



## “PATTERN OF CLINICAL MANIFESTATION OF HIV IN PATIENTS OF TUBERCULOSIS DIAGNOSED BY DIFFERENT DIAGNOSTIC MODALITIES”

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### ABSTRACT

In developing countries, TB is one of the most common opportunistic infections in people who are seropositive for HIV-1. The risk of developing tuberculosis (TB) is estimated to be between 20-37 times greater in people living with HIV than among those without HIV infection. In 2009, there were 9.4 million new cases of TB, of which 1.2 (13%) million were among people living with HIV. With a high prevalence of TB infection in India, the problem of TB related to HIV infection also poses a major public health challenge, particularly in the high HIV burden States. The exact magnitude of HIV among TB patients is unknown as routine surveillance of HIV among TB patients is not undertaken. HIV screening has been done in 129 patients of tuberculosis diagnosed by chest x-ray, sputum AFB, FNAC lymphnode and histopathological examination. Out of them , 17 cases were reactive for HIV. Among Sputam positive cases of AFB, 4(8.1%) were seropositive for HIV. Cough, chest pain, diarrhoea and oral thrush were commonest clinical manifestation. This study shows a pattern of clinical manifestation of HIV and tuberculosis.

**KEYWORDS:** HIV, Tuberculosis, Seropositive, AIDS, ELISA, AFB



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## INTRODUCTION

The hallmark of HIV infection is progressive depletion and dysfunction of CD4 cells and macrophages which have the central role in antimycobacterial defences and dysfunction of these cells places the patient with HIV infection at high risk for primary infection or reactivation of tuberculosis. Epidemiologic evidence indicates that HIV infection increase the risk of progressive disease from new infections. Similarly mycobacteria and their products are powerful stimulators of macrophages and CD4 cells. Coexisting with HIV they induce HIV replication, accelerating immune depletion and progression of HIV to AIDS. There is a distinct interplay between HIV and the immune defenses. Typical non-progressors (those who have been infected with HIV but do not show symptoms) display several responses that are different than those of progressors. Non-progressors show more TH1-type cytokines like IL-2 and IFN- $\gamma$  and an elevated response by CD4+ T-cells and cytotoxic CD8+ T-cells towards HIV is observed.<sup>1</sup> In HIV, CD4+ T cell depletion removes the 'policeman' of TB control in the lung resulting in dissemination of Mycobacterium tuberculosis. Consequently, disseminated tuberculosis (DTB) and extrapulmonary tuberculosis (EPTB) are more common. On the other hand, the activated macrophages also release proinflammatory cytokines, such as tumor necrosis factor and IL-1, which enhance HIV replication. The mycobacteria and their products also enhance HIV replication by inducing nuclear factor kappa-B, the cellular factor that binds to promoter regions of HIV. Therefore, the fact that HIV-TB interplay is a bidirectional response anchored by the cytokines has improved our understanding of the natural progression and clinical course of HIV and TB. In fact, sites of active TB infection act as epifoci of HIV replication independent of HIV disease activity. The genetic diversity of locally replicating HIV strains is also more. These findings have renewed our impetus for

prevention, early recognition and effective treatment for both diseases<sup>2</sup>.

In a patient with tuberculosis, the possibility of associated HIV infection should be thought of if there is generalized lymphadenopathy, oral candidiasis, chronic diarrhea not responding to standard anti-diarrhoeal treatment for more than a month, herpes zoster recurrent pneumonia, bacteraemia especially with Salmonella typhimurium, oral hairy leukoplakia, persistent painful genital ulceration of Kaposi's sarcoma<sup>3</sup>. There presence of the following symptoms should alert the clinician to the possibility of associated HIV infection in a patient with tuberculosis; weight loss more than 10 kg or more than 20 percent of the original body weight, pain on swallowing (oral candidiasis) and burning sensation of the feet (peripheral sensory neuropathy). It is estimated that worldwide nearly 2 billion people are infected with Mycobacterium tuberculosis; 30 million are HIV infected and 5 to 6 million are dually infected with mycobacterium tuberculosis and HIV<sup>4</sup>. The clinical presentation of tuberculosis in HIV infected patients varies depending on the severity of immunosuppression. In patients with earlier stages of HIV disease, clinical presentation of tuberculosis tends to be similar to that observed in persons without immunodeficiency. Pulmonary disease is the most common, often with focal infiltrates and cavities. In patients with more marked immunodeficiency, with CD4+ counts of less than 200/m<sup>3</sup>, the features of tuberculosis are often atypical, with a much greater frequency of extrapulmonary involvement, especially of the lymph nodes. Diffuse pulmonary disease without cavitations often involving the lower lobes and prominent mediastinal or paratracheal adenopathy are often seen in patients with advanced HIV disease. The radiological shadows in the lungs may change rapidly. Patients with advanced HIV disease more often have military tuberculosis and

involvement of the lymphatic system, central nervous system (parenchymal and meningeal), soft tissue, bone marrow, liver and other viscera<sup>5,3,6</sup>.

## MATERIALS & METHODS

Study on the screening of TB patients of greater Gwalior region for HIV was carried out during the period of one year, at tertiary care centre. The blood samples were collected chiefly from patients admitted in TB Medical Wards and patients attending the outpatient department of a tertiary care centre. Total 129 TB patients were finally enrolled for the study.

## RESULTS

These TB patients were selected on the following basis:-

1. Patients who were not having any other metabolic disorders like Diabetes, Thyroidism, Cardiac problems.
2. Patients having any one of the positive finding (on X-ray, sputum smear, FNAC, Histopathological Examination).

Following investigations has been done :

1. ELISA Test for HIV detection :  
Kit manufactured by Bio Standard Diagnostics Pvt. Ltd.<sup>7</sup>
2. AFB (Zeihl Neelson Stain)
3. GIEMSA STAINING FOR FNAC
4. Haematoxylin and Eosin staining for Histopathological examination of biopsies submitted.

**TABLE 1**  
**DISTRIBUTION OF CASES ACCORDING TO HIV STATUS REGARDING SEROPOSITIVITY AND SERONEGATIVITY**

S. No.	HIV Status	Total No. of Cases
1	Seropositive	17 (13.2%)
2	Seronegative	112 (86.8%)
Total		129 (100%)

**TABLE 2**  
**DISTRIBUTION OF TUBERCULOSIS CASES ACCORDING TO DIAGNOSTIC METHODS AND THEIR RELATION WITH HIV**

S. No.	Diagnostic Methods	Total	HIV	
			Seropositive	Seronegative
1	X-ray	76 (58.9%)	16 (21.05%)	60 (78.9%)
2	AFB (Sputum)	49 (37.9%)	4 (8.1%)	45 (91.8%)
3	FNAC and other smear cytology	15 (11.7%)	1 (6.6%)	14 (93.3%)
4	HPE	10 (7.7%)	0 (0%)	10 (100%)
Total		129 (100%)		

**TABLE 3**  
**DISTRIBUTION OF TB CASES ACCORDING TO SPUTUM SMEAR BY AFB AND ITS RELATION WITH HIV**

S. No.	AFB	Total	HIV	
			Seropositive	Seronegative
1	Sputum positive	49 (37.9%)	4 (8.1%)	45 (91.8%)
2	Sputum negative	80 (62.1%)	13 (16.2%)	67 (82.7%)
Total		129 (100%)		

**TABLE 4**  
**PATTERN OF CLINICAL MANIFESTATIONS (RESPIRATORY)**  
**IN 129 TB CASES AND THEIR RELATION WITH HIV STATUS**

S. No.	Respiratory Complaints	Total	HIV	
			Seropositive	Seronegative
1	Cough	86 (66.6%)	11 (12.7%)	75 (87.2%)
2	Expectoration	75 (58.1%)	6 (8%)	69 (92%)
3	Chest Pain	51 (39.5%)	9 (17.6%)	42 (82.3%)
4	Breathlessness	18 (13.9%)	0 (0%)	18 (100%)
5	Haemoptysis	4 (3.1%)	0 (0%)	4 (100%)
Total		129 (100%)		

**TABLE 5**  
**PATTERN OF CLINICAL MANIFESTATIONS (NON RESPIRATORY)**  
**AND RELEVANT HISTORY WITH ITS RELATION TO HIV**

S. No.	Non respiratory complaints	Total	HIV	
			Seropositive	Seronegative
1	Fever	112 (86.8%)	17 (15.17%)	95 (84.8%)
2	Weight loss	75 (58.1%)	15 (20%)	60 (80%)
3	Diarrhoea	28 (21.7%)	13 (46.4%)	15 (53.5%)
4	Oral thrush	7 (54.2%)	3 (42.8%)	4 (57.1%)
5	Past H/o TB	44 (34.1%)	5 (11.36%)	39 (88.6%)
6	Family H/o TB	21 (16.27%)	4 (19.04%)	17 (80.9%)
Total		129 (100%)		

## DISCUSSION

The incidence of HIV co-infection with tuberculosis varies from 0.5% in Delhi<sup>7</sup> to 37.8% in Imphal<sup>8</sup>. The present study showed incidence of 13.1% in Gwalior region, which is almost similar to 12.1% incidence in Pune<sup>9</sup>, and 15.28% incidence in Mumbai<sup>10</sup>.

### **HIV seropositivity in tuberculosis patients as reported in various studies published from India**

In Mumbai, the HIV seroprevalence in tuberculosis patients increased from 2.56% in 1988 to 11.3% in 1995<sup>11</sup>. However, reports from certain other parts of India indicate that HIV seroprevalence in tuberculosis patients is low there, as shown by prevalence of 0.7% in Ajmer<sup>12</sup>, 0.8% in Lucknow<sup>13</sup>, 1.0% in Calcutta<sup>14</sup>. In Miraj, HIV seroprevalence in tuberculosis patients in 1995 was reported as 9.2%<sup>15</sup>. HIV seroprevalence in tuberculosis patients in Pune has been shown to increase

from 3.2% in 1991 to 20.1% in 1996<sup>16</sup>. In Chennai, HIV seroprevalence increased from 0.77% in 1991 to 3.4% in 1993<sup>17</sup>. Whereas in 1996 in Chennai HIV Seroprevalence in pulmonary tuberculosis patients was reported as 17%<sup>18</sup>. From Pondicherry, there is report of increase in HIV seroprevalence among tuberculosis patients from 2.65% in 1991 to 10.4% in 1993<sup>19</sup>.

### **Distribution of tuberculosis patients according to sputum status and their relation with HIV**

Elliott et al. 1994<sup>20</sup> reported that 57% HIV seropositive showed sputum positive in AFB while 76% seronegative for HIV also showed sputum positivity. Ravi Mehrotra et al. 2006<sup>4</sup> showed that out of total 130 sputum positive cases only 6 (4.6%) were HIV seropositives and 124 (95.3%) were seronegative for HIV. Similarly Hussain T. et al. 2006<sup>21</sup> at Agra

reported sputum positivity in 15 (4.4%) seropositives for HIV and 325 (95.5%) in seronegative for HIV out of 340 cases. The findings in the present study showed sputum positivity in 4 (8.1%) HIV seropositives and 45 (91.8%) HIV seronegatives these are in accordance with the findings of workers mentioned above.

***The pattern of clinical manifestations in HIV positive tuberculosis patients showing wide variations in symptoms.***

S.K. Agarwal et al. 2003<sup>22</sup> reported weight loss (93.5%), fever (87.1%) and cough (74.2%) as the most common manifestations while Ravi Mehrotra et al. 2006<sup>4</sup> found weight loss (100%), fever (63.6%) and cough (54.5%) in that order. The present study also showed that out of 129 tuberculosis cases 17 were HIV seropositive. Fever was seen in 17 (100%), weight loss 15 (88.2%), diarrhea 13 (76.4%) followed by cough 11 (69.7%). These findings correlate well with the findings of other workers.

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## CONCLUSION

The incidence of HIV coinfection in tubercular patients was found to be (13.1%) i.e. 17 patients were HIV seropositive. Out of 17 cases of tuberculosis seropositive for HIV only, 4 cases (23.5%) turned out to be sputum smear positive. Evidence suggests that microscopy for AFB in sputum may be less sensitive in diagnosing pulmonary tuberculosis when HIV infection is present, especially in severely immunocompromised patients. Among the 17 HIV seropositive cases most common symptom was fever (100%) followed by weight loss (88.2%) than diarrhea (76.4%).

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