Comparative Study of Radiological Features of Pulmonary Tuberculosis in HIV Infected Patients in Correlation with CD4 Counts

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ABSTRACT
Tuberculosis, an ancient disease, and a major public health problem which is now complicated by relentless spread of HIV & AIDS pandemic and the emergence of multi drug resistant strains.HIV and TB, each disease speeds up the progress of the other. The study was conducted to compare various radiographic presentation of pulmonary tuberculosis in HIV positive patients with CD4 count more than 200 / µL and CD4 count < 200 / µL. 100 HIV positive patients with pulmonary tuberculosis of 20 – 70 years of age (mean age 39.53 ± 10.82) were selected for the study. Their mode of X-ray presentation and CD4 cell counts were studied. X-rays were reported by Radiologist and statistical comparison were analysed using Z test and χ2 test. CD4 count of 35 cases were more than 200 / µL and 65 cases were less than 200 / µL. It was observed that patients with CD4 count > 200 /µL shows higher incidence of upper zone distribution of alveolar, higher incidence of cavity and higher incidence of fibrosis as compared to patients with CD4 count < 200 /µL. Multiple cavities are more often found in patients with CD4 count >200/ µL. Patients with CD4 count < 200 / µL shows higher incidence of mid and lower zone infiltrate, higher incidence of pleural effusion, higher incidence of adenopathy and higher incidence of miliary mottling as compared to patients with CD4 count > 200 / µL.
Keywords: *Tuberculosis, HIV, CD4, Cavity, Fibrosis, Infiltrates, Pleural effusion, Miliary mottling, Adenopathy.*

INTRODUCTION

The AIMS AND OBJECTIVES is 1.To compare the characteristic radiological presentation of Pulmonary TB in HIV positive patients in relation to degree of immunosuppression (CD4 count). 2. To determine the percentage of patients with atypical Chest X-ray in HIV positive individuals in correlation with CD4 counts. 3. To determine the relationship between atypical Chest X-ray and CD4 counts.

MATERIALS AND METHODS

The study was conducted in Siddhartha Medical College and Government General Hospital, Vijayawada, Andhra Pradesh during the period December, 2013 to October, 2015.

Inclusion criteria

1. All subjects had to be confirmed HIV
2. All subjects had to be confirmed pulmonary tuberculosis(X-ray, smear or both)
3. Age group between 20-70 years.

Exclusion Criteria

1. Age more than 70 years and less than 20 yrs.
2. Patient who received anti tuberculosis treatment before presentation.

Sputum AFB

Two separate first morning deep cough specimen of sputum was collected in a sterile disposable bottle and immediately sent to hospital laboratory for AFB staining. If the patient had non-productive cough, sputum was induced using hypertonic saline via-air powered nebulizer. Sputum specimen was stained with Zeil Neelsen's method for microscopy.

Chest Radiograph

At the time of admission, before starting anti tuberculous drug, chest X-ray PA (Postero-anterior) view were taken in all patients. Chest X-ray is divided by conventional method into three zones upper, mid and lower zones.

Upper Zone: Area of lung above the lower border of the second rib anteriorly

Mid Zone: Area of lung between the lower border of second rib and lower border of fourth rib anteriorly.

Lower Zone: Rest of the lung below the mid zone.

The radiograph of each case were evaluated for

a) Pulmonary infiltrates

b) Pulmonary cavity

c) Pleural effusion

d) Hilar adenopathy

e) Pulmonary fibrosis

f) Pericardial effusion

g) Pneumothorax

h) Volume loss

i) Bronchiectasis

j) Miliary mottling

Blood investigation

1. Complete haemogram
2. Erythrocyte sedimentation rate
3. Blood sugar

4. All patients with pleural effusion were subjected to pleural aspiration and analysis of pleural fluid.
5. HIV status by enzyme linked immunos-orbant assay.
6. CD4 T-cell count.

RESULTS

100 subjects participated in the study, of whom 60 were males and 40 were females.

1. The age of patients is between 20 – 70. Means age 39.53 ± 10.82

All the subjects were of low socio-economic class. Only 30 (30%) had smear positive tuberculosis, while the remaining 70 (70%) had smear negative tuberculosis.

By stratification of CD4 T lymphocyte count, 35 cases (35%) had CD4 count > 200 cells / µL and 65 cases (65%) had CD4 count < 200 cells/ µL

Age Vs CD4 T Cell count

Age	CD4>200 (n=35)	CD4 < 200 (n=65)	Total	Test Applied
20 – 30	4 (11%)	13(20%)	17	
30 – 40	12 (34%)	28(43%)	40	
40 – 50	10 (29%)	13(20%)	23	
50 – 60	5 (14%)	10(15%)	15	$\chi^2 = 6.618$
60 – 70	4 (11%)	1(2%)	05	$p = 0.157$

2.

Sex Vs CD4 T Cell count

Sex	CD4>200 (n=35)	CD4<200 (n=65)	Total	Test Applied
Male	21 (60%)	39 (60%)	60	$\chi^2 = 0.00$ $p = 1.00$
Female	14 (40%)	26 (40%)	40	$Z = 0.0$ $p = 1.00$

3. **Radiological findings in Individuals with CD4 count > 200 cells / µL**

(This group had radiological findings in the following frequency)

a) 31 cases (89%) had pulmonary infiltrates

b) 12 cases (34%) had pulmonary cavity

c) 3 cases (9%) had pleural effusion

d) 10 cases (29%) had adenopathy

e) 3 cases (9%) had fibrosis

f) 3 cases (9%) had Bronchiectasis and

g) No miliary mottling

**Radiological findings in Individuals with CD4 count < 200 cells / µL**

(This group had radiological findings in the following frequency)

a) 55 cases (85%) had pulmonary infiltrate

b) 8 cases (12%) had pulmonary cavity

c) 11 cases (17%) had pleural effusion

d) 35 cases (54%) had adenopathy

e) 1 case (2%) had fibrosis

f) 3 cases (5%) had miliary mottling and

g) 1 case (2%) had Bronchiectasis
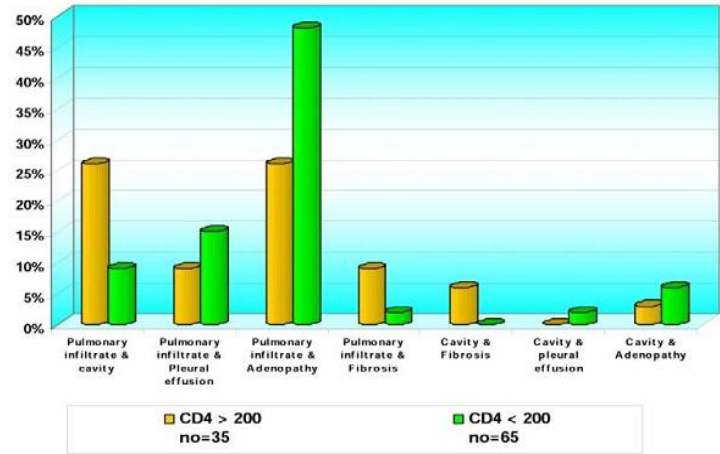
Frequency of Radiographic Features

Radiographic Feature	CD4 > 200		CD4 < 200		Test applied	Significance
	No (n=35)	%	No (n=65)	%		
Pulmonary infiltrates	31	89%	55	85%	x^2 = 0.296, p=0.587 Z = 0.57, p = 0.572	NS
Cavity	12	34%	8	12%	x^2 = 6.86, p=0.009 Z = 2.44, p = 0.015	HS
Pleural effusion	3	9%	11	17%	x^2 = 2.127, p=0.145 Z = 1.26, P = 0.208	NS
Adenopathy	10	29%	35	54%	x^2 = 5.872, p=0.015 Z = 2.57, p = 0.010	HS
Fibrosis	3	9%	1	2%	x^2 = 2.93, p=0.087 Z = 1.41, p = 0.157	NS
Miliary mottling	0	-	3	5%	x^2 = 1.665, p=0.197 Z = 1.77, p = 0.07	NS
Bronchiectasis	3	9%	1	2%	x^2 = 2.93, p=0.087 Z = 1.41, p = 0.157	NS
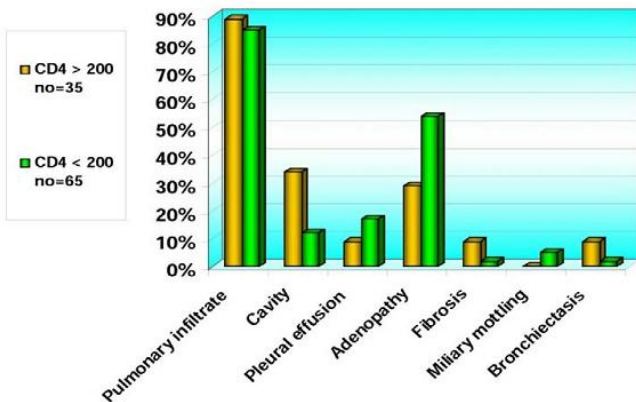
Combination of Radiographic Features

Radiographic Feature	CD4 >200		CD4 <200		Test Applied	Significance
	No (n=35)	%	No (n=65)	%		
Pulmonary infiltrates & cavity	9	26%	6	95%	x^2 = 4.848, p=0.028 Z = 2.01, p= 0.045	NS
Pulmonary infiltrates & Pleural effusion	3	9%	10	15%	x^2 = 0.934, p=0.334 Z = 1.05, p= 0.296	HS
Pulmonary infiltrates & Adenopathy	9	26%	31	48%	x^2 = 4.579, p=0.032 Z = 2.28, p = 0.023	NS
Pulmonary infiltrates & Fibrosis	3	95	1	2%	x^2 = 2.93, p=0.087 Z = 1.41, p= 0.157	NS
Cavity &Fibrosis	2	6%	0	0%	x^2 = 3.79, p> 0.05 Z = 1.46, p= 0.145	NS
Cavity &Pleural effusion	0	0%	1	2%	x^2 = 0.544, p> 0.05 Z = 1.01, p= 0.314	NS
Cavity &Adenopathy	1	3%	4	6%	x^2 = 0.521, p=0.471 Z = 0.80, p= 0.427	NS

3A) *Pulmonary infiltrate and CD4 count*

In the CD4 count > 200 cells / µL group

12 cases (34%) had predominant upper zone infiltrates

7 cases (20%) had predominant middle zone infiltrates

12 cases (34 %) had infiltrates in multiple zones No case of lower zone infiltrates

In the CD4 count < 200 / µL group

8 cases (12%) had predominant upper zone infiltrates

16 cases (25%) had predominant middle zone infiltrates and

13 cases (20%) had predominant lower zone infiltrates

18 cases(28 %) had infiltrates in multiple zones

TB- PULMONARY INFILTRATES

PULMONARY INFILTRATE vs ZONE

Zones	CD4 >200 No (n=35)	%	CD4 <200 No (n=65)	%	Test applied	Significance
Upper	12	34%	8	12%	x^2 = 6.868, p=0.009 Z = 2.44, p = 0.015	HS
Middle	7	20%	16	25%	x^2 = 0.274, p=0.601 Z = 0.54, p = 0.592	NS
Lower	0	0%	13	20%	x^2 = 8.046, p=0.005 Z = 4.03, p = 0.000	HS
Multiple	12	34%	18	28%	x^2 = 0.471, p=0.493 Z = 0.68, p = 0.499	NS

3B) *Cavity Vs CD4 Count*

In the CD4 count > 200 / µL group

4 cases (11%) had a single cavity

8 cases (23%) had multiple cavity and

2 out of total 12 cases (6%) had air fluid cavity

In the CD4 count < 200 group

7 cases (11%) had single cavity

1 case (2%) had multiple cavity and

1 out 8 cases (2%) had air fluid cavity

TB CAVITY

CAVITY vs CD4 count

Cavity	CD4>200 No (n=35)	%	CD4<200 No (n=65)	%	Test applied	significance
Total Cavity	12	34%	8	12%	x^2 = 6.868, p=0.009 Z = 2.44, p = 0.015	HS
Single	4	11%	7	11%	x^2 = 0.010, p=0.920 Z = 0.10, p = 0.921	NS
Multiple	8	23%	1	2%	x^2 = 2.481, p=0.115 Z = 1.91, p = 0.056	NS
Air fluid Cavity	2	6%	1	2%	x^2 = 1.363, p=2.43 Z = 0.99, p= 0.321	NS

Cavity Vs Zone

In the CD4 count > 200 / µL group

10 cases (29%) had predominant upper zone cavity

5 cases (14%) had predominant middle zone cavity and

4 cases (11%) had predominant lower zone cavity

In the CD4 count < 200 / µL group

2 cases (3%) had predominant upper zone cavity

5 cases (8%) had predominant middle zone cavity and

2 cases (3%) had predominant lower zone cavity.

CAVITY vs ZONE

Zone	CD4>200 No (n=35)	%	CD<200 No (n=65)	%	Test applied	Significance
Upper	10	29%	2	3%	x^2 = 2.748, p=0.249	NS
Middle	5	14%	5	8%		
Lower	4	11%	2	3%		
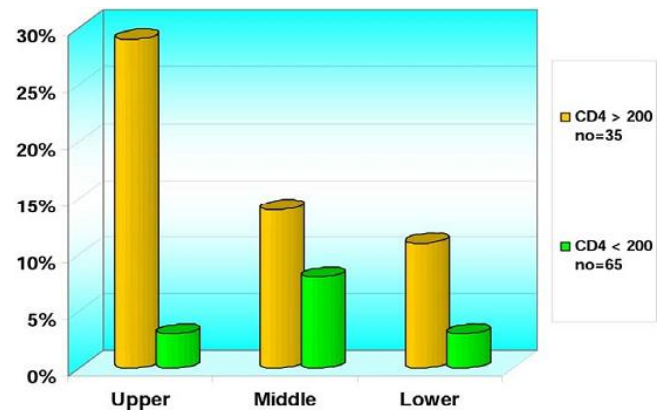
3C) *Pleural effusion Vs CD4 count*

In the CD4 count > 200 / µL group

3 cases (9%) had pleural effusion

All cases are associated with ipsilateral pulmonary infiltrates.

In the CD4 count < 200 / µL group

11 cases (17%) had pleural effusion. Out of the 11, 10 cases (15%) associated with ipsilateral infiltrates

1 case (2%) of pleural effusion had no pulmonary infiltrates.

TB – PLEURAL EFFUSSION

TB- B/L HILAR LYMPHADENOPATHY

PLEURAL EFFUSSION vs CD4 count

Radiograp hic Feature	CD4>200		CD4<200		Test applied	Significi cance
	No (n=35)	%	No (n=65)	%		
Pleural effusion	3	9%	11	17%	x^2 = 1.318, p=0.251 Z = 1.26, p = 0.208	NS
PE with ipsilateral Pulmonary infiltrates	3	9%	10	15%	x^2 = 0.934, p=0.314 Z = 1.05, p = 0.296	NS
PE with out Pulmonary infiltrates	0	0%	1	2%	x^2 = 0.544, p=> 0.05 Z = 1.01, p = 0.314	NS
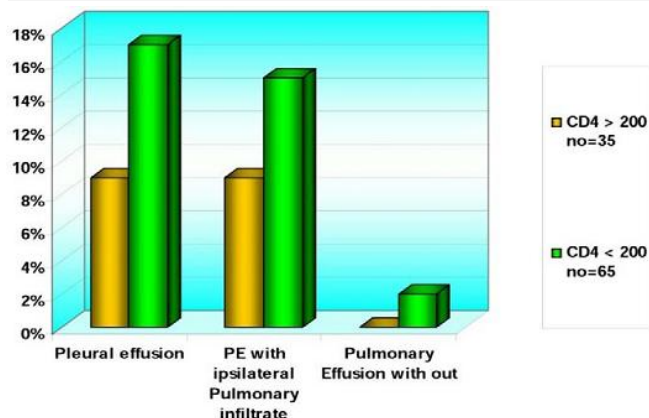
3D) *Adenopathy Vs CD4 Count*

In the CD4 count > 200 / µl group

10 cases (29%) had adenopathy

Out of that, 4 cases (11%) had unilateral hilar adenoapthy and 6 cases (17%) had bilateral hilar adenopathy

In the CD4 count < 200 / µL group

35 cases (54%) had adenopathy.Out of that, 10 cases (15%) had unilateral hilar adenopathy and 25 cases (38%) had bilateral hilar adenopathy.

ADENOPATHY vs CD4 count

Radiographic Feature	CD4 > 200		CD4 < 200		Test applied	Significance
	No n=35	%	No n=65	%		
Total case of Adenopathy	10	29%	35	54%	x^2 = 5.872, p=0.015 Z = 2.57, p= 0.010	HS
U/L Hilar Adenoapthy	4	11%	10	15%	x^2 = 0.296, p=0.587 Z = 0.57, p = 0.572	NS
B/L Hilar adenopathy	6	17%	25	38%	x^2 = 4.834, p= 0.028 Z = 2.43, p = 0.015	HS

3E) *Fibrosis Vs CD4 count*

In the CD4 count > 200 / µL group,3 cases (9%) had fibrosis

In the CD4 count < 200 / µL group**,**1 case (2%) had fibrosis

3F) *Bronchiectasis Vs CD4 count*

In the CD4 count > 200 / µL group, 2 cases (6%) had Bronchiectasis

and in the CD4 < 200 / µL group,no case of Bronchiectasis found

3G) *Miliary Mottling Vs CD4 count*

In the CD4 count > 200 / µL group,no case of military mottling

And In the CD4 < 200 / µL group,3 cases (5%) had military mottling

MILIARY TB

3H) *FIBROSIS vs CD4count*

Radiographic Feature	CD4 > 200		CD4 < 200		Test applied	Significance
	No n=35	%	No n=65	%		
Total case of Fibrosis	3	9%	1	2%	$\chi^2 = 2.93$, p=0.087 Z = 1.41, p= 0.157	NS
Miliary Mottling	0	0%	3	5%	$\chi^2 = 1.665$, p=0.197 Z = 1.77, p= 0.07	NS
Bronchiectasis	2	6%	0	0%	$\chi^2 = 3.790$, p > 0.05 Z = 1.46, p= 0.145	NS
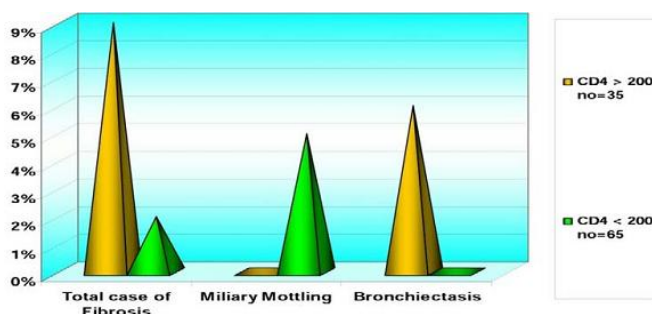
DISCUSSION

100 HIV positive patients with pulmonary tuberculosis were taken up for analysis. Out of which, CD4 count of 35 patients was > 200 and rest 65 patients had CD4 count < 200 /μL. **Frequency of Radiographic Features**

In the present study, statistically significant radiological findings were observed in patients with CD4 count > 200 / μL as compared to patients with CD4 count < 200 / μL.

1. Pulmonary infiltrate:

In the present study, patients with preserved immunity (CD4count > 200 / μL) showed significantly higher incidence of upper zone distribution of alveolar infiltrates as compared to patients with CD4count < 200(34% Vs 12%, P = 0.009). Patients with CD4 count < 200 / μL, showed a significantly higher incidence of mid and lower zone infiltrates as compared to patients with CD4 count > 200. (25% Vs 20%, P = 0.601, 20% Vs 0%, P = 0.005)

Maj Debnath and Colleagues reported significantly higher incidence of upper zone infiltrates in HIV positive group with preserved immunity.

Batung Wanayo et al reported higher incidence of mid and lower zone infiltrate in HIV positive patients with less CD4 count as compared to HIV positive patients with preserved immunity. Similar observation was made by Perlman DC et al and Abouya L et al.

2. Pulmonary Cavity

Patients with preserved immunity (CD4 count > 200) showed higher incidence of cavity as compared to patients with CD4 count < 200 / μL (34% Vs 12%, P=0.009). E. Tshibwabava – Tumba et al reported low incidence of cavitation in HIV positive cases with low immunity. Maj Debnath et al also reported similar observation(85.2% Vs 53.3%, p=0.10). In patients with preserved immunity, cavities are multiple as compared to patients with low immunity. (23% Vs 2%, P = 0.115) .In the initial stages of HIV infection, the form of pulmonary tuberculosis presented was similar to that seen in the patient without HIV, with typical pattern of cavitation. However when CD4 counts begins to drop, the cavitation ceases to occur. *With CD4 count between 200–500, the most frequent pattern of pulmonary TB is cavitation, that becoming less so when these counts drops below 200 cells / μL.* In another study conducted by Perlman Dc, El-

Sadr WM,Nelson ET, Matts JP, Telzak EE, Salomon N et al found cavitation was the most common finding in chest X-ray of patients where CD4 T cell counts were equal to or greater than 200 and was considerably more common among such patients than among those presenting with counts below this value (20% Vs 7%) .

Another study conducted by Keiper MD, Beumont M, Elshami A, Langlots CP, Miller WT found lower values of cavitation (28.9%) in patients with CD4 count < 200 and 53% in those with CD4 count > 200..Similar findings were reported by Jones BE et al(22% Vs7%,p=0.08) and Abouya et al (63.9% Vs 30.9%, p=0.01).This indicates that in areas of high TB prevalence, HIV positive patients develop the disease in a phase in which their cellular immunity is relatively intact (prior to developing AIDS) and therefore present with cavitation. This hypothesis is consistent with experimental data that indicate that cavity formation requires a strong lymphocyte reactivity to the mycobacterium tuberculosis antigen.

3. Pleural Effusion

In the present study, higher incidence of pleural effusion was found in patients with CD4 count < 200 as compared to patients with CD4 count >200cells/µL. (17% Vs 9%, p = 0.251).

Debanath et al reported significantly higher incidence of pleural effusion (28% Vs 10%, p < 0.01) and adenopathy (36% Vs 8%, p < 0.001) in HIV patient with CD4 count < 200 as compared to patients with CD4 count > 200. Kawooya VK, Kawooya M, Okwera A97 compared the occurrence of pleural effusion with degree of immunosuppression.

They observed that 36.8% of patients with pleural effusion had normal or moderate immune status where as 63.2% of patients with pleural effusion had high degree of immuno suppression. Similar results were obtained by Perlman DC et al (22% Vs12.9%,p=0.1)

4. Adenopathy

In the present study we found that adenopathy in chest X-ray is more common in group with ≤ 200 CD4 cells as compared with > 200 CD4 cell group (54% Vs 29%, p = 0.015).Similar observation was reported by Jones BE and colleagues ,they found HIV infected pulmonary tuberculosis with adenoapthy had lower CD4 cell count than those without adenopathy (34% Vs 14%, p = 0.04). Keiper MD, Beumont M, Elshami A, Langlots CP94, found that intrathoracic lymphnode enlargement is more common in patients with AIDS

than in HIV positive without AIDS as well as being more common in HIV positive with CD4 < 200 than in patients with CD4 > 200 (30% Vs 7%,p=0.01).

Higher prevalence of lymph node enlargement in HIV positive patient with lower CD4 have also been found in other studies. Therefore intrathoracic lymph node enlargement in adult with pulmonary TB strongly suggests the presence of severe immunosuppression. Often lymphadenopathy is the dominant or only finding in severely immunosuppressed patients. Jasmer et al found HIV infected patients with necrotic lymphadenopathy were 26 times more likely to have mycobacterial infection than HIV infected patients without necrotic lymphadenopathy.

5. Pulmonary fibrosis

There was low incidence of fibrosis in chest X-ray in patients with ≤ 200 CD4 count compared to patient with high CD4 count (2% Vs 9%, p=0.087). Debnath et al reported less incidence of fibrosis in patients with CD4 count < 200 as compared to patients with CD4 > 200. This finding suggests that the ability to form fibrotic scar is directly related to CD4 cell count. i.e., the level of cell mediated immunity.

6. Miliary Mottling

In our study we found that miliary pattern on chest X-ray has been reported to occur more frequently in severely immuno suppressed patients than in relatively immuno competent patients. (5% Vs 0%, P = 0.197).

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