

CLINICAL AND LABORATORY PROFILE OF SPUTUM POSITIVE PULMONARY TUBERCULOSIS AMONG HIV SEROPOSITIVE AND HIV SERONEGATIVE PATIENTS- A CROSS-SECTIONAL STUDY

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ABSTRACT

BACKGROUND

The global impact of the converging dual epidemics of TB and HIV is one of the major public health challenges. The increasing rate of HIV infection in many countries has had an impact on TB epidemiology. As the prevalence of pulmonary tuberculosis is increasing among HIV seropositive patients with a wide range of immune status and clinical presentations, the present study was undertaken to assess the clinical and laboratory profile of sputum positive pulmonary tuberculosis among HIV seropositive and HIV seronegative patients.

MATERIALS AND METHODS

The present one year cross-sectional study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 104 patients with sputum positive pulmonary tuberculosis patients during the period of January 2009 to December 2009. Routine investigations such as blood group, haemogram that is haemoglobin, total count, differential count, erythrocyte sedimentation rate, sputum smears for AFB and chest x-ray were done.

RESULTS

Seroprevalence of HIV among pulmonary tuberculosis patients was 23.08%. On examination anaemia, undernourishment, lymphadenopathy and the presence of opportunistic infections like oral candidiasis, herpes zoster stain and genital lesions were more predominant among HIV seropositives compared to HIV seronegatives. Mean Hb and TLC were significantly low among HIV seropositives compared to HIV seronegatives. Chest x-ray showed varied presentation. Upper zone infiltration, cavitation and fibrosis were more commonly involved among HIV seronegatives compared to HIV seropositives.

CONCLUSION

HIV seropositive PTB patients commonly present with fever, weight loss and loss of appetite, while cough with expectoration, haemoptysis, breathlessness were more common with HIV seronegative patients. Cavitation, fibrosis and fibrocavitary lesions were predominantly seen among HIV seronegatives, while infiltration and miliary mottling was present in HIV seropositives.

KEYWORDS

Pulmonary Tuberculosis, HIV, Fibrosis, Cavitation, Haemoptysis.

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BACKGROUND

About one-third of world population suffers from mycobacterium tuberculosis (MTB) infection. Tuberculosis (TB) continues to be the most important cause of morbidity and mortality worldwide killing approximately two million people each year.¹

It is estimated that there are about 14 million cases of TB in India, about two million new cases occur annually and home of one-fourth the world's TB prevalence.²

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Fuelled by high prevalence of Human Immunodeficiency Virus (HIV) infection, the incidence rate of TB is very high as TB is the most common opportunistic infection in HIV seropositive patients, when the immune system weakens as a result of HIV infection.¹ The life time risk of developing tuberculosis is 60% in HIV seropositive patients compared to 10% in HIV seronegative patients.²

Human immunodeficiency virus related PTB can present across a wide range of immune status, and its clinical presentation also varies accordingly. In the early stage of HIV infection, clinical manifestations of TB are quite similar to that of HIV seronegative patients; however, at a later phase atypical features are common.³

Most common symptoms of PTB are cough with expectoration and weight loss. Constitutional symptoms like fever, night sweats, generalised weakness, loss of appetite and other respiratory symptoms like chest pain, haemoptysis and breathlessness.

Weight loss and fever are more common in HIV seropositive PTB patients than in those who are HIV seronegative. Conversely, cough and haemoptysis are less common in HIV seropositive PTB than in those are HIV seronegative as there is less cavitation, inflammation and endobronchial irritation.⁴

The chest x-ray (CXR) pattern also varies among HIV seropositive and HIV seronegative patients. Classical pattern is more common in HIV seronegative, that is upper lobe infiltration, cavitation, pulmonary fibrosis while interstitial infiltration are common in middle and lower zones and less cavitation in HIV seropositive.⁵

As the prevalence of PTB is increasing among HIV seropositive patients with a wide range of immune status and clinical presentations, the present study was undertaken to assess the clinical and laboratory profile of sputum positive PTB among HIV seropositive and HIV seronegative patients.

Aims and Objectives

The objective of the present study was to study the clinical and laboratory profile of sputum positive PTB among HIV seropositive and HIV seronegative patients.

MATERIALS AND METHODS

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on patients with sputum positive PTB during the period of January 2009 to December 2009. The study design was one year cross-sectional study.

Inclusion Criteria

- Patients diagnosed to have sputum positive PTB proved by laboratory reports that is;
 - Two or more initial sputum smear examinations positive for AFB, or
 - One sputum smear positive for AFB and CXR abnormalities consistent with active PTB as determined by a clinician, or
 - One sputum smear positive for AFB, which is also culture positive for MTB.

Exclusion Criteria

- Chronic Obstructive Pulmonary Disease (COPD).
- Bronchial asthma with secondary infection.
- Non-tubercular Pneumonia and Bronchiectasis.
- Patients of PTB, presently on Anti-Koch's Treatment (AKT) of more than two weeks duration.

The study was approved by the Ethical and Research Committee of Ethics Committee, Jawaharlal Nehru Medical College, Belgaum. Patients admitted in the wards of Medicine and Respiratory Department at KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum were evaluated based on selection criteria. The selected patients were briefed about the nature of the study, the interventions used and a written informed consent was obtained. A thorough clinical examination was conducted and the

findings were also recorded. Routine investigations such as blood group, haemogram that is haemoglobin, total count, differential count, erythrocyte sedimentation rate were done.

Chest x-ray was done and evaluated for lesions involved like infiltration, cavitation, fibrosis, fibrocavitary lesions and miliary mottling along with different zones involved. Other tests like serum urea, serum creatinine, serum sodium and serum potassium were carried out. HIV status was confirmed by voluntary counselling and testing centre along with CD4 count.

Statistical Analysis

The results were tabulated and the data was analysed using rates, ratios and percentages for different clinical manifestations. The data was compared using chi-square (x²) test, 'Z' test and student's 't' test.

RESULTS

The present study was conducted in the Department of Medicine, KLES Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum on 104 patients with sputum positive PTB during the period of January 2009 to December 2009. The HIV ELISA was done in all 104 patients to confirm HIV seropositivity. The data obtained was tabulated and analysed as below.

Symptoms	Patients	
	Number	Percentage
Cough with expectoration	104	100.00
Fever	80	76.92
Night sweats	25	24.04
Haemoptysis	6	5.77
Weight loss	61	58.65
Loss of appetite	59	56.73
Chest pain	7	6.73
Breathlessness	4	3.85
Generalised weakness	39	37.50
Diarrhoea	3	2.88

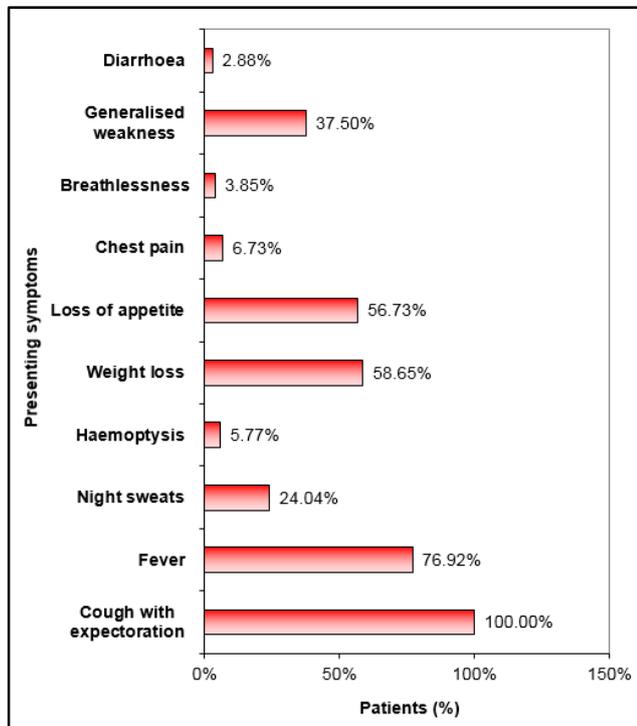
Table 1. Presenting Symptoms

In the present study, among 104 patients all patients (100%) presented with cough with expectoration, 76.92% of patients had fever, 58.65% had weight loss, 56.73% had history of appetite; 37.50% had generalised weakness and 24.04% of patients had history of night sweats. History of chest pain, breathlessness, haemoptysis and diarrhoea was seen in 7.73%, 3.85%, 5.77% and 2.88% of patients respectively.

Physical Findings	Patients	
	Number	Percentage
Pallor	48	46.15
Lymphadenopathy	30	28.85
Oral candidiasis	18	17.31
Herpetic scar	13	12.50
Genital lesions	4	3.85

Table 2. Physical Findings

In the present study on physical examination 46.15% of patients had pallor, 28.85% had lymphadenopathy, 17.31% had oral candidiasis, 12.50% of patients had herpetic scar and genital lesions were present in 3.85% of patients.



Graph 1. Presenting Symptoms

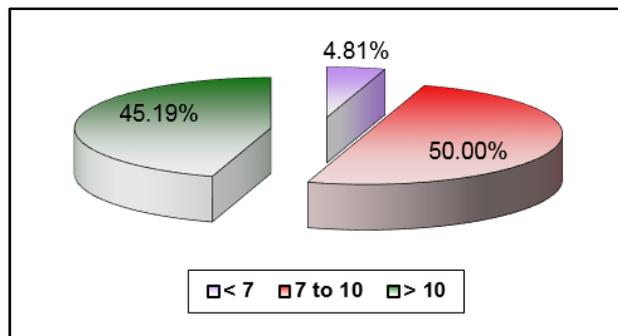
Signs	Patients	
	Number	Percentage
Cavitation	40	38.46
Fibrosis	90	86.54
Infiltration	11	10.58

Table 3. Respiratory System Examination

In the present study, on systemic examination 86.54% of patients had signs of fibrosis, 38.46% of patients had signs of cavitations and 10.58% of patients had signs of infiltration.

Haematological Parameters	Range	No.	%
HB (gm%)	Less than 7	5	4.81
	7 to 10	52	50.00
	More than 10	47	45.19
Total Count (Cells/mm ³)	Less than 4000	3	2.88
	4000 to 11000	46	44.23
	More than 11000	55	52.88
ESR (mm)	0 to 20	0	0.00
	More than 20	104	100.00

Table 4. Haematological Parameters

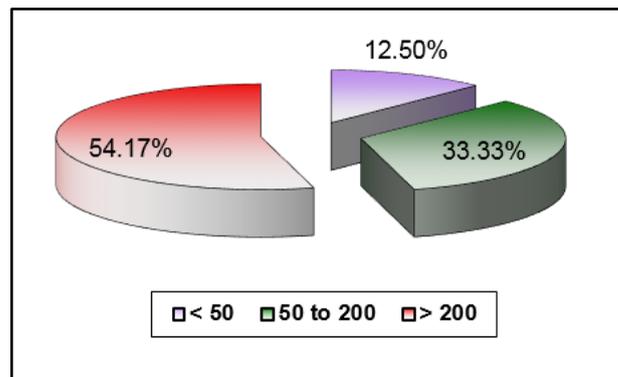


Graph 2. Haemoglobin Levels (gm Percentage)

In this study, majority of the patients (50%) had haemoglobin levels between 7 to 10 gm% followed by more than 10 gm% in 45.19%. Haemoglobin levels were less than 7 gm% in 4.81% of patients. In the present study, 52.88% of patient's total leucocyte count was more than 11,000, 44.23% of patients had in the range of 4000 - 11,000 and 2.88% of patients had less than 4000 cells/mm³. All patients had their ESR raised more than normal (100%).

CD4 Count (Cells/mm ³)	Number	Percentage
Less than 50	3	12.50
50 to 200	8	33.33
More than 200	13	54.17

Table 5. CD4 Count among HIV Seropositive Patients



Graph 3. CD4 Count among HIV Seropositive Patients (Cells/mm³)

In the present study, majority (54.17%) of HIV seropositive patients had CD4 count more than 200 cells/mm³ followed by 50 to 200 cells/mm³ (33.33%) and less than 50 cells/mm³ (12.50%).

Biochemical Parameters	Range	Number	%
Urea (mg/dL)	Less than 10	0	0.00
	10 to 39	78	75.00
	More than 39	26	25.00
Serum creatinine (mg/dL)	Less than 0.5	2	1.92
	0.5 to 1.3	84	80.77
	More than 1.3	18	17.31
Serum sodium (mEq/L)	Less than 130	5	4.81

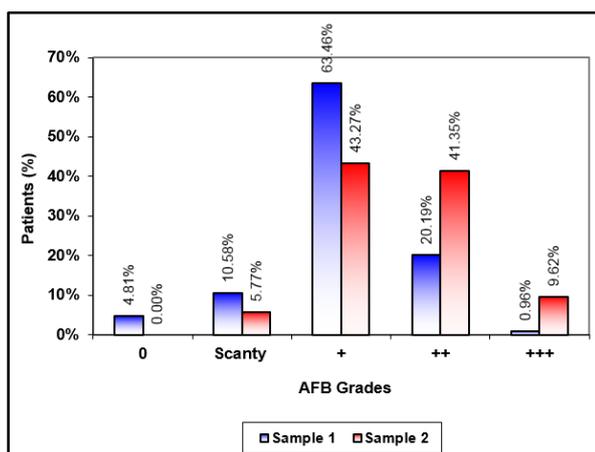
	130 to 145	89	85.58
	More than 145	10	9.62
Serum potassium (mEq/L)	Less than 3	5	4.81
	3 to 5	94	90.38
	More than 5	5	4.81

Table 6. Biochemical Parameters

In the present study, 75% of patient's blood urea levels were within the normal range and 25% of patients had elevated blood urea levels; 80.77% of patient's sr. creatinine levels were within normal range, 17.31% of patients had elevated sr. creatinine levels and 1.52% of patient's serum creatinine levels were less than 0.50 normal range; 85.58% of patient's sr. sodium levels were within normal range, 9.62% of patients had elevated sodium levels and 4.81% of patients had low sr. sodium levels; 90.38% of patients sr. potassium levels were within normal range, 4.81% of patients had elevated sr. potassium levels and 4.81% of patient's potassium levels were low.

AFB Grades	Sample 1		Sample 2	
	Number	Percentage	Number	Percentage
0	5	4.81	0	0.00
Scanty	11	10.58	6	5.77
+	66	63.46	45	43.27
++	21	20.19	43	41.35
+++	1	0.96	10	9.62

Table 7. Sputum Smear Examination



Graph 4. Sputum Smear Examination

In the present study, 63.46% of patients were recorded as grade + (1+), 20.19% as grade ++ (2+), 10.58% as scanty, 4.81% as grade 0 and 0.6% as +++ (3+) on sputum

smear examination for AFB. In sample 2, 43.27% of patients were recorded as grade ++ (2+), 9.62% as +++ (3+), 5.77% as scanty on sputum smear examination for AFB.

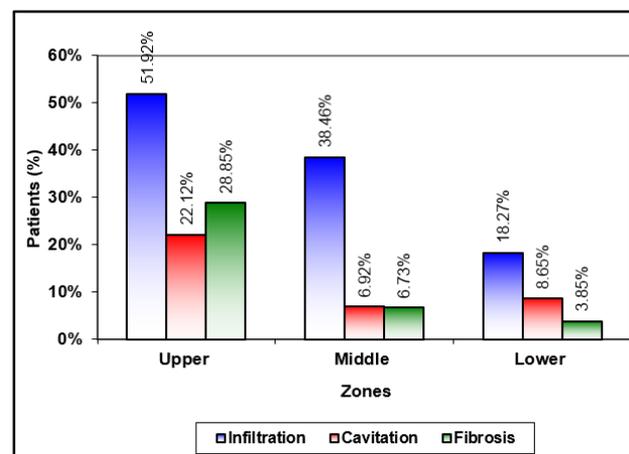
Chest X-ray Findings	Patients	
	Number	Percentage
Infiltration	70	67.31
Cavitation	39	37.50
Fibrosis	40	38.46
Fibrocavitary Lesion	34	32.69
Miliary Mottling	4	3.85

Table 8. Chest X-Ray Findings

In the present study among 104 patients, 67.31% of patients on chest x-ray had infiltration, 37.50% had cavitation and 38.46% had fibrosis. The fibrocavitary lesions were seen in 32.69% and miliary pattern was present in 3.85% patients.

Chest X-Ray Findings	Zones					
	Upper		Middle		Lower	
	No.	%	No.	%	No.	%
Infiltration	54	51.92	40	38.46	19	18.27
Cavitation	23	22.12	10	9.62	9	8.65
Fibrosis	30	28.85	7	6.73	4	3.85

Table 9. Chest X-Ray Findings involving different Lung Zones



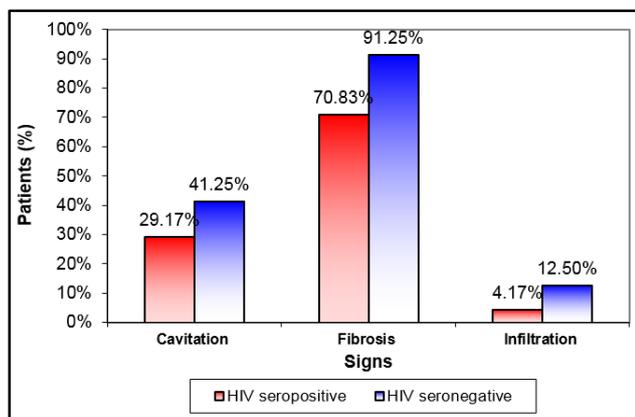
Graph 5. Chest X-Ray Findings involving different Lung Zones

In the present study, 51.9% of patients had upper zone infiltrations. 38.46% of patients had middle zone infiltration and 18.27% of patients had lower zone infiltration.

22.12% of patients had upper zone cavitation, 9.62% of patients had middle zone cavitation and 8.65% of patients had lower zone cavitations.

Signs	HIV Seronegative (n = 80)		HIV Seropositive (n = 24)		Z	P
	Number	Percentage	Number	Percentage		
Cavitation	33	41.25	7	29.17	1.07	> 0.05
Fibrosis	73	91.25	17	70.83	2.57	< 0.01
Infiltration	10	12.50	1	4.17	1.16	> 0.05

Table 10. Respiratory System Examination Findings



Graph 6. Respiratory System Examination Findings

In the present study, 91.25% of patients among HIV seronegatives had signs of fibrosis compared to 70.83% HIV in seronegatives and this difference was statistically significant ($p < 0.01$). In the seronegatives, 41.25% and 12.5% of patients had signs of cavitation and infiltration compared to 29.17% and 4.17% in the HIV seronegatives.

Haematological Parameters	HIV Seronegative (n = 80)		HIV Seropositive (n = 24)		T	DF	P
	Mean	SD	Mean	SD			
Hb (gm%)	10.1	1.92	8.2	0.88	4.690	102	< 0.005
TLC (cells/mm ³)	12465.8	3950.62	7039.2	2049.57	6.458	102	< 0.001
ESR (mm)	62.4	26.60	59.70	25.36	0.441	102	> 0.05

Table 11. Haematological Parameters

In the present study, the mean haemoglobin percentage and TLC in the HIV seropositive patients were significantly low compared to HIV seronegatives. However, no statistically significant association was found with regard to ESR.

DISCUSSION

In the present study, majority (100%) of the patients had cough with expectoration, fever (76.92%), weight loss (58.65%), loss of appetite (56.73%) and generalised weakness (37.50%) (Table 1).

A study¹ conducted at a Teaching Hospital of Northwest Ethiopia showed that among PTB patients, 93% had low-grade fever, 90.3% had weight loss, 86% had night sweats and 82.5% had cough with expectoration.

In this study, patients had a wide spectrum of physical signs on examination. Majority of the patients had pallor (46.15%) and lymphadenopathy (28.85%). Other signs like oral candidiasis, herpetic scar and genital lesions were present in 17.31%, 12.50% and 3.85% of patients respectively (Table 2).

On respiratory system examination 86.54% of patients had signs of fibrosis, 38.46% had signs of cavitation and 10.58% had signs of infiltration (Table 3).

A study¹ done in Ethiopia among PTB patients found 47.1% of patients had sign of fibrosis, 77% of patients had signs of cavitation and 50% of patients had signs of infiltration.

In the present study, majority (50%) of the patients had moderate anaemia (Hb 7 to 10 gm%) and severe anaemia was present in 4.85% of patients (Hb less than 7 gm%) (Table 4).

A study⁶ done in Tanzania showed 75.6% of patients had moderate anaemia and 24.4% had severe anaemia. In this study, 44.23% of patients had TLC in the range of 4000 to 11000 and 52.88% of patients had leucocytosis and 2.88% had leucopaenia. All patients had elevated ESR levels (Table

4). Among the patients with PTB co-infected with HIV, 54.17% of patient’s CD4 count levels were more than 200 cells/mm³ and 33.33% had in between 50 to 200 cells/mm³, whereas 12.5% had CD4 count less than 50 cells/cm³ (Table 5).

In this study, blood urea was normal in 75% and serum creatinine in 80.77% of patients. Serum sodium levels were normal among 85.5% of patients and in 90.38% of patient’s serum potassium levels were within normal range; 4.81% of patients had hyponatremia (Table 6).

On sputum examination, majority of patient’s sputum smear for AFB showed 63.46% of patients in the sample 1 and 43.27% of patients in sample 2 were recorded as Grade + (1+) followed by Grade ++ (2+) in 20.19% in sample 1 and 41.35% in sample 2 (Table 7).

In this study chest x-ray findings among 104 patients showed 67.35% had infiltrations, 37.50% had cavitation and 38.46% had fibrosis. The fibrocavitary lesions were seen in 32.69% and miliary mottling was present in 3.85% of patients (Table 8). The upper zone involvement was more predominant with regard to infiltration, cavitations and fibrosis (Table 9).

Comparison of Clinical and Laboratory Profile among HIV Seropositives and HIV Seronegatives

The seroprevalence of HIV among PTB patients in this study was 23.08%. Studies^{3,4} done in Jamaica and AIIMS, New Delhi have reported a prevalence of 11.6 to 20% among PTB patients.

In the present study, majority of the patients presented with symptoms of cough with expectoration, fever, night sweats, loss of weight and loss of appetite. Fever, loss of weight, loss of appetite and generalised weakness were more predominant among HIV seropositive patients compared to HIV seronegative (Table 10).

These findings were comparable to a study⁵ conducted in Manipur, where cough with expectoration was present among HIV seronegative and weight loss, loss of appetite and generalised weakness among HIV seropositives. Another study¹ done in Ethiopia showed similar presentation where cough with expectoration, haemoptysis, chest pain, breathlessness were more in HIV seronegative and weight loss, loss of appetite and diarrhoea in HIV seropositives. A Study⁷ done in Chennai reported similar clinical profile of symptoms. All patients presented with cough with expectoration, which reflects mild immunosuppression with higher CD4 count.

In the present study among HIV seropositive patients, 33.33% of patients were known HIV earlier and history of contact with sputum smear positive PTB was present in 20% of HIV seronegatives compared to none in HIV seropositive. In the present study, patients had a wide spectrum of physical findings on examination. Other findings like lymphadenopathy was seen in 33.33% in HIV seropositive compared to 27.50% in HIV seronegative. This is comparable to a study¹ done in Ethiopia, where 29% of patients among HIV seropositive had lymphadenopathy compared to 22% in HIV seronegative; 54.17% of patients among HIV seropositive had pallor compared to 43.75% in HIV seronegative patients.

In the present study clinical findings on respiratory system examination showed 41.25% of patients with signs of cavitation, 91.25% with signs of fibrosis in the HIV seronegative compared to 29.17% and 70.83% in the HIV seropositives (Table 10). This is comparable to a study¹ conducted in Ethiopia where 68.2% of patients had sign of cavitations; 56.4% had sign of fibrosis in the HIV seronegative compared to 31.8% and 43.6% in HIV seropositive patients. History of cough, expectoration and haemoptysis and sign of cavitation as well as coarse crepitation in the chest were independent predictions of sputum smear positive TB. 12.50% of patients in the seronegative had sign of infiltration compared to 4.17% in HIV seropositives.

In the present study, haematological parameters such as mean haemoglobin and TLC were significantly lower in HIV seropositives (8.2%) compared to HIV seronegatives. Mean ESR (mm) levels were comparable in HIV seropositive and HIV seronegative patients (Table 11).

This sputum positive for AFB were recorded at a lower grade among HIV seropositive due to low CD4 counts and less number of patients with cavitory lesions (Table 11).

In this study, the chest x-ray findings showed, fibrosis, cavitation and fibrocavitory lesions were more common in the HIV seronegative compared to HIV seropositive patients. However, infiltrative lesions and miliary mottling were more common in HIV seropositives compared to HIV seronegative patients (Table 10).

This is comparable to study¹ conducted in Ethiopia, where 50% of patients had fibrosis and 13.3% had miliary mottling among HIV seropositive compared to HIV seronegatives. Another study⁸ in Chennai showed 83.33% of patients had fibrocavitory lesions among HIV

seronegatives compared to 11.15% in HIV seropositives. Another study⁹ showed cavitory lesions were less common (29% vs 36.1%) among HIV seropositive patients as compared to HIV seronegative patients.

Another study⁸ done in Chennai showed 91% and 39% of patients among HIV seronegative had diffuse infiltrates and cavitation compared to 65% and 18% in HIV seropositives.

Among HIV seropositive patients typical radiological features of post primary TB, that is upper zone infiltrates were less common, while atypical features such as mid and lower zone infiltrates were more common in seropositive patients. It has been shown that in mild immunosuppression the appearance is often classical, while in severe immune suppression it is atypical.

Miliary mottling was seen in 12.5% among HIV seropositive compared to 1% in HIV seronegative. This could be probably due to more dissemination due to low CD4 count and severe immune suppression (Table 29). This is similar to a study¹⁰ done in Chetput, Chennai showed 11% patients among HIV seropositives had miliary mottling compared to 1% among HIV seronegatives.

CONCLUSION

Seroprevalence of HIV among pulmonary tuberculosis patients was found to be 23.08%.

HIV seropositive PTB patients commonly present with fever, weight loss and loss of appetite, while cough with expectoration, haemoptysis, breathlessness were more common with HIV seronegative patients.

On examination anaemia, undernourishment, lymphadenopathy and the presence of opportunistic infections like oral candidiasis, herpes zoster and genital lesions were more predominant among HIV seropositives compared to HIV seronegatives.

On respiratory system examination, signs of fibrosis and cavitation were more predominant in HIV seronegative compared to HIV seropositives.

Mean Hb and TLC were significantly low among HIV seropositives compared to HIV seronegatives. Sputum smear examinations for AFB showed higher grades among HIV seronegatives and low grades among HIV seropositives. Chest x-ray showed varied presentation. Cavitation, fibrosis and fibrocavitory lesions were predominantly seen among HIV seronegatives, while infiltration and miliary mottling was present in HIV seropositives. Upper zone infiltration, cavitation and fibrosis were more commonly involved among HIV seronegatives compared to HIV seropositives.

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