ORIGINAL ARTICLE

Chest radiological features of pulmonary tuberculosis in HIV-positive and HIV-negative patients

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ABSTRACT

Background: Pulmonary tuberculosis (PTB) is a leading cause of illness and death in individuals with HIV. While chest X-rays are commonly used for diagnosing PTB, HIV can alter X-ray findings, potentially delaying diagnosis and leading to misinterpretation, which can exacerbate disease progression and complications.

Material and Methods: This prospective, single-center observational study was conducted at The Aga Khan University Hospital in Karachi, Pakistan from May 2023 to April 2024. This study compared the radiological features of PTB in HIV-positive and HIV-negative patients using chest X-rays, CT scans (when CXRs were unavailable), and blood tests, including HIV results and CD4 counts. Statistical analysis was performed using SPSS version 19, with significance set at $p < 0.05$. Ethical approval and data confidentiality were ensured.

Results: A total of 116 patients (mean age 52.23 years; 70.7% male) were analyzed. PTB was diagnosed via sputum in 75.9% of cases, with HIV co-infection present in 16.4% (median CD4 count 119 cells/mm^3). The PTB + HIV group was younger (42.16 vs. 54.21 years, $p < 0.0001$) and had a higher male proportion (94.7% vs. 66.0%, $p = 0.012$). Alveolar infiltrates were more common in the co-infection group (78.9% vs. 45.4%, $p = 0.007$), while cavitary infiltrates were exclusive to the PTB-only group (27.8%, $p = 0.006$). Upper lobes were predominantly affected in the PTB-only group, whereas lower lobes were more involved in the co-infection group.

Conclusions: Recognizing atypical radiological patterns is essential for the timely diagnosis and treatment of PTB in HIV-positive patients, as co-infection complicates management due to drug interactions and the increased risk of drug resistance, particularly in TB-endemic areas.

Keywords: HIV, Pulmonary tuberculosis, Co-infection, Chest radiography

BACKGROUND

Pulmonary tuberculosis (PTB) is caused by *Mycobacterium tuberculosis (MTB*), a slow-growing, aerobic bacterium with a waxy cell wall that resists Gram staining. Discovered by Robert Koch in 1882, MTB requires specialized staining methods like Ziehl–Neelsen or auramine for identification.[1] According to the WHO, 10.6 million people were infected with PTB in 2021, with Pakistan ranking 5th among high-burden countries, reporting a prevalence of 348 per 100,000 populations.[2,3] PTB spreads through the airborne route and can manifest as primary, secondary, or miliary TB, primarily affecting the lungs in about 90% of cases. Symptomatic PTB presents with low-grade fever, night sweats, productive cough, occasional hemoptysis, and weight loss.[4]

In primary PTB, chest X-rays may appear normal, but common findings include hilar or mediastinal lymphadenopathy, pleural effusion, and pulmonary consolidation.[5] Post-primary PTB usually involves the upper lobes.[6,7] Diagnosis is confirmed by isolating M. tuberculosis from bodily fluids or tissues.[8]

Human Immunodeficiency Virus (HIV) significantly increases the risk of PTB, with those living with HIV being 30 times more likely to develop the disease. PTB is a leading cause of death in HIV-infected individuals, accounting for one in five HIV-related deaths. Advanced immunosuppression in HIV patients increases the risk of extra pulmonary and disseminated TB, with common presentations including lymphadenitis and pleural involvement, often leading to

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severe illness if not diagnosed and treated promptly. [9, 10, 11, 12]

Research has explored the radiographic findings in HIV and PTB co-infection. A study in southern Nigeria found that bilateral cavitary lesions, patchy opacities, and hilar opacities were more prevalent in individuals with PTB/HIV co-infection compared to those with PTB alone.[13] The current study aimed to identify chest radiological patterns in PTB patients with and without HIV, using chest X-rays as the primary diagnostic tool.

MATERIAL AND METHODS

A prospective, single-center observational study was conducted at The Aga Khan University Hospital in Karachi, Pakistan from May 2023 to April 2024. Patients were included if they were 18 years of age or older, with a diagnosis of PTB confirmed by microbiological testing, had undergone chest imaging i.e.: Chest X-rays or CT scans and confirmed for HIV using ELISA testing. Individuals were excluded if they were under 18 years of age, lacked chest imaging, had a negative or unverified diagnosis of PTB, had extra pulmonary TB, or had pre-existing interstitial or structural lung diseases, and had drug resistant PTB verified through microbiological testing. Additionally, patients with concurrent lung infections or malignancies were also excluded from the study.

Eligible patients enrolled in the study were followed with chest X-rays, CT scans when available, HIV test results (CD4 counts for HIV-positive individuals). Chest CT scans were accessible for review in 4 HIV-positive patients and 15 HIV-negative patients. The radiological investigations were initially interpreted by pulmonologist and subsequently reviewed by a radiologist to enhance the accuracy and consistency of the findings of our study. The study received approval from the hospital's ethical review committee (ERC 2023-8652-24644) dated 20th April 2023, and a waiver of informed consent was granted.

Statistical analysis was performed using SPSS version 19. Descriptive statistics were reported as means ± standard deviations or medians with interquartile ranges for quantitative variables and as frequencies and percentages for qualitative variables. Fisher's exact test, unpaired t-test, and Chi-square test were utilized for comparative analyses, with statistical significance defined as $p < 0.05$.

RESULTS

A total of 116 patients were included, with a mean age of 52.23 ± 13.43 years. Of these, 70.7% (n=82) were males. The most prevalent comorbidity was diabetes mellitus, affecting 38.8% (n=45) of patients (Table-I).

PTB was diagnosed via sputum in 75.9% (n=88) of cases, bronchoscopy in 22.4% (n=26), and tissue biopsy in 1.7% (n=2). AFB smear was positive in 60.3% (n=70) of patients, AFB culture in 85.3% (n=99), and Gene Xpert in 95.7% (n=111). HIV positivity was detected in 16.4% (n=19) of PTB patients, with a median CD4 count of 119 cells/mm³ (IQR= 65.00 – 307.00). The majority of patients (95.7%, n=111) were treated, while 4.3% (n=5) were lost to follow-up (Table-I).

Among the 97 patients with HIV -ve PTB, the mean age was 54.21 ± 12.56 years, compared to 42.16 ± 13.49 years in the HIV +ve PTB group ($p < 0.0001$). Male predominance was noted in both groups, with 66.0% (n=64) in the PTB group and 94.7% (n=18) in the co-infection group, Hypertension was significantly more common in the PTB-only group (39.2%, n=38, $p = 0.016$). No other comorbidities showed significant differences between the groups (Table-II).

Consolidation was the most prevalent radiological finding, present in 64.7% (n=75) of all patients. Alveolar infiltrates were the second most common finding, seen in 50.9% (n=59) of patients, with a significant predominance in the PTB + HIV group (78.9%, n=15) compared to the PTB-only group (45.4%, n=44) ($p = 0.007$) as shown in Figure-II and Figure 03. Reticular infiltrates were observed in 27.6% (n=32) of patients, more frequently in the PTB-only group (32.0%, n=31) compared to the co-infection group (5.3%, n=1). Cavitary infiltrates were exclusive to the PTB-only group (27.8%, n=27, $p = 0.006$) as shown in Figure-I.

In the right lung, the most commonly affected lobe was the upper lobe, exclusively observed in the PTB-only group (57.7%, n=56, $p < 0.0001$). The right middle lobe was affected in both groups, with no significant difference (37.1%, n=36 vs 26.3%, n=5, $p = 0.368$). Conversely, the right lower lobe was significantly more involved in the co-infection group (73.7%, n=14 vs 5.2%, n=5, $p < 0.0001$).

In the left lung, the upper lobe was similarly affected only in the PTB-only group (52.6%, n=51, $p < 0.0001$), while the lower lobe was predominantly affected in the

co-infection group (78.9%, n=15 vs 4.1%, n=4, p < 0.0001). Overall, patients with PTB + HIV co-infection exhibited a clear pattern of lower lobe involvement, while those with PTB without HIV showed predominantly upper lobe involvement.

Table-I: Clinical characteristics of patients with PTB Only and PTB + HIV co-infection.

Clinical Characteristics	Total (*n*=116)
PTB Diagnosis	
Sputum	88 (75.9%)
Bronchoscopy	26 (22.4%)
Tissue	2 (1.7%)
AFB Smear	70 (60.3%)
AFB Culture	99 (85.3%)
Gene Xpert	111 (95.7%)
CD4 Count (cells/mm^3)	119.00 (65.00 – 307.00)
Outcomes	
Lost to Follow Up	5 (4.3%)
Treated	111 (95.7%)

PTB, Pulmonary Tuberculosis; HIV, Human Immunodeficiency Virus; and AFB, Acid-Fast Bacilli. Values are presented as Mean ± Standard Deviation (SD), Median and Interquartile Range (IQR), and Frequency.

Table-II: Comparison of Clinical Characteristics between PTB Only and PTB + HIV Co-Infection

Clinical Characteristics	PTB Only (*n*=97)	PTB + HIV Co-Infection (*n*=19)	*P* value
Age (Years)	54.21 ± 12.56	42.16 ± 13.49	**<0.0001**
Gender			
Female	33 (34.0%)	1 (5.3%)	**0.012**
Male	64 (66.0%)	18 (94.7%)	
Comorbidities			
Diabetes Mellitus	41 (42.3%)	4 (21.1%)	0.083
Hypertension	38 (39.2%)	2 (10.5%)	**0.016**
Ischemic Heart Disease	10 (10.3%)	0 (0.0%)	0.364†
Chronic Liver Disease	5 (5.2%)	1 (5.3%)	1.000†
Malignancy	3 (3.1%)	0 (0.0%)	1.000†
Chronic Kidney Disease	5 (5.2%)	0 (0.0%)	0.590†
AFB Smear	58 (59.8%)	12 (63.2%)	0.784
AFB Culture	83 (85.6%)	16 (84.2%)	1.000†
Gene Xpert	92 (94.8%)	19 (100.0%)	0.590†

PTB, Pulmonary Tuberculosis; HIV, Human Immunodeficiency Virus; and AFB, Acid-Fast Bacilli. Values are presented as Mean ± Standard Deviation (SD) and Frequency (%). †Fisher's Exact Test

Table-III: Comparison of radiological abnormalities between PTB only and PTB + HIV co-Infection.

Radiological Features	Total (*n*=116)	PTB Only (*n*=97)	PTB + HIV Co-Infection (*n*=19)	*P* value
Right Upper Lobe	56 (48.3%)	56 (57.7%)	0 (0.0%)	**<0.0001**
Right Middle Lobe	41 (35.3%)	36 (37.1%)	5 (26.3%)	0.368
Right Lower Lobe	19 (16.4%)	5 (5.2%)	14 (73.7%)	**<0.0001**†
Left Upper Lobe	51 (44.0%)	51 (52.6%)	0 (0.0%)	**<0.0001**
Left Lower Lobe	19 (16.4%)	4 (4.1%)	15 (78.9%)	**<0.0001**†
Cavitation	27 (23.3%)	27 (27.8%)	0 (0.0%)	**0.006**†
Consolidation	75 (64.7%)	61 (62.9%)	14 (73.7%)	0.368
Reticulonodular Infiltrates	32 (27.6%)	31 (32.0%)	1 (5.3%)	**0.017**
Hilar Lymphadenopathy	12 (10.3%)	9 (9.3%)	3 (15.8%)	0.413†
Fibrosis	6 (5.2%)	6 (6.2%)	0 (0.0%)	0.587†
Pleural Thickening	13 (11.2%)	13 (13.4%)	0 (0.0%)	0.123†
Miliary Pattern	5 (4.3%)	5 (5.2%)	0 (0.0%)	0.590†

Alveolar Infiltrates	59 (50.9%)	44 (45.4%)	15 (78.9%)	**0.007**
Air Fluid Level	3 (2.6%)	3 (3.1%)	0 (0.0%)	1.000†
Tree in Bud Infiltrates	14 (12.1%)	14 (14.4%)	0 (0.0%)	0.122†

PTB, Pulmonary Tuberculosis; and HIV, Human Immunodeficiency Virus Values are presented as Frequency (%). †Fisher's Exact

Figure-I: Chest X-ray PA view of HIV negative PTB patient demonstrating non-homogenous patchy infiltrates on Right mid zone with thick walled cavity on right side.

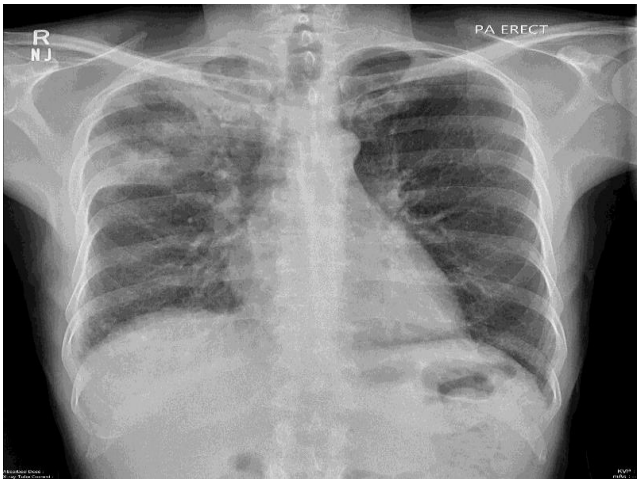

Figure-II: Chest X-ray PA view of HIV negative PTB patient demonstrating alveolar infiltrates in right upper zone.

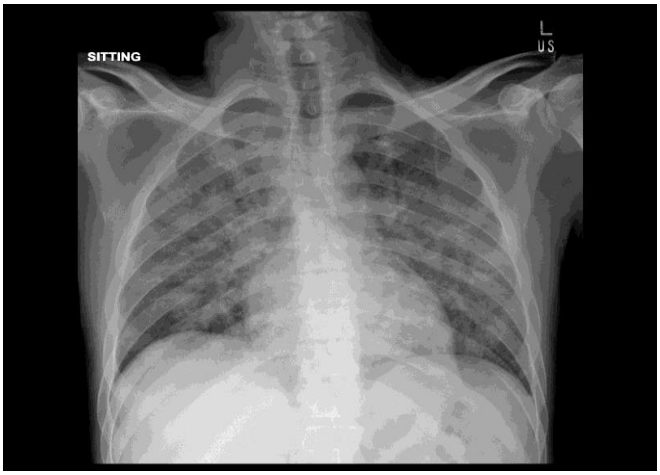

Figure-III: Chest X-ray AP view of HIV positive PTB patient demonstrating bilateral alveolar infiltrates in both lungs.

DISCUSSION

In this study, we identified radiological differences between patients of PTB with and without HIV infection using Chest X-ray as primary diagnostic tool. Our findings reveal significant differences in the demographic and radiological profiles of these two groups, contributing valuable insights to the diagnosis of PTB in the context of HIV co-infection.

In our cohort, there was male predominance in PTB + HIV co-infected group. This trend aligns with previous research highlighting the vulnerability of male populations to HIV-associated TB.[17] On chest radiography, while consolidation was the most prevalent finding across all patients, significant differences were observed when comparing other features between the two groups. Alveolar infiltrates were more prevalent in the co-infected group, whereas reticular infiltrates were more commonly observed in the PTB-only group. The absence of cavitation in HIV co-infected patients in our study is supported by existing evidence that individuals with HIV are less likely to present with cavitations compared to those without HIV.[16] This finding is further supported by studies from Aline Been ***et al***., L B Hirakata ***et al***. and Jese Kistna ***et al***. which reported significantly lower rates of cavitatory infiltrates in HIV-TB co-infected patients.[16,18,19]

Similarly, Sunita Grover ***et al***. observed no cavitary lesions in HIV-PTB co-infected patients on chest X-rays [20]. This is probably because HIV-positive patients do not develop the strong cell-mediated response needed to produce granulomas and ensuing cavities.[16, 21, 22] As HIV progresses and CD4+ T-lymphocyte counts decrease, the risk of developing active PTB increases, and the likelihood of atypical clinical and radiologic presentations also rises. These HIV-related changes in PTB presentation can lead to diagnostic challenges, particularly in patients who are unaware of their HIV-positive status.[14] These findings highlight the need for clinicians to be vigilant in recognizing these atypical presentations in HIV co-infected patients and screen patients timely.

Several studies, including those by A M Saks ***et al*** and A N Leung ***et al***., have reported higher rates of lymphadenopathy in co-infected patients.[23,24] In contrast, our findings showed no significant differences in lymphadenopathy between the PTB-only and PTB-HIV co-infected groups.

Our study found a significant difference in involvement of different lobar segments of lungs between the two groups. The upper lobes were predominantly affected in the PTB-only group, whereas the lower lobes were more commonly involved in HIV-positive patients. According to Sunita Grover ***et al*** upper lung zone involvement was more frequent in HIV-negative patients, and mid-lower zone involvement was characteristic of HIV-positive patients.[20] This variation in radiological manifestations reflects the impact of immunosuppression on TB X-ray findings.[20] Most patients in both studies had CD4 counts below 200 cells/µL, which likely contributed to the higher number of atypical findings.[20]

Our study provides valuable insights to clinicians through identification of specific radiological features, such as cavitary infiltrates, that are exclusive to PTB-only patients, thus providing actionable information that can help clinicians tailor treatment strategies. Our study identifies specific radiological features of PTB in both groups, thus equipping health care workers with information to make more informed decisions based on Chest X-rays which is usually the primary diagnostic tool in low resource income countries. The statistically significant differences in radiological findings (e.g., alveolar infiltrates in co-infected patients, p=0.007; reticular infiltrates more common in PTB-only patients, p=0.017) provide robust, evidence-based data that can influence clinical guidelines. This data can be incorporated into algorithms for diagnosing PTB and PTB + HIV in resource-constrained settings, further improving the quality of care provided.

LIMITAIONS

This study has several limitations, including a relatively small sample size, being single center study and the exclusion of important variables, such as the use of immune suppressants and the duration of antiretroviral therapy in HIV PTB positive patients and presence of drug resistance in PTB patients. Additionally, due to the low-resource setting and limited access to advanced imaging technologies, we used chest X-rays as primary diagnostic tool for radiological comparison between the two groups in our study.

Future research should aim to address these limitations by including larger, more diverse populations and examining the impact of these additional factors on the presentation and outcomes of PTB in HIV co-infected patients.

CONCLUSION

In conclusion, our study highlights key differences in radiological characteristics of PTB patients with and without HIV co-infection. In HIV-positive patients with pulmonary tuberculosis (PTB), the radiological presentation differs significantly from those without HIV, with a higher prevalence of lower lobe involvement and atypical patterns like the absence of cavitation. Clinicians should be vigilant in identifying these unique radiological features on Chest X-rays to ensure early diagnosis and treatment, especially in regions with a high TB burden and where accessibility to advanced imaging is difficult. These insights are crucial for preventing misdiagnosis, improving patient outcomes, and mitigating the risk of drug resistance in co-infected individuals.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Mir Musaib Alavi: Data collection, curation, validation, drafting and editing of manuscript, data interpretation, final approval, agreement to be accountable for all aspects of the work

Javaid Ahmed Khan: Conceptualization, supervision, revision of manuscript and suggestions, study design., final approval, agreement to be accountable for all aspects of the work

Iffat Khanum: Data acquisition, resources acquisition, supervision, questionnaire design, final approval, agreement to be accountable for all aspects of the work

Salva Shariq: Data collection, literature search, manuscript writing, final approval, agreement to be accountable for all aspects of the work

Sameen Alavi: Data curation, statistical analysis, interpretation of data and visualization, final approval, agreement to be accountable for all aspects of the work

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