Impact of CD4 Count on sputum smear for AFB in HIV –TB Co infection

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Abstract

Background: Human immunodeficiency virus (HIV) infection is a major threat in the world population and in the control of tuberculosis in developing countries. HIV-TB co infected patients with CD4 counts above 200 cells/cu µl, are likely to have typical symptoms and most of the sputum shows positive for acid fast bacilli (AFB). Patient withCD4 count less than 200 are with high risk of getting (Tuberculosis) TB, but diagnosis is difficult as there is more chances of sputum becoming negative, which requires sputum culture for diagnosis of (TB). Although sputum smear negativity is high in most cases of dual infection, particularly in patients with low immunity, it is an essential component in the diagnosis of tuberculosis in countries like India.

Methodology: A cross sectional study of 50 HIV-TB patients admitted to tertiary care hospital were studied for correlation between CD4 count and sputum smear results.

Results: 50 HIV-TB patients studied for a period of 1 year. Majority were in the age group of 30-40 years 20 (78%). In the study 29 (58%) were males and 21(42%) were females. The common presentations were cough 48 (96%), fever 44 (88%), weight loss 42(84%) and diarrhoea 25(50%). Mean CD4 count being 146.6±88. Most patients had CD4 count < 200 cells/cu µl. Mean CD4 count in sputum positive TB was 254.8±77.3 and in sputum negative TB was 97.2±33.8.

Conclusion: Patients with CD4 count > 200cells/cuµl are likely to have sputum positive pulmonary TB and typical presentations. Patients with CD4count < 200cells/cuµl are more of sputum negative pulmonary TB with atypical presentations which poses diagnostic difficulty and needs newer diagnostic tests.

Key words: HIV-TB co infected patients, CD4 count, Sputum for AFB

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-5478.2016.00030.3

Introduction

TB is the leading cause of death among adults. India contributes to 30% of world TB burden. Normally 10% of those infected with TB bacilli will get disease in their life time. However co-infection with HIV increases life time risk of developing TB from 10% to 60%[1,2]. The risk of developing TB increases as CD4 count progressively decline[3,4]. About 2 million HIV-TB coinfection is estimated in India and 3,20,000 people will die. 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[6,7,8,9]. Risk of death in HIV infected persons with TB is twice as high as that in HIV infected patients without TB[10,3]. Even though extra pulmonary TB is common in hospitalised patients, pulmonary TB is common in community[11,12]. High frequency of negative sputum smears common with dual infection, may requires sputum culture, chest radiograph and nucleic acid amplification tests for diagnosis. Chest radiograph may be less useful and normal in7-14% of patients[13,14]. Clinical presentation of TB in HIV patients depends on CD4 T cell count. Typical symptoms, upper lobe disease and sputum smear positive are common with patients having CD4 count >200 cell/cu µl. Atypical clinical and radiographic presentation, extra pulmonary disease and miliary TB are common with CD4 count < 200 cells/cu µl. Routine TB screening for all HIV seropositive patients offers opportunity to identify and diagnosis of TB[3]. Most frequent method of TB detection involves microscopic examination of AFB. However to be considered smear positive a specimens needs to contain 10^5 bacilli/ml with sensitivity varying from 43-51%. Methods to improve speed on sensitivity include fluorescence microscope and alternate processing methods such as concentration techniques and same day sputum collection[15].

Materials and Methods

A study was carried out at tertiary care hospital in the department of microbiology for a period of 1 year. After taking ethical approval from institutional ethical committee, 50 HIV-TB co infected patients were studied.

Diagnosis of HIV was done by HIV Coombs test, if positive confirmed by Tridot method (in vitro immunofilteration membrane) by diagnostic enterprises. Pulmonary TB was diagnosed among HIV patients by clinical examination, sputum examination, chest X ray and complete haemogram, liver function tests, and renal function tests were also done. According to the RNTCP guidelines, two sputum

specimens (spot, early morning) were collected for diagnosis of pulmonary tuberculosis. Sputum smears were prepared and subjected to Ziehl Neelson Staining (ZN) to identify the acid fast bacilli (AFB). Smear were screened as per standard protocol and graded according to RNTCP guidelines. Radiographic chest x rays and blood examination results of all patients were collected. All samples were subjected to CD4 count by Flow cytometry.

Results

Out of 50 HIV patients with tuberculosis, 29 were males and 21 were females. The age of study subjects ranged from 19- 63 years. The mean age was 39.2±9.67. Maximum numbers of patients 20 (40%) were in 30-39 years age group.

Table 1: Age and sex distribution

Age group (years)	Male		Female		Total	
	No. of cases	Percentage	No. of cases	Percentage	No. of cases	Percentage
< 21	1	3.4	1	4.8	2	4
21-29	2	6.9	3	14.3	5	10
30-39	13	44.8	7	33.3	20	40
40-49	8	27.6	7	33.3	15	30
50-59	4	13.8	2	9.5	6	12
> 60	1	3.4	1	4.8	2	4
Total	29	100	21	100	50	100

Common constitutional symptoms reported were fever 44(88%), weight loss42 (84%). Cough48 (96%) was the common respiratory symptom followed by breathlessness 24 (48%). Physical examination revealed that BMI > 18.5 kg/m2 in 52%. Pallor seen in 52%. Among the patients studied, pulmonary TB was seen in 38(76%) and extra pulmonary TB in 9(18%) and disseminated TB in 3 (6%). Out of 50 patients with X-ray evidence of TB, 16 (32%) were sputum positive TB while 34(68%) were sputum negative.

Abnormal x-ray findings included upper zone infiltrative lesions seen in 7(14%) cases, mid and lower zone infiltrative lesions in 13(26%) cases, bilateral infiltrative lesions + miliary seen in 19(38%), fibrocavitory lesions in 6(12%) and extrapulmonary lesions (pleural effusion/ mediastinal node) seen in 5 (10%).

In the study CD4 > 200 cells/cu µl was seen in 12 (24%) patients and 50-200 cells/cu µl in 33 (66%) and < 50 cells/cu µl in 5 (10%) patients. Mean CD4 count in the study was 146.6±88. Mean CD4 count among males was 145.6± 89.8 and in females was 147.6±87.8.

Table 2: CD4 Counts and number of patients

Cd4 count	No. of patients	Percentage
>200	12	24
51-200	33	66
< 50	5	10
Total	50	100

Table 3: Mean CD4 Counts and sex

Sex	No.	Mean	Standard deviation	Minimum	Maximum
Male	29	145.6	89.9	20	290
Female	21	147.6	87.7	35	377
Total	50	146.6	88.0	20	377

Mean CD4 count in patients with sputum positive TB was 254.8±77.3 and in sputum negative TB was 97.2±33.8. Mean CD4 count among extra pulmonary TB was 142.3±55.3 and in disseminated TB was 49.7±14.6.Mean CD4 count was found to be significantly high in patients with sputum positive TB. Mean CD4 count was also high in extrapulmonary TB. Mean CD4 count in disseminated and sputum negative pulmonary TB is significantly low (F=29.8 p< 0.001HS). 100% of sputum negative TB, 88.9% of extrapulmonary TB and 100% of disseminated (miliary) TB had CD4 count < 200 which is found to be highly significant (P< 0.001).

Sputum positive pulmonary TB seen in 14 patients, out of these 11(78.6%) are withCD4 count > 200 and 3(21.4%) are with CD4 count < 200. Sputum negative pulmonary TB seen in 24 patients, among these all were having CD4count < 200, which is found to be statistically significant.(p<0.001)

Table 4: CD4 Ranges and clinical manifestations of TB

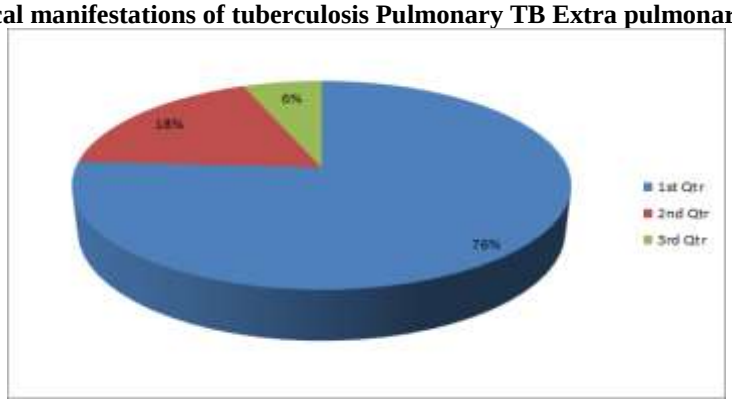
	-ve PTB	+ve PTB	Disseminated	EPTB	Total
< 50	3(12.5%)	0	2(66.7%)	0	5(10%)
50-200	21(87.5%)	3(21.4%)	1(33.3%)	8(88.9%)	33(66%)
>200	0	11(78.6%)	0	1(11.1%)	12(24%)
Total	24(100%)	14(100%)	3(100%)	9(100%)	50(100%)

85.7% patients with upper zone lesions had sputum positive TB and 14.3% had sputum negative TB. 92.3% patients with mid and lower zone lesions had sputum negative TB. This is found to be statistically significant. (p < 0.001HS)

Table 5: Sputum positivity and X-Ray zones

Sputum Positivity	Zones		Total
	Upper lesions	Mid/lower lesions	
-ve PTB	1 (14.3%)	12 (92.3%)	12 (60%)
+ve PTB	6 (85.7%)	1 (7.7%)	8 (40%)
Total	7 (100%)	13 (100%)	20 (100%)

Graph 1: Clinical manifestations of tuberculosis Pulmonary TB Extra pulmonary Disseminated



Discussion

In this study, out of 50 patients studied, 58% of patients were males and 42% females, this is comparable to other studies[17,18]. Most of the patients were in the age group of 30-39 years with mean age of males being 40.13 years and the females 38.28 years[19,16] which is comparable to other studies[17]. Most common constitutional symptom was fever (88%) and the most common respiratory symptom was cough (96%) which is similar to other studies[20,16,18]. Pulmonary tuberculosis ranked as the most common clinical manifestation (76%), followed by extra pulmonary tuberculosis in 18% and disseminated tuberculosis in 6%[18] comparable to other studies[21,16,20].

In this study sputum positivity was found to be low compared with other studies. Among X ray finding infiltrative lesions were more common (78%) than the fibrocavitory lesions. Among these infiltrative lesions, 14% was in the upper zone and 76% in mid and lower zone and bilateral infiltrative + miliary mottling seen in 38%.

Extrapulmonary manifestations are seen in 10%. Among the extrapulmonary manifestations, lymphadenopathy was seen in 8(16%) followed by pleural effusion 8(16%), meningitis 3 (16%) and ascites 1 (2%) which is also comparable with other studies. Mean CD4 count in the present study was 146.6±88.0. Among males count was 145.6±89.8 and in females 147.6±87.8 which is compared with other studies[17,20]. CD4 count >200 cells /cuµl was seen in 22% patients while < 200 cells/cuµl in 78% of patients.

In the present study, mean CD4 count in the sputum positive AFB was 254.8±77.3, in sputum negative TB was 97.2± 33.8, in EPTB was 142.3± 55.3 and in disseminated TB 49.7±14.6. This difference was statistically found to be significant with a P value <0.001 and it shows disseminated TB, sputum negative TB and extrapulmonary TB occurs more frequently with lower CD4 counts.

In the present study 24 patients were diagnosed as sputum negative pulmonary TB. Among these all were having CD4 count < 200 cell/cuµl and none were having CD4 > 200cells/cuµl. 14 sputum positive pulmonary TB were seen, among these 11 (78.6%) are with CD4 count > 200 and 3 (21.4%) are withCD4 count < 200cells/cuµl.

It shows sputum negative pulmonary TB are more in patients with CD4 count< 200cells.These patients pose diagnostic problem and requires further work up.

Among chest X ray findings upper zone lesions found to be more in CD4 count>200 group while mid and lower zone lesions are common in CD4 count < 200 group, which is found to be statistically significant with ($p< 0.001$). This is compared with other studies[24].

Conclusion

In this study common manifestation of TB in HIV infected was pulmonary TB with more number of sputum negative TB. A high proportion of pulmonary + extrapulmonary TB was also found.

HIV patients with CD4 count < 200 were having high risk of developing TB, but the sputum negative and atypical pulmonary TB are more as CD4 count decline below 200, which poses diagnostic difficulty. Sputum positive pulmonary TB with typical form seen withCD4 count >200cell/cuμl, were ease to diagnosis of TB.

Inspite of advanced research in diagnosis of TB, HIV-TB co infection requires high suspicion. Because of poor performance of sputum smear microscopy in HIV infected patients particularly with low CD4 count, newer diagnostic tests are urgently required.

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How to cite this article: Swarooprani N.B, Wadekar MD, Rajakumar S. Impact of CD4 Count on sputum smear for AFB in HIV- TB co infection. Indian J Microbiol Res 2016;3(2):126-129.