

A Study of HIV-TB Co-infection and its Determinants at a Tertiary Care Hospital in Goa

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ABSTRACT

Introduction: Since the discovery of HIV in the 1980's, there has been an alarming upsurge of Tuberculosis across the globe. TB is the most common and usually the first opportunistic infection in people living with HIV. Both HIV and TB together form the cursed duet, each one fast forwarding the progression of the other. **Aims & Objectives:** To study the epidemiology & various determinants of HIV-TB co-infection in HIV positive patients attending ART center at Goa Medical College (GMC), Goa. To study the prevalence of HIV- TB co-infection. **Settings and Design:** It was a three year record based retrospective observational study carried out at the antiretroviral therapy center of a tertiary care Hospital in the state of Goa.

Material and methods: Study group comprised of 342 cases of HIV-TB co-infected patients above 15 years of age, and the control group was formed by equal number of non TB, HIV infected patients diagnosed during the same period. Various determinants like age, gender, occupation, educational status, mode of transmission of HIV, addictions, CD4 counts etc were compared. **Statistical analysis:** was done by calculating percentages and proportion by SPSS 14.0 version and Chi-square test was used for statistical significance, with P values less than 0.05 considered as statistically significant.

Results: The prevalence of HIV-TB co-infection during the study period was found to be 26.6%. The incidence of co-infection was found to be higher in males (60.8%), in those who were semiskilled workers and with level of education up to secondary school and all these were found to be statistically significant. Alcohol consumption, low CD4 counts and Co-morbid illness like anemia were also found to be statistically significant.

Conclusions: Higher HIV-TB co-infection prevalence rate in the state warrants upgradation of disease control programs with efforts to increase awareness about the prevention and spread of both the diseases and their effective management.

Keywords: HIV, Tuberculosis, Determinants, TB- HIV, Epidemiology, Co-infection

Globally, there were 1.2 million TB deaths amongst HIV negative and an additional 0.25 million deaths among HIV positive individuals.¹ Nearly half a million new cases of drug resistant TB were diagnosed worldwide (of which 78% had MDR TB), with 27% being contributed by India.¹ About 9.2 lakh people living with HIV (PLHIV) got diagnosed with TB, with nearly 3 lakh deaths due to HIV-TB co-infection in 2017 with Africa accounting for 84% of all deaths.²

HIV increases the rate of conversion from latent TB infection to active TB disease by attacking the immune system. Also, TB causes faster progression of HIV to full blown AIDS in HIV positive individuals. A high degree of suspicion is therefore required with better improved diagnostic modalities like CBNAAT, CBNAAT Ultra, Line Probe Assay, along with phenotypic methods like solid and liquid AFB culture including MGIT on pulmonary and extra-pulmonary specimens.

Various factors are associated with increased risk of co-infection: poverty, poor living conditions, malnutrition, drug abuse, alcoholism, unemployment & homelessness, having either a direct or indirect influence on the duo. Also, low BMI, anemia, helminthic infections are associated with co-infection. Low CD4 count and poor adherence to ART are poor prognostic factors in co-infected patients.³

This study was undertaken to evaluate the HIV-TB co-infection, which is first of its kind in this part of India.

Current research aimed to study the epidemiology & various determinants of HIV-TB co-infection in HIV positive patients attending ART center at Goa Medical College (GMC), Goa and to study the prevalence of HIV- TB co-infection.

MATERIAL AND METHODS

The retrospective observational study was carried out at the Anti Retroviral Therapy (ART) center of Goa Medical College (GMC) Bambolim, a Tertiary Care Hospital, between January 1st 2013 to December 31st 2015.

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Variable	Number (n) and frequency (%)		P value	
	Study group	Control group		
Age (years)	15-24	19 (5.5%)	29 (8.4%)	0.298
	25-34	94 (27.4%)	109 (31.8%)	
	35-44	134 (39.1%)	132 (38.5%)	
	45-54	62 (18.1%)	49 (14.3%)	
	55-64	25 (7.3%)	22 (6.4%)	
	65-74	7 (2.0%)	3 (0.8%)	
	>75	1 (0.29%)	0 (0%)	
Gender	Male	208 (60.8%)	170 (50%)	0.009
	Female	133 (38.8%)	170 (50%)	
	Transgender	1 (0.29%)	0 (0%)	
Educational status	Illiterate	118 (34.5%)	72 (21%)	0.009
	Primary School	51 (14.9%)	39 (11.4%)	
	Secondary School	166 (48.5%)	202 (59%)	
	Graduation	7 (2.0%)	29 (8.4%)	
Occupation	Skilled worker	21 (6.1%)	102 (29.8%)	0.001
	Semiskilled worker	151 (44.1%)	106 (30.9%)	
	Students	6 (1.7%)	8 (2.3%)	
	Prison inmates	2 (0.5%)	0 (0%)	
	Commercial sex workers	2 (0.5%)	0 (0%)	
	Housemaids	16 (4.6%)	5 (1.4%)	
	Housewife	49 (14.3%)	73 (21.3%)	
	Retired	4 (1.1%)	5 (1.4%)	
Unemployed	91 (26.6%)	43 (12.5%)		
Religion	Hindu	263 (76.9%)	258 (75.4%)	0.249
	Catholic	48 (14.0%)	61 (17.8%)	
	Muslim	31 (9.0%)	23 (6.7%)	
Marital Status	Married	213 (62.2%)	224 (65.4%)	0.159
	Widow	67 (19.5%)	50 (14.6%)	
	Divorced	16 (4.6%)	16 (4.6%)	
	Single	43 (12.5%)	52 (15.2%)	
	Live in Relationship	3 (0.8%)	0 (0%)	
Mode of transmission of HIV	Heterosexual	308 (87.7%)	302 (88.5%)	0.065
	Blood transfusion	3 (0.8%)	6 (1.7%)	
	Unsafe infections	1 (0.2%)	3 (0.8%)	
	Mother to child	7 (2.0%)	12 (3.5%)	
	Unknown	31 (9.0%)	15 (4.3%)	
	Injectable drug abuse	0 (0%)	1 (0.2%)	
	Male sex with male	0 (0%)	2 (0.5%)	
	Non pan & tobacco chewing	247 (72.2%)	272 (79.5%)	
CD4 count	0-100	105 (30.7%)	39 (11.4%)	0.001
	101-200	84 (24.5%)	47 (13.7%)	
	201-300	55 (16%)	67 (19.5%)	
	301-400	44 (12.8%)	68 (19.8%)	
	401-500	16 (4.6%)	45 (13.1%)	
	>500	38 (11.1%)	76 (22.2%)	
	Comorbid condition	Anemia	151 (45%)	
Diabetes mellitus		24 (7%)	7 (2%)	
Hypertension		1 (0.2%)	2 (0.5%)	
Hepatitis B		3 (0.8%)	3 (0.8%)	
VDRL		3 (0.8%)	3 (0.8%)	
Hepatitis C		0 (0%)	1 (0.2%)	
Dyslipidemia		2 (0.5%)	0 (0%)	
HIV 2 Infection		1 (0.2%)	0 (0%)	
Bronchial Asthma		0 (0%)	1 (0.2%)	
No comorbidities		150 (43.8%)	249 (74.1%)	

Table-1: Sociodemographic determinants of HIV-TB co-infection:

Sampling methods and Participants: Patients were divided into 2 groups, the study group- comprising of HIV-TB co-infected patients, and the control group- comprising of HIV patients without TB. Confidentiality was maintained throughout, and the study was approved by the Institutional Ethics Committee.

The inclusion criteria for the study were all HIV Positive patients, more than 15 years of age, with and without TB (Pulmonary, Extra pulmonary & Disseminated). Also, only those with completed records were included in the study.

Patients who had one or both sputum samples positive for AFB, or with high clinical suspicion with chest X-Ray suggestive of TB or histo-pathological evidence of TB were included in the study. Also, all these patients were counselled and tested for HIV by ELISA by triple test/strategy 3 method including Combi AIDS Rs Advantage, Meriscreen test and AIDS scan.

Patient records were collected from the records at the ART center retrospectively, with the help of a pre- designed semi-structured questionnaire specially prepared to collect certain required variables for the study. A matching control group comprised of equal number of HIV patients not suffering from TB registered during the study period, selected randomly.

STATISTICAL ANALYSIS

All the data collected was entered in a master chart in MS Excel Database. Thereafter SPSS software 14.0 was used for statistical analysis. Various descriptive variables like proportion and percentage were used and Chi- Square test was used as the test for statistical significance. P value less than 0.05 was considered statistically significant.

RESULTS

Socio demographic characteristics

A total of 684 patients (342 cases and 342 controls) were included in the study. More than half of the total patients (n= 380, 55.2%) were males, and 75.1% of all patients were in the age group of 15- 35 years (not statistically significant). Also, more of the co-infected patients were illiterate as opposed to the control patients having secondary education indicating that illiteracy was a risk factor for HIV-TB co-infection. About 44% of the study patients were semiskilled workers & 26.6% were unemployed (see table 1) as opposed to majority (30.9%) being skilled workers in the control group with only 12.5% unemployment. This clearly showed that unemployment and lesser skill were associated with more HIV-TB co-infection with statistical significance (P=0.001). Marital status of the study group was not found

		Number (n) and Frequency (%)		P value
		Study Group	Control Group	
Alcohol consumption	Alcoholic	185 (54%)	110 (32.2%)	0.001
	Non Alcoholic	157 (46%)	232 (67.8%)	
Smoking status	Smokers	68 (19.9%)	52 (15.3%)	0.258
	Non Smokers	274 (80.1%)	290 (84.7%)	
Pan and Tobacco Chewing	Pan and Tobacco chewers	95 (27.8%)	70 (20.5%)	0.062
	Non Pan and Tobacco chewers	247 (72.2%)	272 (79.5%)	

Table-2: Addictions in HIV TB patients

Variable		Number (n) and frequency (%)
Type of TB	Pulmonary	155 (45.3%)
	Extra pulmonary	
	Pleural effusion	58 (17%)
	Lymph node	51 (14.9%)
	Abdominal	25 (7.3%)
	TB meningitis	24 (7.0%)
	Spine	6 (1.8%)
	Pericardial effusion	1 (0.3%)
	Breast	1 (0.3%)
	Genitourinary	1 (0.3%)
Disseminated	20 (5.9%)	
Treatment Received	CAT I DOTS	230 (67.2%)
	CAT II DOTS	87 (25.4%)
	Non DOTS	9 (2.6%)
	CAT IV DOTS	5 (1.4%)
	Private Anti TB Drugs	11 (3.2%)
Treatment outcome	Treatment Completed	107 (31.3%)
	Defaulter	66 (19.2%)
	Death	71 (20.8%)
	Cured	76 (22.2%)
	Failure	21 (6.1%)
	Transfer out	1 (0.3%)

Table-3: TB Disease & Treatment Related determinants:

to be statistically significant.

Host and Clinical Factors related characteristics

More than 88% of all patients had heterosexual mode of acquisition of HIV and nearly 58% had their CD4 counts less than 300 (statistically significant $P=0.001$). Almost 74% of control group had no co-morbidities versus 49.8% of the HIV-TB co-infected patients who had co-morbid illnesses, anemia being the most common association in the study group with statistical significance ($P= 0.001$).

Almost 49% patients in the study group had extra-pulmonary TB, with 17% having TB pleural effusion followed by 14.9% having TB lymphadenitis. Whereas, in patients with Pulmonary TB (45% of the total number), majority (92%) had the sputum negative variety. Also 72.8% of patients in the study group were newly diagnosed patients of TB and were started on CAT 1 DOTS of which nearly 32.7% patients had defaulted TB treatment or were lost to follow up & death was the outcome in 20.8%.

Environmental characteristics:

Nearly 54% of co-infected patients were alcohol consumers and alcohol consumption was a positive association and showed statistical significance ($P=0.001$). Surprisingly, such a statistically significant positive association was not found with cigarette smoking or Pan and tobacco chewing in our study.

DISCUSSION

TB is the most common opportunistic infection in HIV infected individuals. HIV positive individuals are 20 to 30 times more prone to get TB disease with an annual risk of 8-10% versus 10% lifetime risk in those who are HIV negative. HIV also increases the risk of conversion of latent TB infection to active TB disease.

HIV causes defective macrophages & T cells, and also weakens the cell mediated immunity, due to low IL-2 and high IL-10 production, thus reducing ability of an individual to form granulomas and contain or prevent spread of the infection resulting in disseminated, extra-pulmonary and miliary forms of TB.⁶ Also, TB causes increased production of cytokines like TNF-alpha, IL-1, IL-6 by the alveolar macrophages causing increased viral loads, decreased CD4 cell counts, enhanced HIV multiplication, increased survival in the macrophages, and resistance to TNF- alpha mediated apoptosis.^{6,7} Thus each one increases the progression of the other causing "the cursed duet".

The total number of HIV patients in the state in the study period of 3 years were 1,283 of which 362 patients had HIV -TB co-infection. Nearly 20 patients had to be excluded from the study due to incomplete records. Thus, the prevalence of HIV-TB co-infection in our study was 26.6%, similar to Nissapatorn et al (30.3%)¹⁵, Agarwal et al (29.1%)¹⁸ and Dagnra et al (23.7%).¹⁹ Many other studies showed higher and few others showed lower prevalence of the dual infection, probably due to differences in the study settings, differences in the distribution pattern or clustering and differences in the prevalence of either disease alone in the region under study.

The prevalence in our study also was high, indicating rising numbers of both HIV and TB in the state due to migration, increased use of alcohol and other addictive substances and tourist influx, as this state is a popular tourist destination for national and international tourists. This indicates need for upgradation of preventive services and treatment strategies and better health management policies.

In our study, the majority of the co-infected patients were males (60.8%) and majority were in the age group of 25-39 years as this is the most socially, economically productive and sexually active age group and this, was similar to studies by Purshottam A Giri (50.58%),⁸ Hiregoudar (58.8%)⁹, S Kumar et al (61.5%),¹⁰ and many more which showed male preponderance. Males usually tend to have higher chance of co-infection due to more socialization, migration in search of better job opportunities, and coming across more people at workplace and otherwise, thus acquiring TB bacilli and more sexual encounters increasing risk of HIV. Females usually have lower incidence of co-infection (except in few studies in Pakistan and Peru), due to certain factors like differences in social behavior, stigma & discrimination leading to underreporting of cases, and poor public health access in many parts of the world. Also, females tend to have more stress due to biological, economic and cultural role as care givers, thus under reporting or neglecting their health.

Education also plays an important role in co-infection, with majority of studies showing high risk of co-infection with lower education and illiteracy. Better education allows better understanding of the risks of acquiring the co-infection, better application of strategies for prevention and also, understanding need for treatment.¹¹ In contradiction, our study showed majority of patients having secondary school education (48.5% v/s 34.5% being illiterate) similar to studies by Purshottam Giri et al⁸, Hiregoudar et al⁹, Laxmi Gautam et al etc.¹²

Majority of our patients with co-infection were Hindu by religion, but this religious factor did not show any statistical significance, although some customs, beliefs, religious traditions may increase the susceptibility in certain religions. Other statistically insignificant variables studied included Pan and Tobacco chewing, smoking status, residential locality, marital status and mode of acquisition. Majority of our patients were married, and had heterosexual mode of transmission. Multipartnering and promiscuity increases the risk, so also localized pockets and clustering of cases due to prostitution, and other reasons.

Occupation is also a very important determinant of co-infection. Majority of co-infected patients were semiskilled workers, similar to studies by P. Giri et al⁸, Hiregoudar et al⁹, Ramachandra Kamath et al.¹³ Certain occupations increase the likelihood of the co-infection, like drivers, truckers, laborers etc, due to combination of factors like illiteracy, addictions, type of work and working schedule and also due to socioeconomic status. Alcohol consumption is an important determinant, with majority being alcoholics in the co-infected group. Alcohol addiction increases risk of defaulting both TB and HIV treatment, increases spread of

TB disease, also increasing risk of other addictive behaviors like cigarette/Bidi smoking and Tobacco chewing and also risk taking behaviors and promiscuity. This not only causes increased risk of getting co-infected, but increases risk of drug resistant TB and HIV and complications due to it thereafter.

CD4 cell count plays an important role in TB-HIV co-infection with lower CD4 counts indicating lower levels of immune functioning, leading to rapid spread of disease, increased risk of reactivation of latent infection and also higher propensity of acquiring extra-pulmonary TB and other opportunistic infections like *Pneumocystis Carinii* pneumonia, atypical mycobacterial infections, candidiasis, and various others. Nearly 55% of co-infected patients had CD4 counts <200 cells/microlitre, versus 24% in the non co-infected group. This was in accordance with other studies done by Nara Kingkaew et al¹⁴, P. Giri et al⁸, Ramachandra Kamath et al¹³, Laxmi Gautam et al¹² and many more.

Anemia was a very common association with the HIV-TB co-infection, which may be due to various factors like poor nutrition, increased risk of parasitic/ helminthic infestations in co-infected patients, or due to pancytopenia secondary to TB or due to high viral loads and severe immune suppression by HIV, leading to secondary bone marrow suppression and anemia of chronic disease. Other comorbidities seen in co-infected patients were, Diabetes Mellitus, Hepatitis B and syphilis.

The majority of patients in our study were extra-pulmonary TB similar to studies by Hiregoudar et al⁹ and Raginia Ghiya et al¹⁷ with Pleural effusion predominating, followed by Lymph node. Studies by Ramachandra Kamath et al¹³, Veeranoot Nissapatorn et al¹⁵, Christopher Affusim et al¹⁶ showed predominance of pulmonary over extra-pulmonary TB unlike our study where extra-pulmonary TB was predominant (49%). This may be due to the fact that our institution is the only tertiary care center of the state of Goa, all the investigating modalities for diagnosis of extra-pulmonary TB being available. And majority of co-infected group reported to us with CD4 counts of less than 200 leading to more of atypical form and presentation of TB. Amongst the Pulmonary TB patients, sputum negative were in majority. Most of the co-infected patients were new patients of TB started on CAT I DOTS. Also, the treatment success rate in co-infected patients was 53.5% with nearly 19% default rate and 21% deaths. Studies by Mehretu et al²⁰, Hassan et al²¹ and Teshome et al²² showed a lower death and default rate and higher treatment success rate than our study. This was probably due to the fact that, Goa being a highly developing state, with increase in tourism, construction and urbanization, there is a great influx of Migrants and tourists which has greatly contributed to a higher prevalence of co-infection, with higher rates of death and default. Also, a higher number of referred cases from adjoining states, and increased degree of stigma and discrimination due to the smaller size of population has further contributed to the default and treatment failure.

CONCLUSION

This study was the first of its kind in the state of Goa. The higher prevalence of HIV-TB co-infection in the state warrants upgradation of TB-HIV control activities and high degree of suspicion for early diagnosis. Migration and tourism may be responsible for a slightly higher burden of co-infection in the state. Male gender, lower CD4 counts, alcohol consumption, lower level of education and semiskilled work were all associated with co-infection. A higher default and death rate warrants better and improved TB-HIV control program functioning. These socio-demographic factors will help guide the control strategies to target the high risk groups and help in improving the treatment outcomes and disease severity. More such studies in the future will help to gain more knowledge on the dual infection in the state. Active commitment at the political level for intensifying the efforts to curtail both the scourges simultaneously is the need of the hour.

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