A Cross Sectional Study on Impact of Anti Tuberculosis Treatment in Tuberculosis (TB) Human Immunodeficiency Virus (HIV) Co-Infection

Avani G. Gajjar[1], Tinkal Patel[2], Sanjay Kumar Patel[3], Vipul P Chaudhari[4], U C Samudyatha[5], J K Kosambiya[6]

[1,5]Resident, [4]Assistant Professor, [6]Professor & Head, Community Medicine Department, Government Medical College, Surat, Gujarat, India

[2]Professor & Head, Department of General Medicine, Government Medical College, Surat, Gujarat, India

[3]Senior Medical Officer at A.R.T. Centre, Government Medical College, Surat, Gujarat, India

Correspondence : Dr. Tinkal Patel, Email: pateltinkal@yahoo.com

Abstract :

Introduction: TB is the most common opportunistic infection in HIV positive people. HIV-TB co-infection is a fatal combination with higher death rates in developing countries. In cured TB cases in HIV positive people, chances of recurrent also high. ART prevents the progression of HIV, reduces the chances of another opportunistic infection that could make management of care more complicated, and reduces the chances of TB recurring. **Objectives:** To document the profile of HIV positive TB patients availing both Anti-Retroviral (ART) and Anti Koch's Treatment (AKT) at a tertiary care hospital. **Method:** A retrospective descriptive study was conducted using available records of 198 HIV positive TB patients enrolled at an ART Centre of South Gujarat from November 2016 to November 2017. Age at enrollment at ART Centre, sex, native place, ART status, CD4 count were recorded along with detection, category, previous history and treatment of TB. Test of significance (t test) was applied to analyze the difference between CD4 count before and after treatment with AKT. **Results:** Mean age of male (n=123) and female (n=75) patients at the time of HIV detection was mean 37.62 (SD±11.61) years and mean 34.05 (SD±8.85) years respectively. Majority (86.87 %) were migrants from states other than Gujarat, of which 31.31% were from Maharashtra. Among them, 66% patients were on CAT-I AKT and 10.6% had previous history of TB. Among 56.1% patients who had extra-pulmonary TB, common were abdominal TB (47.75%), lymphadenopathy (18.02%) and pleural effusion (16.22%). While 32% of patients had completed their AKT regimen, 68% were on AKT. Among those were missed out (8.6%) and lost to follow up (3.5%) from ART, almost half (41.67%) had been initiated under CAT-II AKT. Mean CD4 count for 84 patients who completed their AKT was increase, this was statistically significant (p=0.001). **Conclusion:** Majority of patients were migrants and extra pulmonary TB was more common in this study group. Mean CD4 count increased significantly after completion of AKT. Prompt treatment and preventing loss to follow up are key to successful treatment completion and cure.

Key Words: HIV positive TB patients, AKT, CD4 count

Introduction:

Worldwide, among people living with HIV most common opportunistic infection is TB. Despite being a preventable and treatable disease, it is also the most common cause of death in HIV-positive adults living in developing countries.[1] Annually, about 1,10,000 people in India are estimated to be HIV-TB co-infected, with the national average for HIV prevalence among incident TB cases at 5%.[2] It is recognized that HIV and TB count for a fatal combination with extremely high death rates (15–18%) reported among HIV infected TB cases notified under the Revised National Tuberculosis Control Program (RNTCP). Further, even among cured TB cases with HIV infection, the risk of

recurrent TB is quite high. TB is estimated to cause about 25% of all deaths among People Living with HIV (PLHIV) in India. The National Framework for Joint HIV/TB Collaborative Activities articulates the national policy for collaboration between NACP and RNTCP for HIV-TB activities to ensure reduction of the HIV-TB burden in India. [3]

HIV-associated immune dysfunction increases the risk of TB disease, is associated with worse TB treatment outcomes, and increases the risk of TB relapse after initial cure.[4,5] Antiretroviral therapy (ART)–mediated immunological recovery is associated with decreased risk of TB, and sequential ART after initiation of TB treatment has been shown to improve outcomes.[4-10]

People living with HIV who have a low CD4 count are at a much higher risk of falling ill from TB infection than HIV negative people. In fact, the risk of developing active TB is estimated to be 26 and 31 times greater in people living with HIV than in those who are HIV-negative. [11]

ART also prevents the progression of HIV, reduces the chances of other opportunistic infections that could make clinical management more complicated, and reduces the chances of TB recurring. However, treating both conditions at the same time can be challenging because of side-effects, pill burden, and drug interactions.

Objectives:

To document the profile of HIV positive TB patients availing both Anti Retroviral Therapy (ART) and Anti Koch's Treatment (AKT) at a tertiary care hospital.

Method:

A retrospective descriptive study was conducted at ART centre, New Civil Hospital, Surat in Gujarat in November 2017. All HIV-TB (198) co-infected patients who were registered between November 2016 and November 2017 at ART center were enrolled in the study.

Study Variables: Information about age at enrollment for ART, native place, sex, on ART status, previous history of TB, type and site of TB and status of AKT were collected from the records available at ART centre. CD4 counts of those patients who had completed the treatment (AKT) in this period at the time of starting and after completion of AKT were also obtained.

Data was entered in MS Excel and analyzed using SPSS. Mean for quantitative variables and frequency for qualitative variables were calculated. Paired t-test was applied to find difference of CD4 count at initiation and completion of AKT.

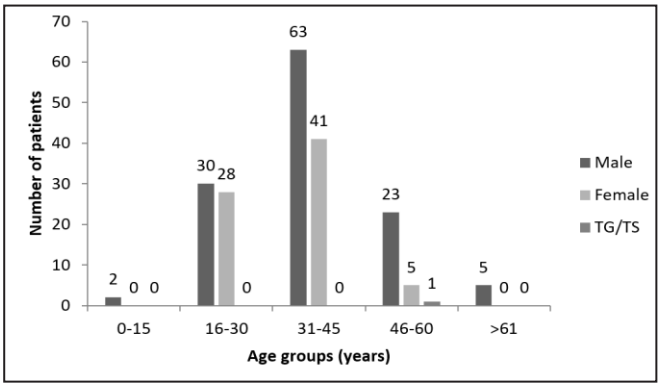
Confidentiality of the participants: This was a retrospective descriptive study using programmatic data. Personal identifiers were not collected.

Ethical Issues: No bio marker will be collected from study participants. Study is approved by Human Research Ethics Committee, Government Medical College Surat and Gujarat State AIDS Control Society.

Results:

Mean age of Male (n=123) and Female (n=75) patients at the time of HIV detection was 37.62±11.61 years and 34.05±8.85 years respectively. (range: 3 years to 70 years). Figure 1 shows that majority belongs to 31-45 years age groups.

Figure 1 : Age- Sex distribution of HIV positive TB patients (n=198)



Majority (86.87%) of them were migrants from states other than Gujarat, namely Maharashtra (31.31%), Uttar Pradesh (18.69%), Bihar (9.6%), Rajasthan (5.05%) and the rest from other states (Madhya Pradesh, Andhra Pradesh, Jharkhand, Odisha, Nepal, West Bengal and Tamil Nadu).

Table 1: Current ART status of PLHIV initiated on AKT in the study period

ART Status	Intensive phase of AKT n= 71 (%)	Continuation Phase of AKT n=63 (%)	Completed AKT Treatment n= 64 (%)
On ART	25 (35.2)	48 (76.2)	53 (82.8)
Transferred out	17 (23.9)	1 (1.6)	3 (4.7)
Missed out	7 (9.9)	4 (6.3)	6 (9.4)
Loss to follow up	5 (7)	2 (3.2)	0 (0)
Opted out	0 (0)	2 (3.2)	0 (0)
Died during the study period	17 (23.9)	6 (9.5)	2 (3.1)

Among those patients who were Missed out/ Loss to follow up (LFU), 87.5% were from states other than Gujarat (n=21).

Table 2: Distribution of HIV positive patients according to their TB Category (n=198)

Type of TB	N (%)	Site of TB (%)
Pulmonary TB	87 (43.94)	
Extra Pulmonary TB	111 (56.06)	Abdominal TB (47.76)
		Lymphadenopathy (18.02)
		Pleural Effusion (16.22)
		TB meningitis (9)
		Spine TB (4.5)
		Milliary TB (4.5)

Table 3: Difference in CD4 count after completion of treatment (n=64)

Cd4 count (cells/cumm)	n	Range of CD4 count at the time of initiation	Mean CD4 count at the time of initiation (±SD)	Range of CD4 count at the end of treatment	Mean CD4 count at the end of treatment with AKT (±SD)	t statistic	p value
Less than 500	56	31-490	210 (±132)	35-1232	287.38 (±260)	2.35	0.02
More than 500	8	543-885	712 (±149)	207-1167	516(±296)	-2.2	0.06

All 198 patients were initiated on treatment, of which, at the time of this study, 35.9% (71) were in Intensive phase of AKT, 31.3% (63) were in Continuation phase and 64 (32.3%) had completed the treatment. Table 1 shows the ART status of the patients initiated on AKT.

Category-I AKT was started in 130 (65.66%) of patients and Category-II AKT in 68 (34.34%) patients. Almost half (41.67%) of those who were missed out and lost to follow up (n=24) were being treated under Category-II.

Table 2 shows that 56.06% had Extra Pulmonary TB and 43.94% had Pulmonary TB. In Extra Pulmonary TB patients majority were suffering from Abdominal TB (47.76%), Lymphadenopathy (18.02%), Pleural Effusion (16.22%), TB meningitis (9%), Spine TB (4.5%) and Milliary TB (4.5%).

Majority of the patients (89.4%) were suffering from first episode of TB while the rest (10.15%) were being treated for recurrent TB. Extra pulmonary TB was more in number than pulmonary TB in both new

cases of TB (n= 98) as well as recurrent cases (n=13), however this was not statistically significant ($\chi 2=0.326$, p=0.646).

Mean CD4 count of patients was 259(±198) cells/cumm. Majority of the patients (n=179) had CD4 count less than 500 cells/cumm.

Among patients who completed treatment, mean CD4 count at the time of initiating AKT was 272(±214) and after treatment it was 315(±273) cells/cumm, and this rise was not statistically significant (t=1.32, p=0.191). Only 8 patients among them had initial CD4 count more than 500 cells/cumm.

There was a significant rise in the CD4 count in patients who initially had CD4 count less than 500 and completed treatment with AKT (Table 3). However, there was no significant difference in the CD4 count at the end of AKT in patients who had CD4 count more than 500 initially.

Discussion:

We designed a retrospective record based descriptive study to document the profile of patients receiving both ART and AKT. The study aimed at documenting the sociodemographic profile, diagnosis and treatment history of TB and difference in CD4 count before and after AKT. Among the 198 records studied, 64 had completed the treatment during the study period. Among 24 Missed Out /LFU from ART, only 6 had history of completed the treatment with AKT.

Retention in Care for ART among HIV positive TB patients: Those who were missed out and lost to follow up (n=24) from ART, almost half (41.67%) had been initiated under CAT-II AKT. Out of 198 HIV-TB patients, 10.15% were being treated for Recurrent TB. A study by Schechter et. al shows that among 91 HIV positive TB patients 75% were cured, 3% were lost to follow-up, 3% had recurrence TB infection and 19% were death. [12]

Distribution HIV positive patients according to their TB Category: During the study period, the National guidelines for TB (RNTCP) recommended two categories of treatment for TB. [13] However, it was revised later. In this study, about 66% patients were on CAT-I and 34% were on CAT-II AKT. Only 10.15% were being treated for recurrent TB while the rest (24%) on CAT-II treatment were either treatment after loss to follow up or treatment after failure.

A study in South India by Sara et. al shows that 50% were on CAT-I, 18.5% were on CAT-II and 31.5% were on others daily Regimens.[14] Distribution HIV positive patients according to their TB type: Extra-pulmonary TB was more common than Pulmonary TB. Among Extra-pulmonary TB cases, 47.75% had abdominal TB most common, 18.02% had lymphadenopathy, 16.22% had pleural effusion and 9% had TB meningitis.

A study in Ethiopia by Alemieet. al shows that 51.8% participants were diagnosed with pulmonary TB. Extra-pulmonary TB were recorded in 44% patients of whom 60.8% had TB lymphadenitis, 10.6% had pleurisy, 9.3% had peritonitis, 7.1% had TB of the spine, 5.2% had cold abscess, 2.9% had Skin TB, 2.5% had TB arthritis and 1.7% had TB osteomyelitis.[15]

Mean CD4 count of HIV-TB patients who Completed AKT at different time intervals: Among patients who completed treatment (n=64), mean CD4 count at the time of initiating AKT was 272(±214) and after treatment it was 315(±273) cells/cumm, and this rise was not statistically significant (t=1.32, p=0.191). Median CD4 at the time of starting of AKT was 210 and after completion of AKT it was 223. The rise in CD4 count was significant in patients who had CD4 count less than 500 cells/cumm initially.

A study in Sweden by Skogmaret et al shows that among 35 patients who had baseline median CD4 count of 188, after 6 months of AKT, median CD4 count increased to 417, among 19 patients who had baseline median CD4 count was 505, after 6 months of AKT median CD4 count decreased to 407 and in

rest 17 patients who had baseline median CD4 count of 243, after 6 months of AKT median CD4 count was not changed. [16]

Conclusion:

Majority of patients were migrants from other states than Gujarat and majority of patients who were lost to follow up were also migrants. The proportion of Pulmonary and Extra-pulmonary cases are mostly equal in this study. There was a significant rise in the mean CD4 count after completion of AKT among those who had lower CD4 count initially.

Recommendation:

Adherence to treatment has been long recognized as the key to successful cure of TB and management of HIV. Tracking of those lost to follow up is crucial because of the advantage of AKT- ART drug adherence has on the CD4 count of the patient, especially among those who had low CD4 counts initially as seen in this study. Since majority of the patients were migrants and majority of those who were lost to follow up were also migrants, we recommend the optimum use of web based monitoring tool like 99DOTs. Greater involvement of networks of HIV positive patients to trace those lost to follow up will also be advantageous.

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Declaration:

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Conflict of Interest: Nil

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