

Study of clinical profile of tuberculosis in HIV infected patients with special reference to CD4 T cell count and its oral manifestation

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Abstract

Aim: To study the clinical profile of tuberculosis in HIV infected patients and to compare the different clinical data with their CD4 counts with reference to oral health. **Material Methods:** Total 100 cases attending Department of Medicine /ART center at RIMS Ranchi were selected and their clinical profile was studied. The variations in clinical presentation with changing CD4 cell count were evaluated. **Results:** Most common presenting symptoms were fever (78%) cough (75%) and breathlessness (62%). Most common associated clinical oral findings were oral candidiasis (34%) and lymphadenopathy (33%). Among extra pulmonary tuberculosis lymphadenitis was the most common presentation (18%). Mean CD4 counts in patients with sputum positive TB was 226.71 ± 52.895 and in sputum negative TB was 108.49 ± 74.684 and in extra pulmonary tuberculosis was 138 ± 52.895 . 85.7%. Sputum positive cases were seen with CD4 counts <50 cells/ micro/l. **Conclusion:** HIV and tuberculosis was closely linked. Most commonly presented with pulmonary involvement and high number of cases showed extrapulmonary involvement and oral manifestations. Hence proper screening is important for proper diagnosis.

Key words: Tuberculosis, HIV, CD4, Candidiasis, Lymphadenopathy.

Introduction

HIV and tuberculosis have been closely linked since the emergence of AIDS. TB is the most common opportunistic infection affecting HIV seropositive individuals and it remains the most common cause of death in patients with AIDS [1]. In 2012 1.1 million (13%) of 8.6 million people who developed TB worldwide were HIV positive and there were 320000 deaths from HIV associated TB [2].

The clinical manifestation of TB in HIV infected patients are quite varied and generally show different patterns as CD4 cell count varies. In patients with relatively high CD4 cell count, the typical pattern of pulmonary reactivation occurs; patients represents with fever, cough, weight loss, night sweats and a chest X-ray revealing evidence of parenchymal lesions [3]. In patients with low CD4 cell counts, extrapulmonary or

disseminated disease is more common. The chest X-ray in these patients may reveal diffuse or lower lobe infiltrates consistent with military spread, pleural effusion and hilar / mediastinal lymphadenopathy. Infection may be present in bone, brain, meninges, gastrointestinal tract, lymph nodes and viscera [4]. The oral manifestations of the lesions due to tuberculosis produce a variety of forms and can occur any where in the oral cavity.

However, they show a predilection for certain areas of the mouth. It is hypothesized, that the oral manifestations of lesions can produce a distinct pattern of oral findings in tuberculosis group of patients [5]. It is important to record the oral findings of lesions in tuberculosis patients and study the pattern of oral lesions. Around eight million people become ill with Tuberculosis every year. Nearly one percent (1%) of the world's population is newly infected with Tuberculosis each year [6]. The case rate varies from one region to

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another and is dependent on factors such as poor living conditions, low socio economic status, low native resistance and compromised immunity from debilitating or immunosuppressed. The HIV pandemic provides further evidence of the interplay between TB infection and immunity. Exposure of tuberculosis carries a 10% annual risk of disease in HIV positive individuals, compared to a 5% lifetime risk in the absence of HIV [7]. Also the emergence of multiple-drug resistance forms of Tuberculosis has raised concerns among health officials in many cities.

Tuberculosis lesions of the mouth by primary inoculation are unusual, most cases occur as a result of Tuberculosis of other parts of the body, generally the lungs [8]. The clinical criteria for diagnosis of oral lesions such as tuberculous ulcers consisting of a stellate ulcer, undermined edges, a granulating floor, ragged and not indurated and is often painful. Although the tongue is the commonest site for oral tuberculous lesions, they may also occur on the gingiva, floor of mouth, palate, lips and buccal mucosa. Oral carcinoma included a non-healing ulcero-proliferative growth with pain, tenderness, limitation or loss of function, bleeding, red, white or mixed red and white areas. It can be flat or elevated. It may covered by necrotic slough. On palpation it may be smooth, granular, rough or crusted with induration of the base and margins. Presence of cervical lymphadenopathy is important clue for diagnosis. The lymphnodes are enlarged firm to hard on palpation usually non-tender unless secondarily infected and is fixed to the underlying structures.

TB oral lesions are a relatively rare occurrence. Studies vary, but the incidence has usually been reported as less than 1% of the TB population. Saliva is believed to have a protective effect, which may explain the paucity of TB oral lesions, despite the large numbers of bacilli contacting the oral cavity mucosa in a typical case of pulmonary tuberculosis.

Other factors that attribute to relative resistance of oral cavity for TB are presence of saprophytes, resistance of striated muscles to bacterial invasion, and thickness of protective epithelial covering. It is believed that the organisms enter the mucosa through a small break in the surface. Local factor that may facilitate the invasion of oral mucosa includes poor oral hygiene, leukoplakia, local trauma, and irritation by clove chewing, and so on. Self-inoculation by the patient usually results from infected sputum or by hematogenous or lymphatic dissemination [9,10].

Oral TB lesions may be either primary or secondary in occurrence. Primary lesions are uncommon, seen in younger patients, and present as single painless ulcer with regional lymph node enlargement. The secondary lesions are common, often associated with pulmonary disease, usually present as single, indurated, irregular, painful ulcer covered by inflammatory exudates in patients of any age group but relatively more common in middle-aged and elderly patients [11].

The identification of a TB lesion in any location in the mouth is an unusual finding and its discovery is usually indicative of underlying pulmonary disease. Therefore, in all cases of oral cavity TB, search for primary site of the disease should always be considered even in the absence of any signs and symptoms.

The oral manifestations of TB can also be in the form of superficial ulcers, patches, indurated soft tissue lesions, or even lesions within the jaw that may be in the form of TB osteomyelitis or simple bony radiolucency [12]. Of all these oral lesions, the ulcerative form is the most common [13]. It is often painful, with no caseation of the dependant lymph nodes. Oral lesions of TB are nonspecific in their clinical presentation and often are not considered in differential diagnosis, especially when oral lesions are present before systemic symptoms become apparent. Primary gingival involvement is more common in children and adolescents than adults [14].

According to various studies only a small percentage (7.8%) of histopathology specimens stain positive for acid fast bacilli [15] Therefore, a negative result does not rule out completely the possibility of TB. Another concern is the occurrence of mycobacterial infection as a part of AIDS. Histologically, an immunocompromised patient may not show granuloma or caseation.

This poses a potential problem in diagnosing TB. HIV-1-associated TB is reaching epidemic proportions in many African countries.

The prevalence and incidence of TB is similar in both HIV-positive and an HIV-negative individual, but the risk of active TB was elevated only for seropositive subjects. Increasing problems with TB may well continue because of the continuing emergence of MDR strains of *M. TB*, which is a major threat, particularly with HIV- and AIDS-infected patients, among whom, mortality rates are high [16]. TB is one of the conditions associated with HIV infection for which cure is possible with appropriate therapy.

This study is an effort to determine the clinical profile of TB in HIV patients with special reference to their CD4 cell count so that appropriate therapy can be given at the earliest.

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.

Material and Methods

Source of Data- HIV positive patients attending the ART center /Department of medicine at RIMS, Ranchi between September 2012 to September 2013 were taken up for the study.

They were considered for evaluation of mycobacterium tuberculosis infections 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 symptoms.

Methods of collection of Data

Sample size- 100 HIV positive cases meeting the criteria for the present study.

Sampling methods- simple random sampling

Inclusion criteria

1. 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. Biochemical analysis and /or positive culture of body fluids suggestive of TB OR
- c. Suggestive histopathology / demonstration of bacilli in clinical specimens OR
- d. Chest X-ray findings (physicians opinion) 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 18 years.

Data was collected by using pretested Performa meeting the objectives of the study. Purpose of the study was carefully explained to patients and consent was taken. All patients were interviewed, detailed history was taken with respect to risk factors and detailed physical examinations were carried out. Appropriate investigations were carried out in respective departments of RIMS.

Investigations

1. Routine baseline investigations like complete hemogram, ESR, LFT/RFT.
2. Sputum –AFB for three samples/ CBNAAT.
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 lymph nodes examined by histopathology and Ziehl- Nelson stain.
6. Other investigation like USG abdomen, CT head/ CT abdomen / whenever appropriate.
7. Cd4 counts by flow cytometry by standard technique from ART center, RIMS, Ranchi.

Results

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

Table -1: Mean age and Sex distribution.

	Number of patients	Mean age \pm SD
Male	76	34.95 \pm 8.7
Female	24	29.58 \pm 5.8
Total	100	33.66 \pm 8.4

The age of study subjects ranged from 19-62. The mean age was 33.66 \pm 8.46 (34.95 \pm 8.77 for males and 29.58 \pm 5.86 for females). Maximum number of patients (46%) was in the 30-39 age groups.

Table -2: Presenting 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
	Anorxia	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	4	4
	Memory loss	0	0
Oral manifestation	Skin lesions (Hairy Leukoplakia,Kaposis sarcoma)	12	12
	Mucous membrane (candidiasis)	43	43

The patients reported with mainly fever (n=78), cough (n=75), breathlessness (n=62), weight loss (n=56), fatigue (n=50) and diarrhea (n=50). Also oral manifestations reported were candidiasis (n=43), Hairy leukoplakia and Kaposis sarcoma (n=12)

Table-3: Mean CD4 counts and different manifestations of tuberculosis.

	N	Mean± SD	SD error
-VE PTB	37	108.49± 74.68	12.278
+VE PTB	14	226.71± 52.89	14.137
Disseminated	6	42.50± 4.41	1.803
EPTB	43	138.02± 58.38	8.904
Total	100	133.78± 76.26	7.626

Out of the 100 cases reported, mean CD4 counts was found (226.71±52.89) in positive pulmonary tuberculosis patients. A total of 43 cases presented with Extrapulmonary tuberculosis with mean CD4 count as 138.02±58.38.

Table-4: CD4 ranges and clinical manifestations of TB.

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

The CD4 count was found mainly between range 50-200 with n=48 and least in >200 CD4 count (n=23). Out of this n=34 EPTB reported with CD4 count in range 50-200 whereas >200 CD4 count n=12 cases of positive TB were seen.

Discussion

In this study out of 100 cases studied, 76% of patients were males and 24% females. This is comparable to study by Deivanayagam CN et al [17] in which 79.25% were males and rest 20.75% were females. This is similar to study by Soumya Swaminathan et al [18] This reflects increased incidence of HIV infection in males and that females in general are less likely to get treatment at a tertiary level hospital for HIV infection.

Most of the cases were in the 30-39 age groups with mean age of males being 34.95 years and a mean age of females 29.58 years. This is comparable to the study done by Deivanayagam CN et al [17] in which 74.94% of patients belongs to 21-40 years and National statistics reported to NACO, 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.

Most common occupation were unskilled laborers (40%), farmers (30%), drivers (10%), which indicates the co-infection affected people of low socio-economic status. Mohanty et al¹⁹ and Zuber Ahmad et al [20] found a similar occupation profile.

Most common constitutional symptom was fever (78%), while the commonest respiratory symptom was cough (75%).

These symptoms are similar to previous studies. The difference in reporting cough as a respiratory symptom in this study may be due to the more number of pulmonary tuberculosis cases in studies by Deivanayagam et al [17] and Soumya Swaminathan et al [18].

In this study diarrhea dominated 50% among the gastrointestinal symptoms, which is more than the Deivanayagam et al [17] study. This difference may be due to the fact that patients selected in this study were having low CD4 count thereby greater immunosuppression.

Oral candidiasis was seen as the most common oral finding followed by hairy leukoplakia, kaposi sarcoma present in 43% and 12% respectively as compared to Soumya Swaminathan et al [18] of 38%, 29% respectively. This finding highlights the importance of oral examination as an important complementary diagnostic means for the early identification and

monitoring of TB infection and HIV HAART regimen therapy.

The lesser number of PTB cases in this study may be due to the referral bias in which more number of severely ill extrapulmonary tuberculosis are referred to RIMS Ranchi which is a tertiary care center.

Another reason could be the low mean CD4 counts in the present study which is responsible for severe immune-suppression and more number of extrapulmonary tuberculosis. (Mean CD4 – 133.78 ± 76.26 in this study compared to CD4 – 192 ± 173 in the study by Soumya Swaminathan et al [18])

In this study sputum positivity was seen in 27.45% of cases as compared to 54% reported by Houston et al and 32.3% by Rajashekharan et al [21].

In this study sputum positivity was found to be low compared with other similar studies in India and abroad. Lesser sputum positivity in the present study may be due to low mean CD4 counts in the present study, with lower CD4 T cell levels; there is decreased prevalence of sputum positive TB while sputum negative and extrapulmonary TB cases increase.

Among the extrapulmonary manifestations lymphadenopathy was seen in 18% followed by pleural effusion in 11% tuberculous meningitis 7%, ascites 5% and pericardial effusion in 2% of cases as compared to Deivanayagam et al [17] with lymphadenopathy 7.88%, pleural effusion 11%, tuberculous meningitis 7% and pericardial effusion 2%.

The Mean CD4 count in the present study was 133.78 ± 75 cells/ micro l. The mean CD4 counts among males were 133.78 ± 75 cells/ micro l and 129.19 ± 79.27 cells/ micro l in females. This difference is not significant.

The mean CD4 counts was similar in a south Indian study by Soumya Swaminathan et al (192 ± 172 cells/ micro l) study by Sharma SK et al [18, 22] from AIIMS reported mean CD4 counts of 106 ± 64 cells/ micro l. 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 86% [22].

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 extra pulmonary 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.

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. Also the oral manifestations presented can help in early screening of which the dentists and the other health professionals should be made aware.

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