

STUDY OF CLINICAL, MICROBIOLOGICAL AND RADIOLOGICAL CORRELATION OF TB: HIV CO-INFECTIONG. Chakradhar Rao¹, G. K. Rajeswari², N. Kalyani³, J. Siva Kalyani⁴, M. V. Shekar Reddy⁵, K. Vasudha⁶**HOW TO CITE THIS ARTICLE:**

G. Chakradhar Rao, G. K. Rajeswari, N. Kalyani, J. Siva Kalyani M. V. Sekhar Reddy, K. Vasudha. "Study of Clinical, Micro-biological and Radiological Correlation of TB: HIV Co-Infection". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 06, January 19; Page: 905-913, DOI: 10.14260/jemds/2015/130

ABSTRACT: BACKGROUND: Tuberculosis, a major public health problem in most of the developing countries is posing a still bigger threat with the epidemic of HIV and association has been termed as "cursed duet". There is significant difference in the clinical profile of tuberculosis in HIV infected compared to immunocompetent host. So prompt diagnosis and treatment of tuberculosis in HIV infected will improve the morbidity and mortality associated with dual infection. So the objective of the study was to determine the clinical profile of TB in HIV infected in relation to CD4 counts. **MATERIALS AND METHODS:** Hundred patients with HIV infection and having symptoms of tuberculosis admitted in the medical wards in Government General Hospital, Guntur were studied. Diagnosis of tuberculosis was based on clinical evaluation, sputum smears, bacteriological and biochemical examination of body fluids, histopathological studies and radiological studies. CD4 T cell counts were done in all patients. **RESULTS:** 51% had only pulmonary tuberculosis, 43% had only extrapulmonary involvement while 6% had disseminated disease. Sputum positivity was seen in 27.45% of pulmonary tuberculosis. Chest X-ray findings were mixed and varied with infiltrative lesions seen in 83.33% and fibrocavitary lesions in 11.11%. 55.55% of infiltrative lesions were seen in mid and lower zones. Mean CD4 counts in this study was 133.78 ± 75 cells/ μ L. Most of the patients with extra pulmonary TB and disseminated TB had CD < 200 cells/ μ L. Sputum positivity and upper zone lesions in chest X-ray were seen more in patients with CD4 > 200 cells/ μ L. **CONCLUSION:** Tuberculosis has a varied clinical presentation in patients with HIV infection. Sputum negative TB, extrapulmonary TB and disseminated TB were common when CD4 < 200 cells/ μ L and chest X-ray findings were atypical when CD4 < 200 cells/ μ L.

KEYWORDS: Pulmonary Tuberculosis; HIV infection; Clinical profile of tuberculosis.

INTRODUCTION: The HIV epidemic has increased the burden of tuberculosis (TB) among young adults, especially in populations where the prevalence of TB infection is high. Infection with HIV is the most potent risk factor for progression to active tuberculosis. Individuals who are infested with *Mycobacterium tuberculosis* have an approximately 10% lifetime risk of developing active tuberculosis, compared with 60% or more in persons infected with HIV and TB. Tuberculosis is the commonest opportunistic infection in HIV/AIDS patients with an attack rate of 7 per 100 person - years. However, HIV infection also greatly increases the risk of developing TB following fresh infection, and the actual proportion of each type in India needs further study.

It is estimated that there are about 14 million cases of tuberculosis in India, about 2 million new cases occur annually, and we are home to 1/4th the world's TB prevalence. The situation is likely to get worse as the prevalence of HIV in the community increases. Therefore, it is important to understand the effect of TB and HIV on each other and take adequate measures to control this dual epidemic.

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The increased morbidity and mortality associated with HIV-TB co-infection makes it essential that there be a clear understanding of the clinical profile tuberculosis in HIV positive patients for the allocation of health care and research resources and for other purposes. Though the data regarding the HIV-TB co-infection from this part of the country is not scanty, change in the trends of its clinical profile makes it essential to further continue study regarding this topic.

This study was conducted in a large teaching hospital with a medical college attached with ART centre and district tuberculosis centre and located in the heart of Andhra Pradesh, thereby attracting representative population from all areas and especially the lower strata of society. Results of this study are therefore relevant to the general public in this part of the country. By studying the clinical profile of HIV-TB co-infection, this study aims to create awareness regarding the infection, so that by effective interventions, this menace could be tackled effectively.

OBJECTIVES:

1. To study the clinical profile of tuberculosis in HIV infected patients.
2. To compare the different clinical and laboratory data with their CD4 counts.

MATERIALS AND METHODS:

SOURCE OF DATA: HIV positive patients admitted in the medical wards in Government General Hospital, Guntur over a period of one year, from June 2013 to May 2014, were taken up. They were considered for evaluation of Mycobacterium Tuberculosis infection on the basis of history of prolonged fever, marked weight loss, cough more than three weeks not responding to antibiotics, and symptoms related to specific organ systems.

METHOD OF COLLECTION OF DATA:

- Sample Size: 100 HIV positive meeting the criteria for the present study.
- Sampling Method: Simple random sampling.

INCLUSION CRITERIA: HIV positive patients (as per WHO criteria) irrespective of their antiretroviral treatment status with consistent clinical features of tuberculosis and

- a. Positive AFB smears or.
- b. Chest X-ray findings (physician opinion) or.
- c. Biochemical analysis and/or positive culture of body fluids suggestive of TB or.
- d. Suggestive histopathology/demonstration of bacilli in clinical specimens or.
- e. Imaging studies suggestive of tuberculosis.

EXCLUSION CRITERIA:

1. Suspected cases of TB who retained ambiguity despite above investigations were excluded.
2. Patients below 12 years.
3. Patients with history of treated or untreated tuberculosis were excluded.

INVESTIGATIONS:

1. Routine baseline investigations like complete hemogram, ESR, LFT/RFT.
2. Sputum-AFB for three samples.

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3. Chest X-ray – P/A view.
4. Biochemical and bacteriological examinations of body fluids in clinically relevant conditions.
5. FNAC/biopsy of accessible peripheral lymphnodes examined by histopathology and Ziehl-Neelson stain.
6. Other investigations like USS abdomen, CT head/CT abdomen/whenever appropriate.
7. CD4 counts by flow cytometry by standard technique using Becton-Dickinson FAC scan.
8. Following statistical methods were applied in the present study:
 - Cross tabs procedure (Contingency coefficient test).
 - Descriptive statistics.
 - Frequencies and percentages.
 - ANOVA-Analysis of variance-two way.

[All the statistical operations were done through SPSS for Windows, SPSS Inc., New York.]

RESULTS:

Age group (in years)	Male		Female		Total	
	No.	%	No.	%	No.	%
< 21	2	2.6	1	4.2	3	3
21-29	23	30.3	10	41.7	33	33
30-39	34	44.7	12	50	46	46
40-49	12	15.8	1	4.2	13	13
50-59	4	5.3	0	0	4	4
60+	1	1.3	0	0	1	1
Total	76	100	24	100	100	100

Table 1: Age and Gender distribution

In this study, 100 HIV patients with Tuberculosis were studied of this 76 were males and 24 were females.

In the present study male: female ratio is 3.5:1. Other studies have also shown the male predominance among HIV infected population. George et al reported male: female ratio of 5:1 in their study of AIDS patients in south India, whereas Cohen et al reported a ratio of 9:1 in their study.^{1,2} Varma T has also reported a male: female ratio of 4:1 in his study of 100 HIV positive patients.³

The age of study subjects ranged from 19-62. The mean age was 33.66 ± 8.46 (34.95 ± 8.77 for males and 29.58 ± 5.86 for females). Most of the people were in the 30-39 age groups. This is comparable to the study done by Deivanayagam CN et al.⁴ in which 74.94% of patients belonged to 21-40 years and National Statistics reported to NACO,⁵ shows 89% of cases were in the age group of 15-44 years. This age reflects the sexually active age group which is commonly affected by the disease.

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System	Symptoms	Number of Patients	Percentage
Constitutional	Fever	78	78
	Weight loss	56	56
	Fatigue/lethargy	50	50
Respiratory	Cough	75	75
	Haemoptysis	10	10
	Breathlessness	62	62
	Chest pain	20	20
Gastrointestinal	Diarrhoea	50	50
	Anorexia	32	32
	Nausea/Vomiting	34	34
	Abdominal distension	10	10
	Jaundice	6	6
Nervous system	Headache	6	6
	Seizures	6	6
	Focal Deficits	2	2
	Altered sensorium	5	5
	Memory loss	0	0
Dermatological	Skin lesions	12	12
	Mucous membrane lesions	8	8

Table 2: Presenting symptoms

- a. Common constitutional symptoms reported were fever (78%), weight loss (56%) and fatigue (60%).
- b. Common respiratory symptom reported were cough (75%), breathlessness (62%) and Chest pain (20%).
- c. Common gastrointestinal symptoms reported were Diarrhoea (50%), anorexia (32%), abdominal distension (10%) and jaundice (6%).
- d. Commonest neurological symptoms were headache (6%), seizures (6%) and focal deficits (2%).
- e. Among dermatological symptoms skin lesions were reported in 12% and oral/genital ulcers in 8%.

In the series reported by Mohanty et al.⁶ fever was the most common complaint, while Deivanayagam et al.⁷ reported cough with expectoration in majority of their patients. In a case series done by Anand K Patel et al, the most common symptom was cough in 47 (94%) patients, while fever was present in 43 (86%) and weight loss in 39 (78%) patients.

Physical finding	Number of Patients	Percentage
BMI < 18.5 kg/m ²	56	56
Pallor	56	56
Icterus	6	6

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Lymphadenopathy	33	33
Oral candidiasis	34	34
Skin lesions	12	12
Mucous membrane lesions (Oral/genital ulcers)	8	8

Table 3: Physical findings

Physical examination revealed that, BMI<18.5 in 56%, pallor in 56%, Icterus in 6%, Lymphadenopathy in 33%, Oral candidiasis in 34%, hyper pigmented macular skin rashes in 12% and oral/genital ulcers in 8%.

Type	Number of Patients	Percentage
Only pulmonary tuberculosis	51	51
Only extra pulmonary tuberculosis	43	43
Disseminated tuberculosis	6	6

Table 4: Clinical manifestations of tuberculosis

- a. Among the patients studied only pulmonary TB was seen in 51(51%) and only extra pulmonary TB in 43 (43%) and Disseminated TB in 6(%)
- b. Out of 54 patients with X-ray evidence of TB, 14 (27.45%) had sputum positive while 40 (78.43) were sputum negative.

Lesion	Upper Zone	Middle Zone	All Zones
Infiltrative	15 (27.77%)	30 (55.55%)	-
Fibro cavitary	2 (3.7%)	4 (7.4%)	-
Miliary mottling	-	-	3 (5.66%)

Table 5: Chest X-ray findings

Out of 54 patients with abnormal X-rays, upper zone infiltrative lesions were seen in 15 (27.77%), upper zone fibrocavitary lesions seen in 2 (3.7%), mid zone/Lower zone infiltrative lesions seen in 30 (55.55%), mid/lower zone, fibro cavitary lesions seen in 4 (7.4%), miliary mottling involving all zones was seen in 3 (5.66%).

CD4 count	Number of Patients	Percentage
>200	29	29
50-200	48	48
<50	23	23

Table 6: CD4 counts and number of patients

CD4 > 200 cells/micro l is seen in 29% of patients while < 200 in 71% of patients. Similar study by Sharma SK et al. from AIIMS reported CD4 < 200 cells/ micro l in 82.6%.⁸

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In the present study mean CD4 count in patients with sputum positive PTB was 226.71 cells / micro l and in sputum negative PTB was 108.49 cells / micro l, in EPTB was 138.02 cells / micro l. and in dis TB is 42.5. cells/micro l. This difference is found to be statistically significant with a p-value <000 and hence it shows disseminated TB, sputum negative TB and EPTB occurs more frequently with lower CD4 counts.

	N	Mean	Sd.deviation	Sd. Error
-ve PTB	37	108.49	74.684	12.278
+ve PTB	14	226.71	52.895	14.137
EPTB	43	138.02	58.386	8.604
Total	100	133.78	76.263	7.626

Table 7: Mean CD4 count and different manifestations of tuberculosis

F=16.432; P<.000 (HS).

Mean CD4 count in patients with sputum +ve TB was 226.71 ± 52.895 and in sputum negative TB was 108.49±74.684.

Mean CD4 count among EPTB was 138 ± 52.895 and in disseminated TB was 42.50 ± 4.416. Mean CD4 count was found to be significantly high in patients with sputum +ve TB (P<.000). Mean CD4 count was found to be significantly low in disseminated TB, EPTB and sputum negative TB.

CD4 Count	-ve PTB	+ve PTB	Disseminated	EPTB	Total
<50 count	18 48.6%	0 0%	6 100.0%	5 11.6%	29 29.0%
50-200 Count	12 32.4%	2 14.3%	0 0%	34 79.1%	48 48.0%
>200 count	7 18.9%	12 85.7%	0 0%	4 9.3%	23 23.0%
Total	37 100.0%	14 100.0%	6 100.0%	43 100%	100 100.0%

Table 8: CD4 ranges and clinical manifestations of TB

81% of the sputum negative TB, 90.7% of extra pulmonary TB had CD4< 200, and 100% of military TB had CD4 < 50.

85.7% of the sputum positive pulmonary TB had CD4 > 200 which is found to be highly significant.

CD4 Count	Lesions			Total
	Infiltrative	Fibrotic	Cavity	
<50 count	18 40.0%	0 0%	0 0%	18 35.0%
50-200 Count	12 26.7%	0 0%	2 40%	14 27.5%

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>200 count	15 33.3%	1 100.0%	3 60%	19 37.3%
Total	45 100.0%	1 100.0%	5 100.0%	51 100.0%

Table 9: CD4 counts and X-ray lesions

CC – 0.296; p < 0.297.

Infiltrative lesions were the most common X-ray finding and was seen in 40% in <50 CD4 count group, 26.7% in 50-200 group and 33.3% in >200 group.

Fibrocavitary lesions were seen in 40% of patients with CD4 counts in the range of 50-200 and 60% patients with CD4 >200. This finding was found to be not statistically significant with P<.297.

CD4 Count	Zone		Total
	Upper	Mid/lower zone	
<50 count	0 0%	18 52.9%	18 35.3%
50-200 Count	0 0%	14 41.2%	14 27.5%
>200 count	17 100.0%	2 5.90%	19 37.3%
Total	17 100.0%	34 100.0%	51 100.0%

Table 10: CD4 counts and X-ray zones

C.C-.676 P<.000.

All patients (100%) with upper zone lesions in chest X-ray had CD4 counts >200.

52.9% of patients with mid/lower zone lesions CXR had CD4 < 50, 41.2% of patients had CD4 50-200 and 5.9% had CD4>200.

Upper zone lesions were more in patients with CD4 counts >200 which is found to statistically significant with P value <.000

CD4 Count	Zone		Total
	Upper	Mid/lower zone	
-ve PTB	6 36.3%	31 90.12%	37 72.5%
+ve PTB	11 64.7%	3 3.3%	14 27.5%
Total	17 100.0%	34 100.0%	51 100.0%

Table 11: Sputum positivity and X-ray zones

CC =.508; p < 0.000 (Highly significant)

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64.7% of patients with upper zone lesions had sputum positive TB and 35.3% had sputum negative TB. 90.12% of patients with mid/lower zone lesions had sputum negative TB. This is found to be statistically significant ($p < 0.000$).

CONCLUSION:

- In this study, most common manifestation of TB in HIV infected was pulmonary TB with more number of sputum negative TB.
- A high proportion of extrapulmonary TB was also found.
- CD4 counts correlated well with the clinical profile of TB, which showed that when CD4 counts were less than 200 cells/ μ l, sputum negative pulmonary TB and extra pulmonary TB were more. Chest X-rays were atypical in the form of lower zone involvement and more of infiltrative lesions.
- So a high level of clinical suspicion is required in diagnosis of TB in HIV infected, especially when they are in the later stages of disease, which is indicated by CD4 counts < 200 cells/ μ l.

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