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Pulmonary Medicine

CLINICAL SPECTRUM OF PULMONARY AND EXTRAPULMONARY TUBERCULOSIS IN HIV SEROPOSITIVE PERSONS WITH REFERENCE TO CD4 COUNT

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ABSTRACT

BACKGROUND: HIV infection is a major threat in the world population and in the control of tuberculosis in developing countries. Infection with HIV is the most potent risk factor for progression to active tuberculosis. Clinical presentation of TB among the HIV infected is dependent on the degree of immune suppression. Patients who are severely immune suppressed are more likely to have atypical clinical and radiographic features, extra pulmonary disease and disseminated disease. Thorough work up may be required to establish the diagnosis.

OBJECTIVES: To study the various manifestations of pulmonary and extra pulmonary tuberculosis in HIV Positive patients and impact of CD4 count on the severity of manifestations of TB.

METHODOLOGY: Observational cross sectional study of 50 HIV positive patients attending Department of pulmonary medicine, Government general hospital, Siddhartha medical college, Vijayawada from March 2016 to February 2017.

RESULTS: 50 HIV patients studied for period of one year. Majority of patients were in the age group of 30- 40 years. 66% were males and 34% females. Low socio economic group were commonly affected. Pulmonary TB (72%) is the most common form. Pleural effusion (30%) is common extra Pulmonary manifestation.Infiltrative lesions (66%) were more common X -ray findings with bilateral infiltrations seen in 28%of cases. Sputum positivity seen in 30% of cases. Mean CD4 count in this study is 162.54±154.37 cells/ μl. Most patients (74%) had CD4 count < 200 cells/ μl. 90.5% of sputum negative TB, 85.6% of extra pulmonary TB had CD4 <200 cells/μl. Majority of patients with upper zone lesions in chest x- ray had CD4 >200 cells/μl.

CONCLUSION : CD4 counts correlated well with clinical profile of TB, which showed that when CD4 counts were < 200 cells/ μl, sputum negative pulmonary TB and extra pulmonary TB were more,Chest x -ray were atypical in the form of lower zone involvement and more of infiltrative lesion.So,a high level of clinical suspicion is required in diagnosis of TB in HIV Infected,especially when they are in the later stage of disease which is indicated by CD4 counts < 200 cells/ μl.

KEYWORDS : HIV patients, Pulmonary TB, CD4 count,Chest x -ray lesions.

INTRODUCTION

HIV infection is a major threat in the global resurgence and in the control of tuberculosis in developing countries. It is estimated that each year about 2.2 million people develop TB in India out of a global incidence of 9.6 million.1.12% of this 9.6 million TB cases are PLWHIV. Tuberculosis remain the leading cause of death among people living with HIV, accounting for around one in three AIDS related deaths.[1]

It is found that in India about 5% of TB patients registered under RNTCP also have HIV infection. Economic burden of TB is extremely high in India between 2006 and 2014 TB cost the Indian economy a massive USD 340 billion. [2]

Thus while country is dealing effectively with HIV burden, TB associated HIV epidemic is posing a great challenge. In contrast to HIV infection, infection with M.tuberculosis can be spread via respiratory droplets and close non sexual contacts.This epidemic of tuberculosis probably represents, the greatest health risk to general public and also health care personnel dealing with these patients.

Therefore it is important to understand the effect of TB and HIV on each other and to take adequate measures to control this dual epidemic. HIV is the most powerful risk factor for progression from TB infection to disease. HIV epidemic will lead to increased number of TB cases including smear positive cases,reactivation of TB and susceptibility to new TB infection.

TB is the most common serious opportunistic infection in HIV patients and is the first manifestation of AIDS in more than 50% of cases in developing countries.The risk of death in HIV infected persons with tuberculosis is twice as high as that in HIV infected patients without tuberculosis. HIV fuels the spread of MDRTB. HIV stigma may lead to inadequate supervision of anti TB chemotherapy and delay in seeking care by TB suspects. HIV infection leads to high default rates because of adverse reactions. Clinical presentation dependent on degree of immune suppression. Patients with preserved immunity with CD4 + T cells count > 200 cell/μl are more likely to have typical symptoms, upper lobe disease and sputum smear positive. Patient who are severely immune suppressed are more likely to have atypical clinical and radiographic presentation,extra pulmonary disease including meningitis and miliary TB and absent cavitation. Because of this atypical presentation thorough work- up may be required to establish the diagnosis.

Effective management of patients with HIV -TB requires timely diagnosis and treatment of active TB and a thorough knowledge of drug interactions between HAART and anti tuberculosis treatment.

MATERIALS AND METHODS
STUDY DESIGN

This is a observational cross sectional study of 50 HIV positive patients with pulmonary or extra pulmonary TB features attending Department of pulmonary medicine, Government general hospital, Siddhartha medical college, Vijayawada from March 2016 to February 2017. Patients were investigated for HIV positivity by HIV coomb's test. Pulmonary TB is diagnosed among HIV positive patients by clinical examination,sputum examination, chest X- ray and blood examinations. Some patients, who are diagnosed as having tuberculosis, are sent for HIV testing.CD4 cells count is tested in all patients with HIV positive and severity of tuberculosis and relation with CD4 count is studied in all patients. The following investigations were done :Routine base line investigations like complete hemogram, ESR, LFT/RFT,Sputum for AFB,Sputum for CBNAAT,Chest X-ray – P/A view, Biochemical and bacteriological examination of body fluids in clinically relevant conditions, FNAC/Biopsy of accessible

peripheral lymphnodes examined by histopathology. Other investigations like US abdomen, CT head/ CT abdomen where ever appropriate.CD4 counts by flow cytometry by standard technique using Becton Dickinson FAC scan.

INCLUSION CRITERIA:
1. HIV seropositive patients with clinical features suggestive of pulmonary and extra pulmonary TB diagnosed by one of the following investigations.
a. Positive AFB smears
b. Radiological features consistent with TB including imaging studies like chest X- ray and CT thorax.
c. Pleural fluid analysis
d. Histopathology suggestive of tuberculosis and / or demonstration of bacilli in clinical specimens.

2. HIV positive patients with and without ART with their respective CD4 count with Tuberculosis

EXCLUSION CRITERIA :
1. HIV positive patients less than 18 years of age.
2. Patients with other immune compromised states.
3. Uncooperative and unwilling patients.

STATISTICAL METHODS
Following statistical methods were applied in the present study –

1. Cross tabs procedure , 2. Descriptive statistics ,3. Frequencies and percentages
4. Two way ANOVA – analysis of variance.

RESULTS
The age of the study subjects ranged from 20-67. The mean age was 35.32±9.08. (35.65±9.57 for females and 35.90±6.89 for males),as depicted in (figure 1). Maximum number of patients were in the 30-39 age group. In this study 50 HIV patients with tuberculosis were studied, of these 33 (66%) are males and 17(34%) are females,as shown in (figure 1). Common occupation among the study group was labourers 40%,followed by farmers 24%, drivers14%, housewives 12%, painter 2%,tailors 2% others 6%,as shown in (figure 2). Common constitutional symptoms reported were fever 82%, weight loss in 36%,as shown in (figure 3). Common respiratory symptom reported were cough 82%, breathlessness in 70%, chest pain in 26%. Gastrointestinal symptoms reported in 38% of patients of which diarrhea and nausea and vomiting are common.Neurological symptoms occurred in 10% of cases of which headache is common. Among dermatological symptoms skin lesions were reported in 40% of patients. Physical examination revealed that BMI <18.5 Kg/m2 in 42%, lymphadenopathy in 10%,icterus in 2%,skin and mucous membrane lesions in 40%. Among the patients studied,pulmonary TB was seen in 36(72%) patients and extra pulmonary features are seen in 14 patients (28%),as shown in (table 1).As shown in (table 2),9(18%) patients have both pulmonary and extra pulmonary features, which include 6 cases pleural effusion, 2 cases of lymphadenopathy,1 case of abdominal TB,because of presence of pulmonary features also, they are considered as pulmonary TB. Out of 36 pulmonary TB cases 21(58%) patients has sputum negative TB and 15 (42%) patients has sputum positive TB . Out of 21 sputum negative pulmonary TB cases 14(66.66%) cases are diagnosed by sputum for CBNAAT test. Remaining 33.33% cases are confirmed by clinical manifestations and x-ray findings.Out of 23 extra pulmonary TB cases in this study 15 (65.22%) patients presented with pleural effusion and 4 (17.39%) patients presented with lymphadenopathy and 4(17.39%) patients presented with ascites. 6 pleural effusion cases, 2 lymphadenopathy cases,1 abdominal TB case are having pulmonary TB features also.As shown in (table 3),among 50 patients with abnormal x- ray findings upper zone infiltrative lesions were seen in 3(6%), mid and lower zone infiltrative lesions seen in 16(32%), bilateral infiltrative lesions + military in 14 (28%), fibrocavitary lesions seen in 3 (6%), pleural effusion seen in 9(18%),normal x-ray findings seen in 5(10%) of patients. In this study CD4 >200 cells was seen in 13(26%) of patients and CD4 between 51-200 was seen in 28(56%) patients and CD4 <50 seen in 9 (18%)patients.74% 0f patients had<200 CD4 count.The mean CD4 count in this study was 162.54±154.37. Mean CD4 count among males was 182.52 ± 180.59 and females was 123.77±73.04.As shown in (table4),in sputum positive TB cases mean CD4count is 280.73±201.44 , and in sputum negative TB cases the mean CD4 count is 103.62±100.54, which is found to be highly significant with p

value<0.01. Mean CD4 count in extra pulmonary cases i.e.in ascites cases it is 97.50±77.48,in cases of lymphadenopathy it is 141.00±9.20, in cases of pleural effusion mean CD4 count is138.27±111.57. Mean CD4 count in patients with both extra pulmonary and pulmonary features is 143.11±112.77. Mean CD4 count in patients with only extra pulmonary features is 124.28±85.27. Mean CD4 counts in cases of chest x-ray finding of upper zone infiltrates is 255.00±3.00,in cases of lower zone and mid zone infiltrates CD4count is 118.31±103.52 ,and in cases of pleural effusion it is 141.00±97.20,in cases of miliary it is 197.43±223.75, and in cases of fibro cavitory lesions it is high 321.67±213.50, as shown in (table 5).100% of patients with upper zone lesions in chest x - ray had CD4 count >200. 12.5% of patients with mid and lower zone lesions in chest x - ray had CD4 >200, 68.75% had CD4 count 50- 200 and 18.75% had CD4 count <50. 66.7% of patients with fibrocavitory lesions had CD4 count >200.
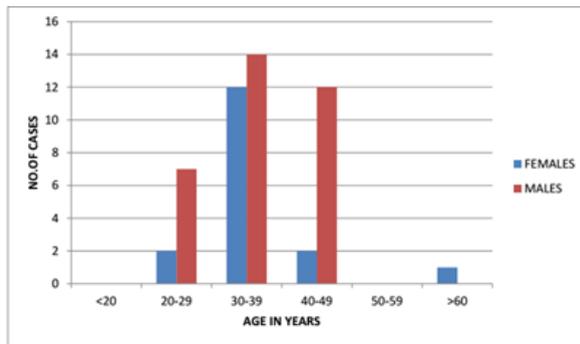

Figure 1.AGE AND SEX DISTRIBUTION
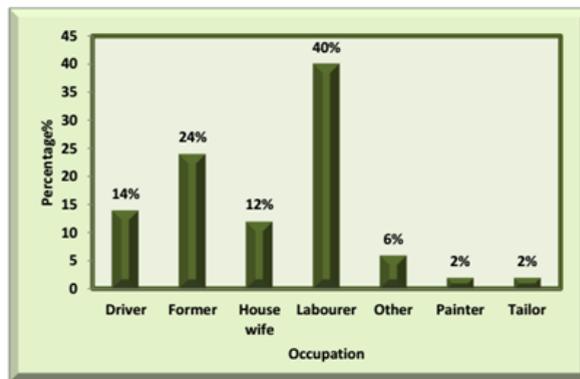
Figure 2.OCCUPATION

Table 1.CLINICAL MANIFESTATIONS OF TUBERCULOSIS

Type	patients	Percent(%)
EXTRAPULMONARY TB	14	28.0
PULMONARY TB	36	72.0
Total	50	100.0

Table 2.EXTRA PULMONARY TUBERCULOSIS FEATURES

Extra pulmonary features	patients	Percent (%)
Ascites	4	17.39%
Lymphadenopathy	4	17.39%
Pleural effusion	15	65.22%
Total	23	100.0%

Figure 3. Bar chart of clinical features: FEVER 82%, COUGH 82%, SOB 70%, WL 36%, CP 26%, NS 10%, CNS 10%, GIT 38% (Percentage% vs Symptoms).
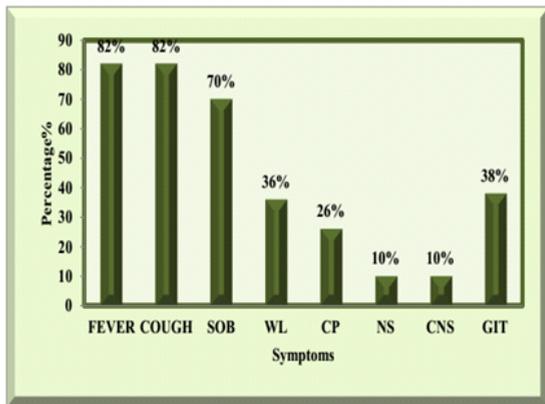
Figure 3.CLINICAL FEATURES

Table 3.CHEST X-RAY FINDINGS

CH X RAY	SPUTUM FOR AFB NEG	SPUTUM FOR AFB POS	Total
UZ INF	0	3	3
	0.0%	20.0%	6.0%
LZ, MZ INF	11	5	16
	31.42%	33.3%	32.0%
Normal	5	0	5
	14.28%	0.0%	10.0%
Pleural effusion	9	0	9
	25.71%	0.0%	18.0%
Miliary , B/L INF	10	4	14
	28.57%	26.7%	28.0%
Fibrocavitary	0	3	3
	0.0%	20.0%	6.0%
Total	36	15	50
	100.0%	100.0%	100.0%
Chi-square=64.03	P-value <0.01		HS

Table 4.CD4 COUNTS AND MANIFESTATIONS OF TUBERCULOSIS

CD4 COUNT	SPUTUM POSITIVE	SPUTUM NEGATIVE	EP	TOTAL
<50	1(6.66%)	6(28.57%)	2(14.28%)	9(18%)
51-200	5(33.33%)	13(61.90%)	10(71.42%)	28(56%)
>200	9(60%)	2(9.5%)	2(14.28%)	13(26%)
TOTAL	15(100%)	21(100%)	14(100%)	50(100%)
Chi-square value =14.18	P-value=0.05		S

Table 5.CD4 COUNTS AND CHEST XRAY FINDINGS

CD4 count	UZ INF	LZ, MZ INF	NORMAL	Pleural effusion	Miliary , B/L INF	Fibro cavitory	Total
<50	0	3	2	0	4	0	9
	0.0%	18.75%	40.0%	0.0%	28.6%	0.0%	18.0%
51-200	0	11	3	7	6	1	28
	0.0%	68.75%	60.0%	77.8%	42.9%	33.3%	56.0%
>200	3	2	0	2	4	2	13
	100.0%	12.5%	0.0%	22.2%	28.6%	66.7%	34.0%
Total	3	16	5	9	14	3	50
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%
Chi-square value =19.28	P-value=0.05						S

DISCUSSION

This study was carried out in the Department of Pulmonary Medicine, Siddhartha Medical College, Vijayawada over a period of one year i.e. March 2016 to February 2017.

In this study, out of 50 people studied 66% of patients were males and 34% females. This is comparable to study by jaryal etal in which 65.5% males and 34.5% females.[3] This is similar to study by zuber etal in which 58% males and 42% females.[4] Most of the people were in the age group 30-39 with mean age of males being 35.90 and the females 35.65.This is similar to the study done by Zuber et al. in which 78% of patients belong to 30 - 40 years and this age reflects the sexually active age group which is commonly affected by the disease.[4]

Most common occupation were unskilled labourers 40%, farmers 24%,drivers 14 %, housewife 12%, which indicates the co- infection affected people of low socioeconomic status. Zuber et al found a similar occupation profile.[4]

Most common constitutional symptom was fever(82%) and most common respiratory symptom was cough (82%). Symptoms were comparable with almost all of the studies. Cough is the main symptom in this study (82%) compared with Deivanayagam etal (85.43%), Sowmya etal (97%) and zuber etal (96%).[4-6] Fever is the second common presentation in this study 82% compared with Devanayagam et al 63.06%, Sowmya etal 79% and zuber etal 85%.[4-6] Lymphadenopathy is seen in 8% of patients and icterus is seen 2% of cases skin and mucous membrane lesions contribute 40% in this study.

Pulmonary tuberculosis ranked as the most common clinical manifestation.72% had pulmonary tuberculosis, extra pulmonary tuberculosis in 28%.Number of cases of pulmonary TB in this study is 72% comparable to Sowmya et al 72%, Deivanayagam et al 83.8% and in Zuber et al it is around 82.42%.[4-6] Lesser number of pulmonary TB may be due to low mean CD4 count 162.5±154.37 as compared to 192±173 in study by Sowmya et al [6] .In this study sputum positivity was seen in 30% of cases.In this study sputum positivity was found to be low compared with Sowmya e tal and Zuber etal studies [4,6]. In these two studies sputum culture was also done.But in other two studies Deivanayagam et al and Praveen Kumar et al only smear examination was done and are comparable to present study other reasons may be due low CD4 count and less number of cavitory lesions in this study.[5,7] In this study CBNAAT test was done among the sputum negative pulmonary TB cases, out of 21 sputum negative cases 14 cases are found to be positive, which shows that CBNAAT is useful investigation in detecting tuberculosis.

Among chest x - ray findings, upper zones lesions were found to be more in CD4 count >200 group while mid and lower zone lesions were common in CD4 counts less than 200 group which was found to be statistically significant. This is compared to study by Andrew Wood etal in which upper zone infiltrates typical of PTB reactivation was found with mean CD4 count of 389 and lower or middle zone infiltrates occurred over a wide intermediate range with mean CD4 counts of 185.[8]

Among the x - ray findings, infiltrative lesions were more common (84%) than the fibrocavitory lesions (6%). Among this infiltrative lesions 6% in the upper zone and 32% in mid and lower zone and bilateral infiltration and military mottling seen in 28% with extra pulmonary manifestations seen in 18%.It is evident that the radiological manifestations are mixed and varied in the present study. This is because the x - ray findings of tuberculosis in HIV infected will depend on the level of immune suppression and most of the patients in the present study had CD4 counts <200 cells/ µl and hence more number of atypical findings.

Among the extra pulmonary manifestations of pleural effusion was seen 15(30%) followed by lymphadenopathy 4(8%) and ascities 4 (8%)/Lymphadenopathy and pleural effusion are the most common manifestations among extra pulmonary tuberculosis similar findings are seen in other studies like Deivanayagam et al and Beena Susheel et al .[5,9]More number of extra pulmonary features in this study is due to the presence of more number of patients with CD4 count less than 200.As the study is done on patients who attended to department of pulmonary medicine, SMC,Vijayawada, the HIV patients with other extra pulmonary manifestations are less as they might have not referred to department of pulmonary medicine.

The mean CD4 count in the present study was 162.5±154.37cells/ µl.

The mean CD4 count among males were 182.52±180.59 cells/ µl and in females 123.77±73.04 cells/ µl. This difference is not significant. The mean CD4 count is similar to South Indian study by Sowmya et al is 192±172 cells / µl and study by Sharma SK et al from AIIMS reported mean CD4 count of 106±64 cells/ µl.[5,10]CD4 > 200 cells/µl is seen in 34% of patients while <200 cells/µl in 66% of patients. Similar study by Sharma SK etal33 from AIIMS reported CD4 <200 cells/µl in 82.6%.[10]

In the present study mean CD4 count in patients with sputum positive AFB was 280.73±201.44cell/ µl and in sputum negative PTB was 103.62±100.54 cells/µl.In EPTB, in Ascites it was 97.5±77.48,in pleural effusion138.27±111.52 and in lymphadenopathy 141.00±9.20. 90.5% sputum negative TB patients had CD4 count <200.

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