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Clinical profile and outcome of HIV-TB Co-Infection at a centre of excellence for HIV care

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ABSTRACT

Background: Tuberculosis (TB) and Human Imuunodeficiency Virus (HIV) co-infection has detrimental effects on both the individual and the health care system especially in resource limited countries like India. Tuberculosis ranks among the most common cause of death in HIV patients. In this review we have analysed the clinical and immunological characteristics of HIV-TB coinfected patients and their clinical outcomes. **Aims and Objectives:** To assess the co-relation between socio-demographic characteristics, clinical and immunological Profile of HIV-TB co-infected patients and the clinical outcome. **Materials and Methods**: A retrospective clinical study of patient records at the Centre of Excellence for anti-retroviral therapy was done. The records of HIV-TB co-infected patients were collected and data extracted pertaining to the socio- demographic characteristics, clinical profiles and outcomes. **Results**: Among the 377 cases included as per criteria, 76.9 % completed the treatment for TB while 23.1% patients died before treatment completion. Twenty-nine point seven percent of the patient population constituted women, while 0.5% was transgenders. Regarding the pattern of tuberculosis, 58.4% patients had extra pulmonary TB while 39.5% and 2.1% of the study population were diagnosed as pulmonary and disseminated TB respectively. Mean baseline CD4 count was 191 cells/mm3 and the mean CD4 count during first and second follow up were 298 and 362 cells/mm3 respectively. There was a statistically significant correlation noted with poor clinical outcomes and low baseline CD4 counts. **Conclusion**: Age, gender, the clinical pattern of tuberculosis and the treatment category did not have a statistically significant association on the outcome. We found that the TB associated mortality in HIV co- infected patients had a direct correlation with the stage of HIV at presentation as there was a strongly significant association between low CD4 counts and adverse clinical outcomes.

Key words: HIV, Tuberculosis, Coinfection, CD-4 Counts

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INTRODUCTION

Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) co-infection is considered one of the most important public health problems in terms of the economic and social impact it has globally. Tuberculosis is the most common opportunistic infection associated with HIV. It is also the leading cause of morbidity and mortality in patients with HIV/AIDS in resource-limited settings.[1]

The immune suppression associated with HIV increases the risk of reactivation of latent tuberculosis and rapid

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progression to active TB infection.[2] HIV infects and destroys CD4+ T lymphocytes. CD4+ T lymphocytes are essential for effective cell mediated immune response to Mycobacterium tuberculosis. Activated T lymphocytes can induce the production of gamma interferon, which activates macrophages. These activated macrophages will limit the further active multiplication of TB bacilli. As the CD4+ function and count declines in HIV, there is a strong predisposition to tuberculosis. AIDS virus infection also interferes with the generation of effector memory CD4 T cell that migrate to the primary site of MTB infection – the lung – and dramatically increases risk of developing active TB. Tuberculosis is more difficult to diagnose and therefore progresses rapidly in HIV positive patients.[3]

The psycho-social challenges include stigma attached to the burden of double disease. Interaction between anti-tubercular and antiretroviral drugs has the potential for producing severe side effects and a long treatment duration of 18 to 24 months.

According to World Health Organization (WHO) report 2016, An estimated 1 million people living with HIV (PLHIV) worldwide fell ill with TB in 2016. TB is the leading cause of death among people with HIV, accounting for some 370,000 people who died from HIV-associated TB in 2016. Globally PLHIV are 21 times (16-27) more likely to fall ill with TB than those without HIV and 37% of deaths among people with HIV due to TB. HIV infected patients are at high risk of mortality from multi-drug resistant and extensively drug-resistant TB.[4]

As per Government of India statistics (2015), India has an estimated 2.1 million people living with HIV (2015). [5,6] In India, 55-60% of AIDS patients reportedly have tuberculosis and it is one of the leading causes of death among people living with HIV/AIDS (PLHA).[7] Collaborative Tuberculosis and HIV activities are essential to prevent, diagnose and treat TB among people with HIV and HIV among TB patients, for an optimal patient care.

AIMS AND OBJECTIVE

To assess the co-relation between socio-demographic characteristics, clinical and immunological Profile of HIV-TB co-infected patients with that of the outcome.

MATERIALS AND METHODS

The records of HIV-TB co-infected patients maintained at the Centre for excellence for anti-retroviral therapy located at Bowring and Lady Curzon Hospital, Bangalore were collected and the data extracted pertaining to socio demographic characteristics, clinical profiles and outcomes. It is an observational cross-sectional clinical study

Inclusion criteria

Subjects living with HIV-1 infection who are followed longitudinally for their HIV health care in the ART Nodal Centre at Bowring and Lady Curzon Hospital, who have been diagnosed with tuberculosis.

We excluded patients with other causes of immune suppression like diabetes mellitus, chronic steroid abuse and immunosuppressive therapy as well as patients with insufficient follow up records

Methodology

The patient details were collected from the records maintained at the centre for excellence for anti-retroviral therapy at Bowring and Lady Curzon hospital.The sociodemographic, clinical and immunological profiles of the patients were compared with the outcomes.

The common trends among the selected profiles were assessed and the difference in outcomes was studied. The aim of the review was to analyse the inference and to know whether appropriate modifications in the line of treatment could be implemented.

Statistical methods

Descriptive and inferential statistical analysis was used in the present study. Significance was assessed at 5% level of significance. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups,

RESULTS

A total of 377 patients were included in our study. Majority of patients (46.4%) were in the age group of 31-40 years of age with the mean age being 38.68±10.12 years (Table-1). Our study showed that there was a strong male predominance comprising almost 70% of the HIV/TB co infection study population.

A total of 58.4% (n=220) of our patients were diagnosed to have Extra-Pulmonary tuberculosis (Table-2). Among the extra-pulmonary TB group, it was observed that lymph node tuberculosis was the commonest presentation in these co-infected patients.

Eighty two point five percent (n=311) of our patients were on category I ATT and 17.5% (n=66) on category II ATT. The category of TB treatment did not have a significant impact on the clinical outcome of the study group as evidenced from the results. The mortality observed was 23.07% (Table-3).

The single most common site of Tuberculosis affection was pulmonary -39.5% (n=149) followed by TB lymphadenitis-23.3% (n=88) (Table-4).

CD-4 counts of the patients were analysed at various points in time of follow up as follows- Time-1-Baseline, Time-2-At end of 6 months and Time-3 at 12 months (Table-5). The mean baseline CD-4 count in these patients were 191.76 ± 171.37 prior to initiating treatment. NR represents the patient group which did not have a serial CD-4 count recording in the subsequent visits.

In this study, we compared different parameters like age, the gender distribution, as to whether each had any statistically significant association with the end point outcome. The results were tabulated as depicted in the tables below.

Age, gender and the clinical pattern of Tuberculosis if taken as independent factors were not found to have a statistically significant impact on the outcome of these patients as shown in the following tables (Table-6, Table-7 and Table-8).

It was observed that patients affected with pleural effusion and Tuberculous meningitis had a statistically significant end-point of adverse outcomes in term of mortality compared with the other clinical TB types (Table-9).

A low baseline CD-4 counts in these patients was shown to have an adverse effect on the clinical outcomes as shown by the p value above (p<0.001).(Table-10) This led to the conclusion that CD-4 counts at presentation

Table 1: Age distribution of patients studied

Age in years	No. of patients	%
11-20	10	2.7
21-30	63	16.7
31-40	175	46.4
41-50	89	23.6
51-60	29	7.7
61-70	10	2.7
>70	1	0.3
Total	377	100.0

Table 2: Distribution of the TB types in study population

Nature of TB	No. of patients	%
Extra Pulmonary TB	220	58.4
Pulmonary TB - sputum negative	87	23.1
Pulmonary TB - sputum positive	62	16.4
Disseminated TB	8	2.1
Total	377	100.0

Table 3: Diagnosed category of patients studied in relation to TB-outcome

Location	TB treatment outcome		Total (%)
	Death (%)	Treatment completed (%)	
Cat I	71 (81.6)	240 (82.8)	311 (82.5)
Cat II	16 (18.4)	50 (17.2)	66 (17.5)
Total	87 (100)	290 (100)	377 (100)

P=0.805, Not significant, Chi-Square test

Table 4: Pattern of TB in patients studied

Location	No. of patients	%
Pulmonary	149	39.5
Lymph node	88	23.3
Abdominal Koch's	67	17.8
Pleural effusion	33	8.8
TB Meningitis	27	7.2
Miliary TB	8	2.1
Spinal TB	3	0.8
Pharyngeal	1	0.3
Genito-Urinary TB	1	0.3
Total	377	100.0

Table 5: CD4 distribution of patients studied

CD4	No. of patients	%	Mean±SD
Ist Analysis (n=377)			
1-50	67	17.8	191.76±171.37
51-100	74	19.6	
101-200	99	26.3	
201-300	56	14.9	
301-500	52	13.8	
>500	29	7.7	
IInd Analysis			
1-50	8	2.1	298.00±188.69
51-100	23	6.1	
101-200	58	15.4	
201-300	58	15.4	
301-500	74	19.6	
>500	35	9.3	
NR	121	32.1	
IIIrd Analysis			
1-50	6	1.6	362.85±196.53
51-100	6	1.6	
101-200	20	5.3	
201-300	34	9.0	
301-500	68	18.0	
>500	33	8.8	
NR	210	55.7	

Table 6: Association of age distribution on the outcome

Age in years	TB treatment outcome		Total (%)
	Death (%)	Treatment completed (%)	
11-20	1 (1.1)	9 (3.1)	10 (2.7)
21-30	13 (14.9)	50 (17.2)	63 (16.7)
31-40	42 (48.3)	133 (45.9)	175 (46.4)
41-50	21 (24.1)	68 (23.4)	89 (23.6)
51-60	6 (6.9)	23 (7.9)	29 (7.7)
61-70	3 (3.4)	7 (2.4)	10 (2.7)
>70	1 (1.1)	0 (0)	1 (0.3)
Total	87 (100)	290 (100)	377 (100)

P=0.548, Not significant, Chi-Square test

as well as those observed during follow up, showing an increment compared with the previous values were associated with a favorable outcome. Patients with a lower CD-4 count and a poor recovery of the same during each of the follow up times had a higher mortality as evidence from Figure-2.

DISCUSSION

Globally and in India, TB is one of the most common opportunistic infections affecting people with HIV. This assumes importance in a country like India which has 2.7 million HIV infections and 23% of the world's incident TB cases. HIV infection is often cited as an important reason for failure to control TB, and for causing a resurgence in TB worldwide.

In our study, 58.4% patients had extrapulmonary TB while 39.5% had pulmonary TB. The mortality among the study population observed was 23.07% which was similar to the findings in a study of HIV-TB co-infected patients in Coastal South India by Kumar N et al where the mortality recorded was18.8%.[7]

A study conducted in Shimla by SK Sharma, Alladi Mohan and Tamilarasu Kadhiravan also supported the observation that the prevalence of extra-pulmonary tuberculosis was more in co infected cases.[8] But, there are reports with pulmonary involvement in higher proportions (73%) as in a study conducted by Shastri et al.[9]

Globally, the TB associated mortality in co-infected patients is three times higher than mortality among TB sans HIV patients. There are a number of possible explanations that have been proposed for the increased mortality among co-infected patients. The location and the extent of TB are influenced by the degree of immunosuppression, often increasing the difficulty of diagnosis and hence delaying treatment initiation, often resulting in higher mortality. Immunological studies have also shown that host responses to M. tuberculosis enhance HIV replication thus accelerating the natural progression of HIV and further depressing cellular immunity.[10] Our study also underscores this in that, there was a strongly significant association between adverse clinical outcomes and low CD4 counts. There are other factors like adherence to treatment, nutrition status of the individual and incidence of drug toxicities though not evaluated in our study which are also important causes contributing to the morbidity and mortality in these patients.[7]

Table 7: Gender distribution of patients studied in relation to outcome

Gender	TB treatment outcome		Total (%)
	Death (%)	Treatment completed (%)	
Female	22 (25.3)	90 (31)	112 (29.7)
Male	65 (74.7)	198 (68.3)	263 (69.8)
TG	0 (0)	2 (0.7)	2 (0.5)
Total	87 (100)	290 (100)	377 (100)

P=0.419, Not significant, Chi-Square test

Table 8: PTB types of patients in relation to the outcome

If diagnosed specify	TB treatment outcome		Total (%)
	Death (%)	Treatment completed (%)	
EPTB	45 (51.7)	175 (60.3)	220 (58.4)
PTB - sputum negative	27 (31)	60 (20.7)	87 (23.1)
PTB - sputum positive	14 (16.1)	48 (16.6)	62 (16.4)
Disseminated TB	1 (1.1)	7 (2.4)	8 (2.1)
Total	87 (100)	290 (100)	377 (100)

P=0.215, Not significant, Chi-Square test

Table 9: Pattern of TB and its outcome

Location	TB treatment outcome		Total (n=377) (%)	P value (%)
	Death (n=87) (%)	Treatment completed (n=290) (%)		
Pulmonary	41 (47.1)	108 (37.2)	149 (39.5)	0.098+
Lymph node	16 (18.4)	72 (24.8)	88 (23.3)	0.213
Abdominal TB	15 (17.2)	52 (17.9)	67 (17.8)	0.883
Pleural effusion	1 (1.1)	32 (11)	33 (8.8)	0.004**
TB Meningitis	11 (12.6)	16 (5.5)	27 (7.2)	0.024*
Miliary TB	1 (1.1)	7 (2.4)	8 (2.1)	0.473
Spinal TB	2 (2.3)	1 (0.3)	3 (0.8)	0.072+
Pharyngeal	0 (0)	1 (0.3)	1 (0.3)	0.583
Genito-Urinary TB	0 (0)	1 (0.3)	1 (0.3)	0.583

Chi-Square test

Table 10: CD4 counts (mean count and SD) in relation to outcome

CD4	TB treatment outcome		Total	P value
	Death	Treatment completed		
Baseline	107.71±114.21	216.10±177.51	191.76±171.37	<0.001**
6 months	220.00±178.06	304.61±188.44	298.00±188.69	0.054+
12 months	330.89±304.09	364.67±189.90	362.85±196.53	0.617

Student t test

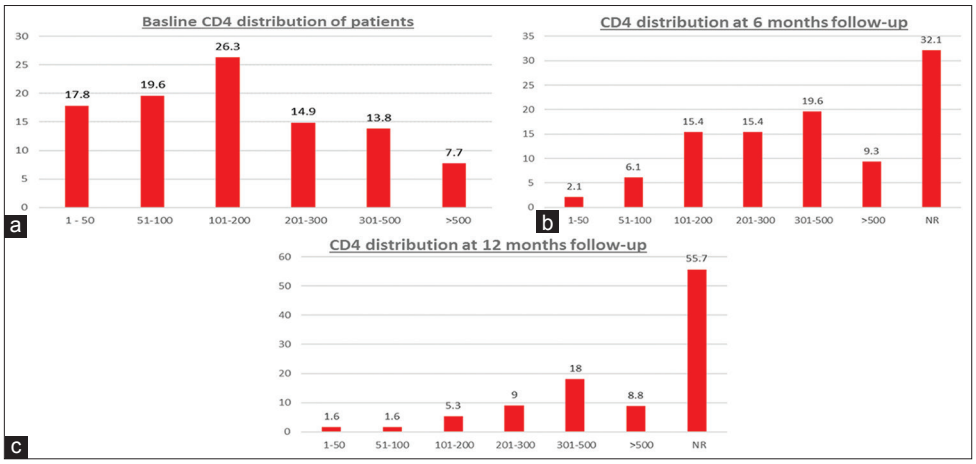

Figure 1(a), 1(b) and 1(c): represents the CD-4 counts of patients at different times of follow up. Among 377 patients in our study 23.1% (n=87) succumbed to mortality during the time course while 76.9% completed the treatment successfully

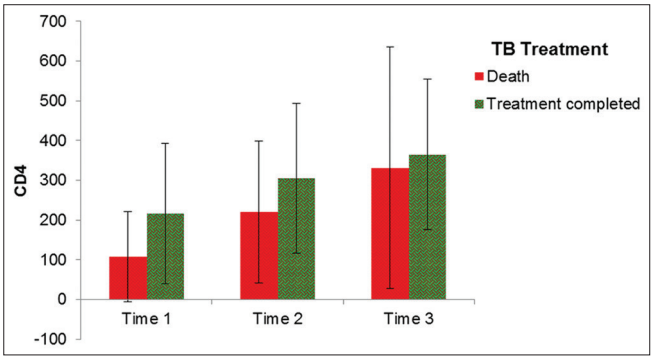

Figure 2: Association of CD-4 counts with adverse outcomes.

The strength of this study lies in the large size of the co-infected cohort, and thus the results are likely to represent the majority of those accessing HIV or TB care in the country.

CONCLUSION

In summary, the majority of co-infected patients had extrapulmonary TB. It was observed that there was a statistically significant increase in adverse outcomes in patients with pleural effusion and TB meningitis. Age, gender, the type of tuberculosis and the treatment category did not have a statistically significant association on the outcome.

We found that the TB associated mortality in co- infected patients did have a direct correlation with the stage of AIDS at presentation as there was a strongly significant association between low CD4 counts and adverse outcomes.

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Authors Contribution:
DTN- Concept and design of the study, reviewed the literature, manuscript preparation and critical revision of the manuscript; **DMT**- Concept, collected data and review of literature and helped in preparing first draft of manuscript; **RK**- Conceptualized study, literature search, statistically analyzed and interpreted, prepared first draft of manuscript and critical revision of the manuscript; **AAT**- Concept, collected data and review of literature and helped in preparing first draft of manuscript; **SKM**- Concept, collected data and review of literature and helped in preparing first draft of manuscript; **AF**- Concept of study, collected data and review of study; **RBC**- Concept of study, collected data and review of study.

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