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Trends of Tuberculosis Co Infection In Hiv/Aids Patients Before and After 2014 –Observational Study at Osmania General Hospital

KEYWORDS: Tuberculosis, National AIDS Control Organisation (NACO) Highly active antiretroviral therapy (HAART), Tuberculosis (TB)

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ABSTRACT *The present study was retrospective hospital based observational study conducted in patients of HIV/AIDS with tuberculosis attending ART centre Osmania General Hospital a tertiary care centre in Hyderabad.*

BACK GROUND: The study was conducted to study trends of Tuberculosis co infection in patients of HIV/AIDS before and after 2014 – observational study at Osmania general hospital .

OBJECTIVE: Tuberculosis is the most common opportunistic infection in patients of HIV/AIDS which is a preventable and curable disease .Early diagnosis and treatment can improve the quality of life in patients of HIV and AIDS.

Tuberculosis can occur at any CD4 count but the prevalence is high in patients with CD4 count <250 cells/µL .As per NACO guide lines ART was started in patients with CD4 count <250 cells/µL before 2014 and from 2014 onwords ART was started in patients with <350 cells/µL.

MATERIAL AND METHODS: It was a retrospective hospital based observational study conducted in patients attending ART centre, Osmania General Hospital from January 2012 to march 2016 .All patients were screened for tuberculosis. Both pulmonary and extra pulmonary tuberculosis patients were included in the study. All patients were on treatment as per NACO guide lines. Patients were categorized in to 2 groups .group 1 includes patients registered during 2012and 2013 with cd4 count <250 cells/µL who were on ART and CD4 >250 cells/µL were not on ART (pre ART) with tuberculosis. Group 2 includes patients registered during 2014and 2015 with count CD4 <350 cells/µL who were on ART and CD4 >350 cells/µL not on ART with tuberculosis (pre ART). All the essential information was collected from the records of ART centre

Introduction:

Tuberculosis (TB) is the most common global infection affecting up to one-third of the estimated 40 million HIV patients [1].There is increased risk of *M.* tuberculosis reactivation from 1 in 10 to 1 in 3 in HIV infection and the likelihood of progressive disease after new infection with *M. Tuberculosis.* Globally, the prevalence of tuberculosis (the number of active cases of disease in a population at any given time) has been falling since 1990, despite the rise in the numbers of new cases up to 2006. This paradox may be explained by and increasing global population (around 1% per annum) and the high mortality in those with new tuberculosis cases infected with HIV [2]. TB is a major cause of death among people living with HIV/ AIDS [3] and may lead to increased HIV disease progression[4]**.** TB is more common in those with advanced immune suppression but can present across a wide spectrum of CD4 counts[5]. As per The World health organisation WHO reports approximately 14 million people have HIV and TB co infection, Worldwide and accounting for 26% of AIDS related deaths. In 2010 the WHO estimated that 39% of new TB cases occurred in people with HIV infection[6]. The risk of active tuberculosis increases as number of CD4 T-lymphocytes fall secondary to HIV infection. Highly active antiretroviral therapy (HAART) for HIV reduces risk of tuberculosis by up to 90%, although risk does not decrease until after 3 months of therapy and never equates to HIV-uninfected individuals[7].

WHO recommends that HIV/AIDS programmes provides isoniazid 5 mg/kg up to a maximum of 300 mg daily for 6–9 months preventative therapy after excluding active tuberculosis for people living with HIV/AIDS and patients should be clinically monitored for toxicity and for active tuberculosis[8]. In early HIV infection, Clinical presentation of TB resembles that observed in immuno-competent persons but in late HIV infection, due to atypical presentation, involvement of in accessible sites and low sputum smear positivity diagnosis may be delayed[9]. Clinical presentation changes with declining CD4 counts. Nonspecific symptoms and extra pulmonary disease are more common with patients with very low counts (<100 cells/µL) and often involves more than one organ. In adults with HIV extra-pulmonary disease accounts around 50% and 10% and has disseminated disease compared to HIV-uninfected adults[10]. HIV and *M.* Tuberculosis co infection *present* special problems in clinical management. Adverse drug events are more common and standard regimens may be less efficacious. High frequency of failure and relapse are common with regimens that do not contain rifampicin[11].Those with drug-susceptible tuberculosis should receive the same 6- month regimen as recommended for HIV-uninfected patients, and a 9–12-month regimen for the treatment of central nervous system tuberculosis[12].

Investigations:

All blood tests were performed on the serum samples as per the strategy and policy prescribed by NACO, Complete blood picture, serum creatinine, Blood urea, serum electrolytes, Liver function tests, Sputum for Acid fast bacilli, Chest radiography, CD4 cell Count, Fine needle aspiration and biopsy, Magnetic Resonance imaging, Comput-

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erized tomography and colonoscopy (if necessary).

Results: Total number of HIV from 2012 to2016 registrations was 4260, out of which 2325 were male, 1913 were female, and 22 were transgender. Total no of patients with tuberculosis from 2012 to2016 were 517 (12.14%). Patients on ART + TB include 371(71.72%) and number of patients with TB on pre ART 146 (28.28%). Patients without tuberculosis were 3743 (87.86).
Out of 4260 HIV registrations in group 1 includes 2624 and 1636 in Group2.

Group1 (2624), on ART 1613 and 341 were on ATT. (21.14%) .Out of 343 TB registrations on ART=ATT were 245(71.85%) and on pre ART were 95(28.15%).

Group2 (1636) HIV registrations 1032 were on ART and 176 were on ATT (17.05%).Out of 176 on ART+ATT were 126 (71.51%) and 50(28.49%) were on pre ART.

Conversion rate of Tuberculosis over a period of 5 years was as fallows.

1) In 2012 Among 1368 HIV registrations, 846 were on ART (CD4 count <250 cells/µL)and 522on pre ART(CD4 count >250 cells/µL). Among them a total of 165 patients (both in ART+ pre ART) TB was detected over a period of five years (2012 to march 2016).

Out of 165 TB patients 128 were on ART+ATT (77.58%) and 37 were on ATT with pre ART (22.42%). Among 128 patients on ART+ATT year wise tuberculosis conversion rate was 92(71.88%) in 2012, 16(12.50%) in 2013, 13(10.16%) in 2014, 5 (3.91%) in 2015, and 2(1.56%) in 2016.

Among 37 patients of pre ART, TB conversion rate year wise was 30(81.08%) in 2012, 2(5.41%) in 2013, 1(2.70%) in 2014, 3(8.11%) in 2015 and 1(2.70%) in 2016.

2)In 2013 among 1256 HIV registrations, 767 were on ART(CD4 count <250 cells/µL) and 489 were on pre ART(CD4 count >250 cells/µL) . Among them a total 176 patients (both in ART+ pre ART) TB was detected over a period of 4 years (2013to 2016).

Out of 176 TB patients 117 are on ART+ATT (66.48%) and 59 were on pre ART (33.52%).

Among 117 patients on ART+ATT year wise tuberculosis conversion rate was, 106(90.60%) in2013, 8 (6.84%) in 2014, 3 (2.50%) in 2015 and 0 in 2016.

Among 59 patients of pre ART, TB year wise tuberculosis conversion rate was, 53(91.38%) in 2013, 3 (5.17%) in 2014, 2(3.45%) in 2015 and 0in 2016

3)In 2014 Among 815 HIV registrations, 532 were on ART(CD4 count <350 cells/µL) and283(CD4 count >350 cells/µL) on pre ART . Among them in a total of 90 patients(both in ART+ pre ART) TB was detected.

Out of 90 TB patients 60 were on ART+ATT (66.67%) and in30 were on pre ART (33.32%).

Among 60 patients on ART+ATT year wise tuberculosis conversion rate was, 47(78.33 %,) in2014, 11 (18.33) in 2015, 2 (2.33%) in 2016

Among 30 patients of pre ART tuberculosis conversion rate was, 27(90%) in2014, 3 (10%) in 2015 and 0 in 2016.

4) In 2015 among 821 HIV registrations, 500 were on ART(CD4 count <350 cells/µL) and 321on pre ART (CD4 count >350 cells/µL) . Among them in a total of 80 patients(both in ART +pre ART) TB was detected.

Out of 80 TB patients 66 are on ART+ATT (76.74%) and 20 were on pre ART (28.24%).

Among 66 patients on ART+ATT year wise tuberculosis conversion rate was, 63(95.55%) in 2015 and 3(4.5%) in 2016.

Among 20 patients of pre ART tuberculosis conversion rate was, 17(85%) in2015,3 (15%)in 2016. (As shown in 1&2).

Table:1: HIV Registrations and TB Registrations

YEAR	HIV REG	Male	Female	Trans gender	Total TB	Total TB %	Not on TB	Not on TB %
2012	1368	752	611	5	165	12.06	1203	87.94
2013	1256	691	557	8	176	14.01	1080	85.99
Total	2624	1443	1168	13	341	26.07	2283	87.00
2014	815	425	384	6	90	11.04	725	88.96
2015	821	457	361	3	86	10.48	735	89.52
2016	1636	882	745	9	176	21.52	1455	88.94
Total	4260	2325	1913	22	517	12.14	3743	87.86

Table:2: showing ART and Pre ART with Tuberculosis

YEAR	ART	Total TB	Total TB %	ART +TB	ART+ TB %	PRE ART	PRE ART +TB	PRE ART+ TB %	Male	Female	TransGender
2012	846	165	19.50	128	77.58	522	37	22.42	107	58	0
2013	767	176	22.95	117	66.48	489	58	33.52	119	57	0
Total	1613	341	21.14	245	71.85	1011	96	28.15	226	115	0
2014	532	90	16.92	60	66.67	283	30	33.33	69	21	0
2015	500	86	17.20	66	76.74	321	20	23.26	67	18	1
Total	1032	176	17.05	126	71.59	604	50	28.41	136	39	1

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Figure :1

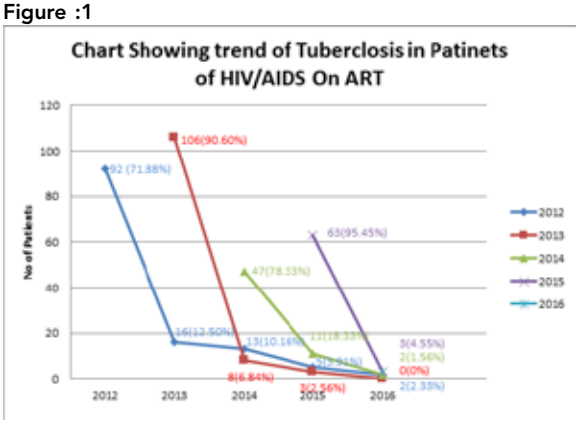

Table :3:Conversion rate of Tuberculosis in patients of HIV/AIDS

Year	Total TB	Total ART+TB	2012		2013		2014		2015		2016	
			No of Pts	%	No of Pts	%	No of Pts	%	No of Pts	%	No of Pts	%
2012	165	128	92	71.88	16	12.5	13	10.16	5	3.91	2	1.56
2013	176	117			106	90.6	8	6.84	3	2.56	0	0
average	171	122.5										
2014	90	60					47	78.33	11	18.33	2	3.33
2015	86	66							63	95.45	3	4.55
average	88	63										

Figure: 2

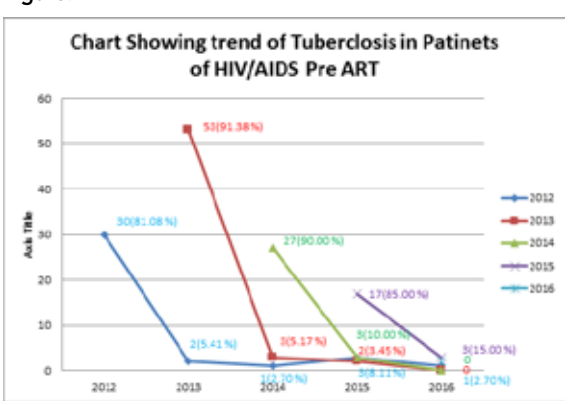

Table: 4: Conversion rate of Tuberculosis inpatients on Pre ART

Year	Total Pre ART+TB	2012		2013		2014		2015		2016	
		No of Pts	%	No of Pts	%	No of Pts	%	No of Pts	%	No of Pts	%
2012	37	30	81.08	2	5.41	1	2.7	3	8.11	1	2.7
2013	58			53	91.38	3	5.17	2	3.45	0	0
Average	47.5										
2014	30					27	90	3	10	0	0
2015	20							17	85	3	15
Average	25										

Discussion:

TB is the most common treatable HIV-related disease and a leading killer of people living with HIV/AIDS (PLWHA). In India, there were an estimated 5.134 million PLWHA at the end of 2004.[13,14]

In December 2010, the WHO endorsed the new rapid molecular GeneXpert® MTB/RIF test as an alternative to direct Ziehl– Neelsen staining of sputum for TB diagnosis[15]. GeneXpert is a close to point-of-care assay, which does not require laboratory isolation facilities and has high specificity and a lower limit of detection of 100–150 bacilli/mL.

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GeneXpert® MTB/RIF also detects rifampicin resistance with 99.1% sensitivity and excludes resistance with 100% specificity. [16, 17] .

The WHO recommends the same 6-month regimen for the treatment of all patients with tuberculosis, regardless of disease site or HIV status: rifampicin, isoniazid, pyrazinamide and ethambutol for the first 2 months, followed by rifampicin and isoniazid for 4 months. [18] .The WHO currently recommends daily administration of TB treatment at least for the intensive phase of therapy in HIV TB co infected persons. All HIV infected patient with active TB should receive trimethoprim - sulphamethoxazole prophylaxis .In patients with HIV and TB co infection (pulmonary and extra pulmonary) ART should be started or continued irrespective of CD4 count and type of TB as early as possible between 2 weeks and 2 months when TB treatment is tolerated. The prevalence of TB, MDRTB in HIV is similar to that in general population[19, 20].

Among Opportunistic infections in HIV, tuberculosis accounts (65%) in Indian patients.

Anti tuberculosis therapy (ATT) must be administered according to the directly observed treatment-short course (DOTS) regimen. As rifampicin is known to enhance the metabolism of protease inhibitors and nevirapine, efavirenz based antiretroviral therapy (ART) is recommended while patients are on rifampicin. [21]

There is declining trend of TB cases in HIV patient's 21.14% in group 1 and 17.05% in group2. In group 1 average no of TB registrations were 177,among them those on ART +TB were 122.5 and those on pre ATT +TB were 47.5 .In-group 2 average no of TB registrations were 88 , among them those on ART + ATT were 63 and those on pre ART +TB were 25. Present study concludes that there is declining trend of TB and this declining trend of TB is more in patients those on pre ART with CD4count>350 cells/μL (group2). The present study also concludes that more number of tuberculosis cases were detected at CD4 count <250 cells/μL (177) compared to CD4 count <350 cells/μL (88).

Conclusion :

The present study concludes that there was almost 50 % reduction in total TB cases, including those on TB+ART cases and those on pre ART +TB. More number of TB cases were there at the time of detection of HIV and there is gradual declining trend in tuberculosis and over a period of 3 to 4 years it is becoming 0 in both the categories. (CD4 <250 cells/μL n ART before 2014 and CD4 <350 cells/μL on ART after 2014). We can expect more no of TB + ART registrations and less number of TB patients on pre ART by initiating ART at CD4 < 350 cells/μL because initiating ART early can prevent opportunistic infections and improved survival may be possible in HIV patients. Overall incidence of tuberculosis is decreasing may be due to increased awareness, improved nutritional status, easy accessibility, increased ART centres and availability of drugs.

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