treatment units in Hyderabad, Telangana, between January and December 2022. Cases were TB patients with HIV; controls were TB patients without HIV. Data were collected using a semi-structured questionnaire. Statistical significance was assessed using the chi-square test and multivariable logistic regression in Epi-Info 7.2.6.6. **Results:** Majority of participants were male in both cases (67.7%) and controls (52.1%). Most belonged to the 30–39-year age group, had secondary education, and had a Class III socio-economic status. Age, sex, education, religion, and marital status were significantly associated with TB–HIV co-infection, while socio-economic status was not significant. **Conclusion:** TB–HIV co-infection was more common among males, individuals aged 30–39 years, those with secondary education, and married individuals. Clinical factors such as overcrowding, low body weight, anemia, and substance use were also more prevalent. These findings highlight the multifactorial nature of co-infection and the need for targeted interventions.

Keywords: Case-control, TB, HIV, Co-infection, determinants

INTRODUCTION

Tuberculosis (TB) and Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) comprise the main burden of infectious diseases in developing countries like India. Infection with both HIV and TB is called HIV/TB coinfection. The dual infection is termed as "accursed duet" Field(V et al., 2016). The risk of coinfection with TB is about 20-37 times higher among PPL-HIV, according to WHO. (Kamath et al., 2013)

Mycobacterium tuberculosis and HIV both impair host immunity. HIV co-infection is a major risk factor for developing active TB, increasing susceptibility to primary infection, reinfection, and reactivation of latent TB. Among individuals with latent TB infection, HIV is the strongest risk factor for progression to active disease. (Bruchfeld et al., 2015)·(CDCTB, 2022)

Globally, TB disease is one of the leading causes of death among people with HIV. (*HIV and Tuberculosis (TB) | NIH*, n.d.) According to India's TB report 2022, India, with a population of 1.4 billion, 1.93 million total (new & relapse) TB cases were notified. This makes India the highest TB burden country in the world. (*WHO Global TB Report 2022*, n.d.)

Under the newer initiative, Pradhan Mantri TB Mukt Bharat Abhiyan, more than 40,000 Nikshay Mitra are supporting over 10.45 Lakh TB patients all over the country. (*WHO Global TB Report 2022*, n.d.)

The determinants influencing TB-HIV co-infection include various social, economic, environmental, and cultural factors. Reports claim that coinfection with HIV and Mycobacterium has a synergistic effect on each other and adversely increases the extrapulmonary disease. (*Sharma: HIV-TB Co-Infection: Epidemiology, Diagnosis... - Google Scholar*, n.d.)

Research showed that in resource-constrained settings, up to 50% of PPL- HIV without treatment but with concurrent TB would die before completion of 6 to 8 months of treatment for TB, some within the first 2 to 3 months of initial treatment. In such a scenario, prophylaxis substantially decreases the risk by about 10%.(Kamath et al., 2013)

Thus, identifying the at-risk people is inarguably important to mitigate the threat of TB-HIV coinfection. Less literature was available in this study setting, and hence, this study was undertaken to assess the determinants of HIV among the TB-infected patients. However, there is limited published data from Hyderabad and similar urban programmatic settings regarding the socio-demographic and clinical determinants of TB-HIV co-infection, particularly using a record-based case-control design. The present study was therefore undertaken with the following objectives: (i) to study the socio-demographic profile of the study subjects; and (ii) to determine the factors associated with TB–HIV co-infection.

METHODS

A retrospective record-based case–control study was conducted at designated district TB centers and 19 affiliated treatment units (TUs) in Hyderabad, Telangana, between January and December 2022. Data were collected from routine program records of adults aged 18 years and above. The sample size was calculated using the standard formula for case–control studies, with the exposure proportions in cases (P1 = 0.125) and controls (P2 = 0.266) derived from Parrikar et al. (Parrikar et al., 2020). Assuming a case-to-control ratio of 1, with 80% power and a 95% confidence interval ($Z_{1-\beta} = 0.84$, $Z_{1-\alpha/2} = 1.96$), the calculated sample size was 121 per group, for a total of 242 subjects (121 cases and 121 controls in a 1:1 ratio). Cases included TB patients co-infected with HIV, while controls were TB patients without HIV, randomly selected from the same records. The inclusion criteria comprised adults aged 18 years and above with TB, with or without HIV reactive serology, and for whom consent was available. Subjects below 18 years of age, those with severe co-morbidities such as cancer or renal disease, and those without consent were excluded. A semi-structured data extraction was used to collect socio-demographic and clinical data, including age, gender, residence, weight, type of TB case (new or retreatment), TB diagnosis, treatment completion status, co-morbid conditions, and HIV treatment status. Socio-economic status was assessed using the Modified Kuppuswamy classification, which is based on the education of the head of the family, occupation, and monthly family income, with participants categorized into Class I (upper) to Class V (lower). Records with missing data were excluded from analysis for the respective variables. Data were entered in Microsoft Excel and analyzed using Epi-Info 7.2.6.6. Quantitative variables were expressed as mean and standard deviation, while qualitative variables were summarised as frequencies and percentages. The chi-square test was used to assess associations, multivariable logistic regression to identify independent determinants of TB–HIV co-infection, and the Z-test to compare mean age between the two groups. A p-value of less than 0.05 was considered statistically significant.

Ethical approval for this study was obtained from the Institutional Ethics Committee (IEC Approval No.: [IEC/OMC/2022/M.No.(7)/Acad-60]) prior to data collection.

RESULTS

A total of 242 subjects were included in this study. The subjects were divided into two groups, comprising 121 cases and 121 controls. The socio-demographic profile is illustrated in Table 1. In our study, the majority were males in both cases (67.7%) as well as the control (52.1%) groups. Among the age groups classified, the majority were in the 30-39-year age group among cases (33.1%) and controls (28.1%). Among the cases, the distribution by educational attainment showed that 42.15% were secondary school, followed by primary school (32.2%), illiterate (14.9%), Intermediate (5.8%), and graduate (4.95%). Whilst controls followed a similar trend of educational attainment, with 55.4% subjects attaining secondary school, followed by primary school (19%), intermediate (14.9%), illiterate (7.4%), and graduate (3.3%). The distribution of socioeconomic status showed that Class III was higher in both cases (35.5%) and controls (37.2%). Among cases, Class II (21.5%) was next to Class III. Furthermore, Class V were 19.8%, Class IV (17.4%), and Class I (5.8%). Controls followed a dissimilar trend, with Class III followed by Class IV (26.4%), Class II (18.2%), Class V (14.1%), and Class I (4.1%). Distribution of the groups by religion showed a majority of Hindus, at 81.8% and 64.5%, respectively. The majority were married among cases (78.5%) and controls (90.1%). Overcrowding was present in 42.9% of cases and 29.8% of controls. (Table1)

Table 1: Socio-demographic profile of study participants

Variables	**Cases**		**Controls**	
	Frequency (n=121)	**(%)**	**Frequency (n=121)**	**(%)**
Sex				
Male	82	67.7	63	52.1
Female	39	32.3	58	47.9
Age				
<20	4	3.3	14	11.6
20-29	17	14.1	24	19.9
30-39	40	33.1	34	28.1
40-49	36	29.7	19	15.7
50-59	15	12.4	11	9.1
60-69	5	4.1	13	10.7
70 and above	4	3.3	6	4.9
Education				
Illiterate	18	14.9	9	7.4
Primary	39	32.2	23	19
Secondary	51	42.15	67	55.4
Intermediate	7	5.8	18	14.9
Graduate	6	4.95	4	3.3
SES**				
Class I	7	5.8	5	4.1
Class II	26	21.5	22	18.2

Class III	43	35.5	45	37.2
Class IV	21	17.4	32	26.4
Class V	24	19.8	17	14.1
Religion				
Hindu	99	81.8	78	64.5
Muslim	22	18.2	43	35.5
Marital status				
Married	95	78.5	109	90.1
Unmarried	26	21.5	12	9.9
Overcrowding				
Present	52	42.9	36	29.8
Absent	69	57.1	85	70.2

**(SES- Socio-Economic Status according to Modified Kuppuswamy classification)

Clinical characteristics were illustrated in Table 2. Variables studied included type of infection, weight, and comorbidities. Cases had a higher proportion of pulmonary infection (87.6%) than extra-pulmonary infection. Among 15 cases of extra-pulmonary TB, 3(2.5%) had pleural effusion, and 6 had TB lymphadenitis (4.9%). Among controls, 58.7% had pulmonary infection and 50(41.3%) were extra-pulmonary, of which, 11(9.1%) had pleural effusion, 8(6.6%) had TB lymphadenitis. A higher proportion of cases and controls weighed less than 50 kg, at 67.7% and 52.1%, respectively.

Co-morbidities such as anemia, diabetes, and hypertension were present among the groups. The most common morbidity was anemia with 20.7% among cases and 25.6% in controls, followed by hypertension (12.4% and 9.1% respectively) and diabetes (4.1% and 8.3% respectively. (Table 2)

Table 2: Clinical Characteristics of the study groups at designated TB centers

Variables	Cases		Controls	
	Frequency (n=121)	**(%)**	**Frequency (n=121)**	**(%)**
Type TB infection				
Pulmonary	106	87.6	71	58.7
Extra-pulmonary	15	12.4	50	41.3
Pleural effusion	3	2.5	11	9.1
TB lymphadenitis	6	4.9	8	6.6
Others(including pericardial, abdominal, genitourinary, and disseminated TB etc)	6	4.9	31	25.6
Weight (In kgs)				
<50	82	67.7	63	52.1
>50	39	32.3	58	47.9
Diabetes mellitus				
Present	5	4.1	10	8.3
Absent	116	95.9	111	91.7
Anaemia				
Present	25	20.7	31	25.6
Absent	96	79.3	90	74.4
Hypertension				
Present	15	12.4	11	9.1
Absent	106	87.6	110	90.9

Table 3 shows the distribution according to addictions, with 44.6% smokers among cases and 29.7% among controls. Alcoholics were 65.2% among cases and 35.5% among the control group.

Table 3: Distribution of study participants according to addiction status

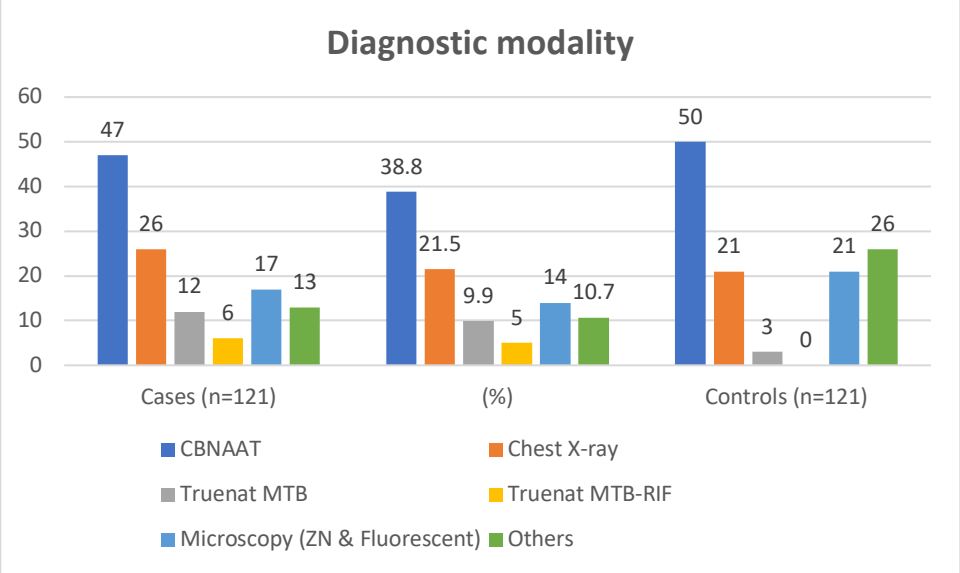
Parameter	Cases		Controls	
	Frequency (n=121)	(%)	Frequency (n=121)	(%)
Smoking	54	44.6	36	29.7
Alcohol	79	65.2	43	35.5

Cases on treatment were 61.9%, completed (36.4%), and lost to follow-up were 1.7%. In the control group, treatment was completed in 65.3%, 30.6% were on treatment. Loss to follow-up was 4.1%. (Table 4)

Table 4: Comparison of treatment status between Cases and Controls

Treatment status	Cases		Controls	
	Frequency (n=121)	(%)	Frequency (n=121)	(%)
On treatment	75	61.9	37	30.6
Completed	44	36.4	79	65.3
Lost to follow up	2	1.7	5	4.1

Figure 1 illustrates the diagnostic modalities for TB-infected subjects. Subjects diagnosed with CBNAAT were present in higher proportions in both groups (n=47 and n=50, respectively). Chest x-ray was the next (26,21), Trunat-MTB (12,3), Trunat MTB-RIF (6,0), Microscopy (17,21).



***CBNAAT – Cartridge-Based Nucleic Acid Amplification Test, MTB – *Mycobacterium tuberculosis*, MTB-RIF – *Mycobacterium tuberculosis* Rifampicin resistance assay, ZN – Ziehl–Neelsen staining**

Figure 1: Distribution of study groups according to diagnostic modality

Table 5: Determinants of HIV among TB patients

Variable	AOR (95% CI)	p-value
Age	0.18 (0.09–0.32)	<0.001
Education	18.58 (7.76–44.50)	<0.001
SES	0.49 (0.21–1.08)	0.078
Sex	20.64 (6.13–69.51)	<0.001
Religion	0.22 (0.07–0.68)	0.009
Marital status	0.15 (—)*	0.004

Determinants of HIV among TB subjects were assessed using the chi-square test and multivariable logistic regression analysis. On univariate analysis, age (p=0.009), education (p=0.005), religion (p=0.002), and marital status (p=0.01) showed significant association, while socioeconomic status was not significant (p=0.38). In multivariable analysis, age, education, religion, and sex remained significantly associated, whereas socioeconomic status was not.

DISCUSSION

This study documented the Sociodemographic profile, clinical characteristics, and determinants of HIV among TB-infected subjects by a case-control study design on 242 subjects enrolled at TB-designated centers. The majority were male in both cases (67.7%) and in controls (52.1%). Most of the cases were in the 30-39 age group in both groups (33.1% and 28.1%, respectively). A similar study by Zeru et al. found that males accounted for 47.5% and females for 52.5%. Subjects aged less than 30 years were 42.4%, and those aged more than 30 years were 57.6%. (Zeru, 2021)

Educational qualification showed secondary school as the highest level of educational attainment, with 42.15% among cases, followed by primary school (32.2%), and 55.4% among controls, followed by 19% of subjects attaining primary school. In Taha et al.'s study, the majority (39.5%) had no formal education, a finding similar to that of another study by Zeru et al. (Zeru, 2021).

The majority belonged to Class III SES (35.5% and 37.2%, respectively), followed by Class II in cases (21.5%) and in controls (26.4%). The least belonged to class I in both groups (5.8% and 4.1%, respectively). Several studies reported that socio-economic status is a strong risk factor for the occurrence of active TB. (Lopez De Fede et al., 2008), (Mackenbach et al., 2008)

The majority were Hindu, at 81.8% and 64.5% among cases and controls, respectively. In a similar study, 6.9% of cases and 75.4% of controls were Hindu. Marital status revealed that the majority in both groups were married (78.5% and 90.1%, respectively). In Taha et al.'s study, 42.6% were married, and 32.1% were widowed.

Overcrowding was present in 42.9% of cases and 29.8% of controls. Studies on TB co-infection with HIV showed that overcrowding at home is a major risk factor for the development of TB among HIV patients. (Taha et al., 2011), (*Investigation of the Risk Factors for Tuberculosis: A Case–Control Study in Three Countries in West Africa | International Journal of Epidemiology | Oxford Academic*, n.d.)

Clinical characteristics showed that cases had a higher proportion of pulmonary infection (87.6%) than of extrapulmonary infection. Few had pleural effusion (2.5%) and TB lymphadenitis (4.9%). Among controls, pulmonary infection was present in 58.7%, followed by pleural effusion in 9.1% and TB lymphadenitis in 6.6%. In another study, the most common form of EPTB was CNS tuberculosis, diagnosed in 22 (33.84%) patients, followed by abdominal tuberculosis in 17 (26.15%), peripheral tubercular lymphadenitis in 14 (21.53%), and pleural effusion in 12 (18.46%) patients. (Jaryal et al., 2011)

In both cases (67.7%) and controls (52.1%), individuals weighed less than 50 kg. In Zeru et al.'s study, 49.7% were less than 50 kg.(Zeru, 2021). A higher proportion had anemia (20.7% and 25.6%) as the morbidity among cases and controls, respectively, followed by hypertension (12.4% and 9.1%) and diabetes(4.1% and 8.3%).In a similar study on TB-HIV co-infection, 45% of cases and 20.8% of controls had anemia, while hypertension was seen in 0.2% and 0.5% subjects, respectively. They also showed other co-morbidities like diabetes (7% and 2%) and hepatitis B(0.8% in each group).

Addictions were assessed, which showed that 44.6% were smokers and 65.2% were alcoholics among cases. In controls, 29.7% were smokers and 35.5% were alcoholics. In Parrikar et al.'s study, smoking status revealed that 19.9% of cases and 15.3% of controls were smokers and alcoholics, were 54% and 32.2% respectively, in each group. (Parrikar et al., 2020) Treatment status revealed that 61.9% of cases and 30.6% of controls were on treatment, and 36.4% of cases and 65.3% of controls had completed their treatment. Regarding follow-up, 1.7% of cases and 4.1% of controls were lost to follow-up. In Parrikar et al.'s study, treatment was completed in 31.3%, and 19.2% were defaulters. (Parrikar et al., 2020)

Finally, the determinants were assessed using multivariable logistic regression. Variables that showed significant association included age (p=0.009), sex (p=0.01), education (p=0.005), religion (p=0.002), and marital status (p=0.01), while socioeconomic status did not show a significant association (p=0.38).

In Kapata et al.'s study, the main determinants that were associated with TB/HIV co-infection were: being in the age-group 24-49 (p = 0.0001); being female (p = 0.0001); re-treatment (p = 0.0001); having extrapulmonary TB (p = 0.02); being married or widowed (p = 0.05 and p = 0.01, respectively). (Kapata et al., 2013)

In Parrikar et al.'s study, the incidence of coinfection was higher in males (60.8%), in semiskilled workers, and in those with up to secondary school education; all of these were statistically significant. (Parrikar et al., 2020) In Zeru et.al study, Bivariate logistic analysis showed that HIV patients with regards to marital status[AOR = 2.6; 95%CI = 1.19–2.89], education status [AOR = 3.74; 95%CI = 2.47–5.66], weight less than 50kg [AOR = 2.54; 95% CI = 1.35 – 4.81], CD4 level < 200cells/mm^3 [AOR = 4.57; 95%CI = 2.38–6.86] were significantly associated with TB/HIV co-infection.(Zeru, 2021)

Limitation

In this retrospective, record-based study, information bias may arise from incomplete, inaccurate, or inconsistent data recording in routine records. Variables such as overcrowding and alcohol use are often based on patient self-report and may be underreported or not documented uniformly by healthcare providers. This can lead to misclassification of exposure status and affect the observed associations.

CONCLUSION

In the present study, the majority of the study groups were male, completed secondary education, belonged to class III socio-economic status, and were Hindus by religion, in both cases and controls. Overcrowding was observed more often in cases than in controls, with a higher proportion of pulmonary infections than of extrapulmonary infections; most cases were less than 50 kg. Addictions such as alcohol consumption and smoking were common. The majority of participants were on treatment, followed by those who had completed treatment and those lost to follow-up. Age 30-39 years, who completed their secondary education and religion by Hindus, and marital status are the determinants that showed statistically significant results in TB- HIV coinfection.

Conflicts of Interest

The authors declare no conflicts of interest.

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