PROSPECTIVE STUDY OF TUBERCULAR MANIFESTATION IN HIV POSITIVE PATIENTS IN VIMSAR, BURLA, SAMBALPUR, ODISHA

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ABSTRACT

BACKGROUND

Tuberculosis is the commonest opportunistic infection in HIV positive patient. This is a major challenge faced by HIV positive patient. There are less number of studies in India.

MATERIALS AND METHODS

This study was carried out at Medicine Department and ART Centre, VIMSAR, Burla to know the epidemiology and clinical profile of HIV and TB co-infection. This is a prospective study in which all adult patients attending our hospital for period of one year with HIV-TB co infection were enrolled. There were 269 patients. The clinical parameters were studied after all detailed history and clinical examination. The diagnosis of tuberculosis was made by relevant investigation like Sputum AFB, Chest X-ray, CSF Study, CT Scan, Pleural Fluid Study, Ascitic fluid study etc.

RESULTS

The data were compiled. Majority of the patients, out of 211 patients, 74 (82.52%) were male, 34 (16.35%) were female & TGTS were-3 (1.42%). Age group mostly affected were 26-35 years (38.1 %) and 36-45 years (38.1%). Extra-pulmonary TB constituted 56.28% and Pulmonary TB-43.72%. 41.99% completed anti-TB treatment and mortality was 12.99%. Mean CD4 count at the time of diagnosis-218; and patients with low CD4 count at the time of diagnosis had high mortality. Extra-pulmonary TB is predominant among HIV TB co-infection and the working-class population. A low CD4 count at the time of tuberculosis diagnosis is associated with a higher mortality and early suspicion diagnosis of tuberculosis and early initiation of ATT in HIV patients reduces mortality and morbidity significantly.

CONCLUSION

Tubercular Co-infection- It most commonly affects the younger economically productive sexually active section of the society. CD4 cell count were inversely related to Tubercular infection in HIV patients. Decrease in CD4 cell count points to increase in Tubercular infection. Males are commonly affected compared to female. Extra-pulmonary tuberculosis is common compared to Pulmonary Tuberculosis.

KEYWORDS

HIV, Tuberculosis, CD4 Cell count, TGTS, AFB, PLHIV, WHO, NACO, RNTCP, UNAID.

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BACKGROUND

The combination of the two deadly diseases TB and HIV continues to increase morbidity and mortality faced by almost all the physicians of the nations. Resurgence of tuberculosis in western countries due to HIV/AIDS is also being contributing significantly for the disease burden on the globe. 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 20 times (16 – 27) more likely to fall ill with TB than those without HIV. PLHIV face the threat of drug-resistant TB. If diagnosis is delayed there is increased risk of mortality from multi drug resistant TB.[1]

Although curable, tuberculosis is estimated to be the single largest cause of death among AIDS patients globally, being responsible for at least 12% - and perhaps up to 30-50% - of all AIDS-related deaths that have occurred.[2] The individual patient level, TB and HIV form a type of "disease complex," with each pathogen manipulating the host response in such a way as to enhance the other pathogen's ability to cause disease pathology. In most cases, mycobacterium is the first pathogen to infect the patient, with HIV infection occurring later. With progressive HIV infection and its associated immune compromise, there is an enhanced risk of reactivation of latent TB infection, an increased likelihood of progressive TB disease from newly

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acquired TB infection, and an increase in recurrent TB or TB relapse. In the cases where HIV infection predates TB infection, such as in mother-to-child transmission of HIV- the generalized immune stimulation that accompanies secondary TB infection, results in driving HIV replication and disease progression.[3] This study describes the clinical and epidemiological features of HIV-TB co-infected patients presented in our hospital.

MATERIALS AND METHODS

Patients were selected among those attending the General Medicine outdoor and indoor department in respective inpatient wards and ART centre between March 2017 and February 2018. All data were collected from the ART center of VIMSAR, Burla, Sambalpur. All HIV positive patients were screened for tuberculosis. Those patients with a strong suspicion of HIV/AIDS infection, were subjected to screening tests for anti-HIV antibodies after pre-test counselling and written consent of patient were taken.

A detailed clinical history and complete general physical and systemic examination findings of HIV/TB patients were recorded. All the routine investigations were done.

Two simple rapid immune binding assays were selected for the HIV serological testing. It was done in the ICTC center of our institute. The approach was consistent with WHO/NACO recommendations.

The diagnosis of tuberculosis was based on the WHO case definition of tuberculosis, according to disease type or pulmonary smear status. All the pulmonary TB suspects were sent to make a sputum smear examination at the RNTCP accredited laboratory in our college. All extra-pulmonary cases were examined individually.

All suspect cases of pulmonary TB gave three sputum specimens to the RNTCP lab. Sputum Negative cases were considered as TB when the chest x ray showed changes consistent with tuberculosis.

RESULTS

Mode of transmission	No.	Percentage
Heterosexual contact	206	97.39
Blood transfusion	1	0.37
Injectable drug abuse	1	0.37
Mother to child		
Homosexual	4	1.85

Mode of Transmission

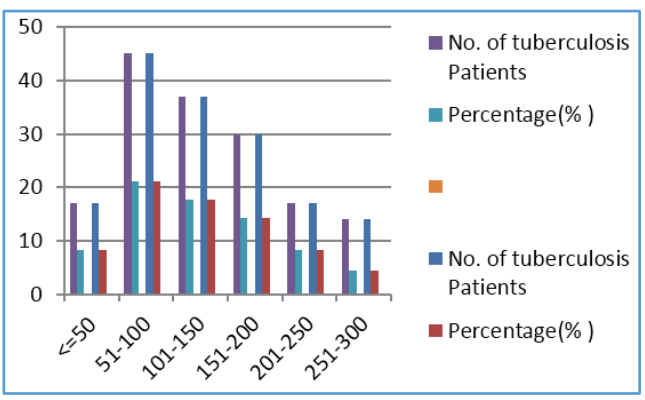
The risk for HIV infection by engaging in unsafe sexual practices, such as having multiple sex partners, unprotected intercourse, sex with high risk partners (e.g., injection drug users, commercial sex workers), and exchanging sex for money or drugs. There is a three-fold risk increase of active TB associated with consumption of more than 40 g alcohol per day, and! or having an alcohol induce disorder.

During the period of study 211 patients qualified to be enrolled. 174 (82.52%) were males and 34 (16.35%) were females. 3 were transgender/transsexuals[4] Age and sex distribution of the patients are shown below.

Age	Male	Female	Trans-gender	Total No. of Patients	Percentage (%)
15-25	18	2		20	9.95
26-35	64	15	2	81	38.50
36-45	65	14	1	80	38.1
46-55	22	2		24	11.26
56-65	3	1		4	1.73
>65	2	0		2	0.86

Table 1

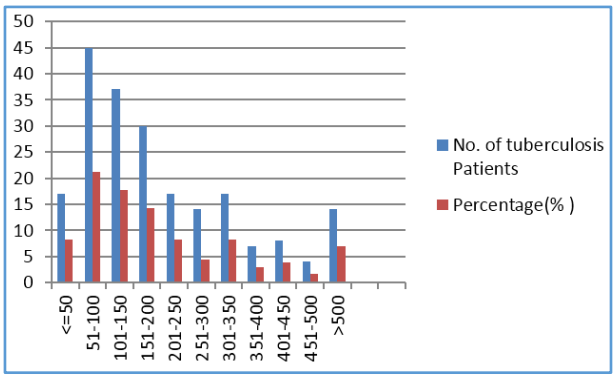
Most of the patients were manual labourers (74 =35.06%); followed by unemployed (33=15.58%); Semi-skilled worker (26=12.12%); self-employed (21=9.96%); House wife (21=9.96); Local transport worker (12=4.76%); mechanic (3=1.30%); Service (5=2.6%) ; truck driver (21=9.96%); Hotel staff (4=1.73%); Student (4=1.73%); Farmer (3=1.3%); factory worker (2 =0.94%).[5]



Graph 1

Occupation	Number	Percentage
Driver	21	9.96
Labourer	74	35.06
Hotel worker	4	1.73
Farmer	3	1.30
House wife	5	2.16
Student	4	1.73
Self-employed	21	9.96
Local transport worker	10	4.76
Service	5	2.60
Semi-skilled worker	26	12.12
Mechanic	3	1.30
Unemployed	33	15.58
Factor workers	2	0.94
Total	**100**	**100**

Table 2. Occupation



Graph 2

135(64.04%) patients were found alcoholic; 109(51.95%) patients were tobacco users, 62(29.44%) were smokers; 63(29.87%) were having no addictions.

Number of married individuals were 163 (77.06%); unmarried =29(13.85%); Divorced/ widowed = 19 (9.09%).

Out of the 163 married persons in the study group 100(47.75%) individuals had a HIV positive partner while 69(32.58%) had a HIV negative partner. 41(19.66%) of them are not aware of their partners HIV status.

Most of the patients (206 = 97.84) are heterosexuals while only 5 (2.16%) are homosexuals and all of them were males.

Out of the 211 cases 92(43.72%) were Pulmonary tuberculosis and 119(56.28%) were extra-pulmonary tuberculosis.

During the study period 92 patients of pulmonary TB; 50(54.46%) patients were sputum positive for AFB and 42(45.54%) were sputum negative out of 119.

Pleural effusion (tubercular) (46 = 38.46%) was the most common type of extra-pulmonary TB in our study group. It was followed by lymph node TB (33 = 27.69%) and gastrointestinal TB (19 =16.15%). 11(9.23%) patients had meningeal TB and 5(3.85%) had multiple sites of involvement. There were 3(1.69%) cases of skin TB and tuberculoma each. 2 cases (1.68%) each of pericardial TB and TB spine were included in the study.

Most of the patients with PTB complained of cough (32=34.78%). Weight loss (18=19.56%) and loss of appetite (20=21.73%) were frequently observed. Fever was seen 10 (10.86%) cases 12 (13.04%) had haemoptysis and another had abdominal distension. [6]

Types of Symptoms		No.	Percentage (%)
	Fever	10	10.86
	Weight loss	18	19.56
	Anorexia (loss of appetite)	20	21.73
	Lymphadenopathy	-	-
Pulmonary	Cough	32	34.78
	Expectoration	1	1.08
	Haemoptysis	12	13.04
	Breathlessness	-	-
	Chest pain	-	-

Table 3. Clinical findings in Pulmonary TB

Types of symptoms		No.	(%)
	Fever	8	6.72
	Weight loss	10	8.40
	Anorexia (loss of appetite)	7	5.88
	Fatigue	1	0.84
	Lymphadenopathy	18	15.12
	Skin Infection	2	1.68
Extra Pulmonary	Cough	28	23.52
	Expectoration	1	0.84
	Haemoptysis	18	15.12
	Breathlessness	2	1.68
	Chest pain	6	5.04
	Nausea / vomiting	2	1.68
	Diarrhoea	8	6.72
	Constipation	-	-
	Jaundice	-	-
	Abdominal distension	7	5.88
	Headache	-	-
	Alter sensorium	1	0.84

Table 4. Clinical Findings in Extra Pulmonary TB

Most of the patients with EPTB had fever 8 (6.72%), weight loss 10 (8.40%) and loss of appetite 7 (5.88%). Abdominal distension 7 (5.88%) and diarrhoea 8 (6.72%) were the major symptoms in gastrointestinal TB, while cough 28 (23.52%) and chest pain 6 (5.04%) were the major symptoms in pleural TB. Neck was the commonest site for TB lymphadenitis 18 (15.12%), Fatigue 1 (0.84%). Most, of the patients with TB meningitis presented with altered sensorium 1 (0.84%).

The CD4 count of the patients at the time diagnosis of TB is given in the following table (mean CD4 count=218 cells/mm3).

Most of the patients with Pulmonary TB 55 (59.41 %) weighed between 41-50 kgs. 22(23.76%) patients weighed 31-40 kgs; 11 (11.88%) patients weighed 51-60 kgs; 2(1.98%) patients were less than 30 kgs. 2(1.98%) were between 61-70 kgs. There was one (0.99%) patient who weighed more than 70 kgs. The mean weight = 44.9 kg; mean BMI = 17.46 kg/m2.

Signs	No. of Tuberculosis patients	Percentage
Body Weight (<30)	2	1.98
Body Weight (31-40)	22	23.76
Body Weight (41-50)	55	59.41
Body weight (51-60)	11	11.88
Body weight (61-70)	2	1.98
Body weight (more than 70)	1	0.99

Table 5. Weight measurement of patients

Out of the 92 cases of PTB in our study, 47(51.49%) patients had infiltrations in their chest x-ray. 19 (20.79%) had fluffy shadows and 10 (10.89%) had non-homogenous patches. Miliary shadows were present in 9(9.9%) cases. 4(3.96%) cases had consolidation and 2(1.98%) had cavity. One (0.99%) chest x-ray had bronchiectatic changes and another one had an isodense shadow.

X-ray findings	No. of Patients	Percentage
Upper zone infiltration	47	51.49
Fibro-cavity lesion	2	1.98
Military shadow	9	9.9
Homogenous patches	10	10.89
Consolidation	4	3.96
Fluffy shadow	19	20.79

Table 6. X-ray findings

Anaemia was a common finding and the mean Hb was 8.6 g/dL.

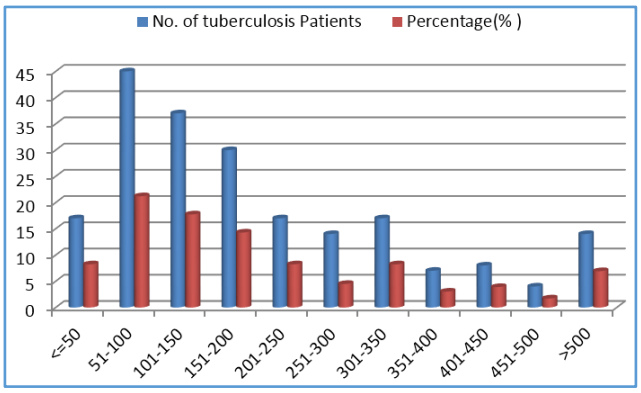
Majority of the patients 181 (86.24%) were started on CAT 1 ATT. 19 (9.29%) patients had CAT 2ATT. 2(1.3%) patients were having MDR TB so started in with CAT 4 DOTS. 3(3.46%) patients had taken therapy.

Out of the 211 patients in our study 89 (41.99%) were declared TB cured after treatment. Another 89(41.99%) patients are continuing the treatment. 27(12.99%) patients died and 8(3.03%) were lost to follow up.

Our study concluded that in the selected population the risk of Tuberculosis increases remarkably when the CD4 count falls below 200 cells/mm. (61.5% of the patients had a CD4 count <=200). The highest number of TB cases were recorded when the CD4 count was between 51 to 100 (21.21%). Though there is a decline in the number of cases as the CD4 count increases, TB is prevalent in all groups. In the study, 78.4% of patients of HIV-TB co-infection were having CD4 count <=200 cells/mm3.[7] The study had 81.6% of patients with CD4 count less than 200 cells/mm3.[8] This contrary data suggest that our study population acquire TB infection even if the CD4 count higher may be because of higher prevalence of TB in general population in this part of the state.

CD4 Count	No. of tuberculosis Patients	Percentage (%)
<=50	17	8.23
51-100	45	21.21
101-150	37	17.75
151-200	30	14.29
201-250	17	8.23
251-300	14	4.49
301-350	17	8.23
351-400	7	3.03
401-450	8	3.90
451-500	4	1.73
>500	14	6.93

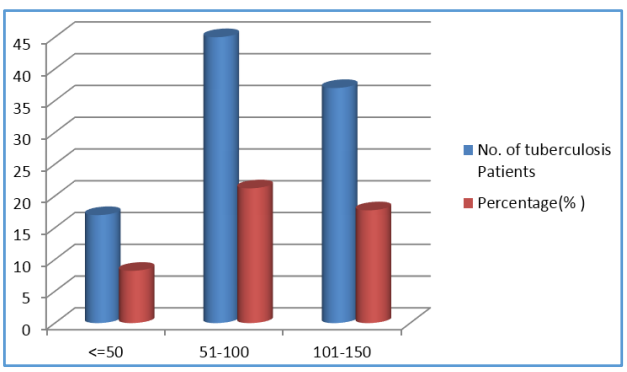
Table 7



Graph 3

	No. of Patients	Percentage
Extra Pulmonary TB	119	56.28
Pulmonary TB	92	43.72
Disseminated TB	-	-

Table 8. Types of Tuberculosis



Graph 4

This clearly shows that EPTB is more common than pulmonary TB in HIV- TB co infection. This can be compared with 54.4% of pulmonary TB and 45.6 of EPTB shown in studies[9]. A study in Thailand had 70% pulmonary and 30% extra pulmonary disease.[10] Among HIV-infected patients with TB extra pulmonary disease are more common, particular in those with advanced immune suppression. This fact can explain the increased number of EPTB cases in our study population as many patients are detected HIV positive at very late stage of the disease. Out of the 92 pulmonary TB cases in our study 50(54.46%) were positive for sputum AFB and the rest 42 (45.29%) were negative.

This apparent predominance of smear negative disease may be partly due to heavy workloads increasing the likelihood of false-negative laboratory errors, and 2). misdiagnosis of other HIV-related pulmonary conditions as smear-negative TB, but severe studies have found that smear-negative disease is actually more common among HIV-positive patients.[11] The level (immune suppression among the HIV-positive patients in the various studies may also have differed. Less severe immune compromised HIV-positive patients tend to have classical cavity TB which is smear-positive. As the level of immunity decreases with advancing HIV disease atypical pulmonary features predominate and smear examinations prove less sensitive.

TB Lymphadenitis	Pleural Effusion	Pericardial Effusion	CNS (TBM)	Abdominal TB	Bone and Joint TB	Skin TB	Tubercular
33 (27.69%)	46(38.46%)	2 (0.99%)	5(0.3.85%)	19(16.15%)	2(0.99%)	3(1.54%)	3

Table 9. Extra Pulmonary Tuberculosis

DISCUSSION

Our study which was conducted for a period of one year revealed that the disease burden of tuberculosis is substantial among the HIV affected population. Tuberculosis still marks as the leading cause of mortality and morbidity among the PLHA group. Total number of patients enrolled in our study was 211 which included all the patients who came to the ART centre of our hospital and the general medicine wards for a period of one year. During the same period of time 269 new cases of HIV were registered in the ART centre and department of medicine of our institute. Among them 211 individuals contracted tuberculosis during the study period.

Among the 211 patients 174(82.68%) were males and 34 (16.45%) were females. 3(1.42%) revealed themselves as transsexuals. This shows a clear preponderance of male population in the disease cohort. These studies showed a clear male majority' in HIV-TB co-infection. Those studies in Iran also showed that males are more affected.[12] But a study in Mumbai showed a marginal female majority as large number of female sex workers were included in that study.[13]

The high prevalence of HIV in males in our study must be due to the high rate of migration of the youth to other states in search of job opportunities where they are exposed to high risk activities. The main regions of migration include Surat in Gujarat, Mumbai, Chennai and Kerala. Another reason for the large male to female disparity may be because the females are often neglected and deprived of health care facilities resulting in an underestimation of their numbers.

The mean age of patients in our study was 37 years and the range was from 15 years to 70 years. The major age groups were 26-35 & 36-45 years which comprised of 76:6% (38.5% and 38.1%) of the study population. This clearly shows that the working population of the society is affected more than the rest as they are more sexually active and also have more chances for exposure to TB infection. This is consistent with the study 26 patients, (11.26%) were between 46-55 years and 23(9.95%) were between 15 and 25 years. Only four patients were above 56 years of age.[14] The decrease in number of elderly population is may be due to the high mortality of the HIV patients in the region. Majority of the participants are manual labourers (74 =35.06%) working either in their native place or in the above mentioned high risk migrant areas. This is consistent with the study in Delhi which had 38.5 % of manual labourers.[15] The dwelling areas of the labourers are congested and are often deprived of adequate ventilation or hygiene which make them prone to infections especially tuberculosis. The Risk for HIV infection by engaging in unsafe sexual practices, such as having multiple sex partners, unprotected intercourse, sex with high risk partners (e.g. injection drug users, commercial sex workers), and exchanging sex for money or drugs.[16]

162 (77.06%) of the patients were married while 29(13.85%) were unmarried. This is contrary to many other studies especially those done outside India and may be due to the social & cultural difference. 19 (9.09%) patients were single due to various reasons like death of the partner, divorce etc. The affected husbands are the viral source for most of village women. Out of the 211 patients with HIV-TB co-infection include 92 (43.72%) patients suffered from Pulmonary TB. The rest 119 patients were diagnosed to have extra pulmonary TB (56.28%).

The relationship between CD4 count and Tuberculosis considered very important as the decline in the level immunity is considered as a major risk for acquisition and reactivation of infections. In our study, 45 (21.21 patients were having a CD4 count between 51-100 at the time of diagnosis of TB 37 (7.75) were in the 101-150 group and 30 (14.29) patient in the 151-200 group. 17(8.23%) patients had less than 50 CD4 cells/ mm3. Another two groups of 17(8.23%) patients each had CD4 count between 210-250 and 301-350. 14(6.93%) patients had CD4 count more than 500. 14(6.49%) had it between 251-300,8(3.9%) between 401-450,7(3.03%) between 351-400 and 4(1.73%) between 451-500. The mean CD4 count of patients having HIV-TB coinfection was 218 cells/mm3. It ranged from 21-1044 cells/mm. It is slightly higher than what had derived from his studies (mean=174).[17] It was even less in studies done in Shimla (mean = 123) and in AIIMS, New Delhi (mean = 120).[18] But in a study the CD4 counts were better than ours (mean = 307; range = *6-1531).*[19]

Our study concluded that in the selected population the risk of Tuberculosis increases remarkably when the CD4 count falls below 200 cells/mm. (61.5% of the patients had a CD4 count <=200). The highest number of TB cases were recorded when the CD4 count was between 51 to 100(21.21%). Though there is a decline in the number of cases as the CD4 count increases, TB is prevalent in all groups. In the study, 78.4% of patients of HIV-TB co-infection were having CD4 count <=200 cells/mm3. The study had 81.6% of patients with CD4 count less than 200 cells/mm3.[20] This contrary data suggest that our study population acquire TB infection even if the CD4 count higher may be because of higher prevalence of TB in general population in this part of the state.

Majority of the patients (181 = 86.24%) were started on CAT 1 ATT. 9(9.09%) patients had CAT 2 ATT. 2(1.3%) patients were having MDR TB so started in with CAT 4 DOTS. 7(3.46%) patients had taken non-DOTS therapy. Out of the 211 patients in our study 89(41.99%) were declared TB cured after treatment. Another 89(41.99%) patients are continuing the treatment. 27(12.99%) patients died and 6

(3.03%) were lost to follow up. This is compared with study in Karnataka with a cure rate of 75.6%; death -11.78%; lost follow up - 3.12% & 9.49% of patients continuing treatment. Low number of cured patients in our study may be because of the large number of patients continuing the treatment. The study had reported death rate of 15.7%.[21]

CONCLUSION

HIV-TB co infection is a major healthcare issue in globally. It most commonly affects the younger economically productive sexually active section of the society. Early suspicion, diagnosis of tuberculosis and early initiation of ATT in HIV patients reduces mortality and morbidity significantly. CD4 cell count were inversely related to tubercular infection in HIV patients. Decrease in CD4 cell count increase in Tubercular infection. Males are commonly affected compared to females. Extra-pulmonary tuberculosis is common compared to Pulmonary Tuberculosis. Therefore, adequate knowledge of the manifestations of tuberculosis in HIV-infected patients is absolutely necessary for optimal management and to reduce mortality and morbidity.

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