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Original Research Article

Demographic, Clinical, Radiological and Microbiological Profile of HIV-TB Coinfected Patients

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Abstract

Background: The rising incidence of tuberculosis among HIV-positive people, estimated at 5-8% per year, the high HIV seroprevalence among tuberculosis patients, the occurrence of tuberculosis among AIDS patients, and the concurrent increase in tuberculosis notifications all point to a link between tuberculosis and HIV. The impact of HIV-TB coinfection on resource-limited countries has alarming social and medical implications, and already overburdened health facilities must now deal with a rapidly growing tuberculosis epidemic. Therefore, our study aimed to assess the demographic, clinical, radiological, and microbiological profile of HIV-TB coinfected patients.

Methods: A total of 150 HIV seropositive adult tuberculosis patients who were admitted to the IPD of the Pulmonary Medicine Department and attended the OPD and ART centre were studied. It is a cross-sectional, observational, descriptive study of HIV seropositive patients with tuberculosis.

Results: The study involved 15-65-year-old patients with respiratory symptoms, including cough (50%), lymphadenopathy (29%), pallor (51%), oral candidiasis (19%), icterus (4%), tachypnoea (13%) and pedal oedema (3%). Extra-pulmonary, pulmonary, and disseminated TB was present in 63%, 28% and 9% of patients. Considering zonal distribution, upper-zone infiltrations were observed in 4% of cases, whereas mid and lower-zone infiltrations were observed in 12%. Furthermore, consolidations (7%), fibro-cavitary lesions (4%), pleural effusion (21%), pneumothorax (1%), and hilar lymphadenopathy (8%) were also found in the patients. Microbiological profiles showed 60% of patients with upper zone lesions exhibited sputum +ve PTB, while 40% had sputum -ve PTB.

Conclusion: Many patients were undernourished, with a BMI of <18.5 kg/m^2. Common symptoms included cough and pallor. Extra-pulmonary TB was the most common type of HIV-TB coinfection. Zonal distribution was more in mid and lower zones. The most frequently encountered radiological findings included pleural effusion and infiltrations. Sputum positivity was more common in upper-zone lesions.

Keywords: HIV-TB Coinfection, *Mycobacterium tuberculosis,* Radiological profile, Microbiological profile, Lesions, PTB

Introduction

HIV-TB coinfection remains a major contributor to infectious diseases in developing countries, particularly in resource-limited countries [1]. The "Unholy Alliance" between HIV and *M. tuberculosis* negatively affects host immunity [2], posing a serious public health and socioeconomic problem. According to the World Health Organization's Global Tuberculosis Report 2014, 1.5 million people died and 9 million contracted TB in 2013, including 3,60,000 HIV-positive adults [3]. The 2020 Global TB Report states that those living with HIV have an 18-fold increased risk of developing active TB illness. They are three times more likely to pass away while receiving treatment, even when on antiretroviral medication (ART) [4]. The India TB report shows an increasing trend of mortality rates among HIV-TB coinfected patients, with 1/5th of the world's TB cases occurring in India [5].

There are 2.31 million HIV-positive adults in India, and 4.9% of new adult TB infections are HIV-positive[6].TB is the most frequent opportunistic infection among HIV-infected patients in India [6], posing a danger even after successful ART initiation [7]. Compared to the HIV-negative population, HIV patients are 100 times more likely to develop active TB [8]. The likelihood of developing tuberculosis in India is estimated to be seven cases per 100 person-years at risk, compared to a 10% lifetime risk for an immunocompetent host [6].

HIV and TB can shorten lifespans without treatment, with untreated latent TB and HIV infection being the strongest risk factors for TB disease progression. 75% of HIV-infected patients with TB had pulmonary involvement [9]. HIV and tuberculosis have a bidirectional and synergistic relationship, with clinical symptoms dependent on immunosuppression levels. An HIV +ve person with a cough lasting longer than 2-3 weeks, weight loss, tiredness, unexplained dyspnea, chest pain, or hemoptysis should be suspected of having tuberculosis and investigated further.

Extra-pulmonary TB is the most common cause of pyrexia of unexplained origin (PUO) in HIV +ve people in underdeveloped countries. The most prevalent extra-pulmonary form of TB is lymph node involvement, with the cervical region being the most common [9]. Persistent glandular lymphadenopathy (PGL) mimics nodal tuberculosis. In contrast to PGL lymph nodes, which are asymptomatic, symmetrical & non-tender, TB lymph nodes are often larger, painless, asymmetric, and matted and may be linked to constitutional symptoms or mediastinal hilar lymphadenopathy on chest X-ray. Diagnosis can be made through FNAC or lymph node biopsy. *Mycobacterium* is a common cause of PUO, especially in immunocompromised patients. However, it isn't easy to diagnose since blood culture utilizing quick culture techniques such as BACTEC is required [9].

To address this serious issue, more emphasis should be given to enhancing TB control programmes in underdeveloped countries where the incidence of HIV and TB is high. Considering this, our study aims to identify the earliest clinical manifestations, TB types, radiological patterns, zonal distributions, and sputum positivity in HIV-TB coinfected patients from India, thereby aiding in early treatment and preventing the coinfection from spiralling into a vicious cycle.

Materials and Methods

The study was conducted in the Department of Pulmonary Medicine (IPD and OPD) and the ART Centre of VSS Medical College and Hospital Burla over two years (December 2012 to November 2014).

Inclusion Criteria

- ✓ Patients aged 15 years and above.
- ✓ Patients who tested positive for HIV according to National AIDS Control Organization (NACO) guidelines.
- ✓ Patients diagnosed with new tuberculosis (both pulmonary and extra-pulmonary) according to WHO criteria.

Exclusion Criteria

- ✓ Patients not willing to give consent or participate in the study.
- ✓ Patients aged less than 15 years or more than 65 years.
- ✓ Patients who had a history of tuberculosis or were diagnosed with TB before being identified as HIV positive.
- ✓ Any new HIV-positive patient who has already been treated for PTB.
- ✓ Patients receiving long-term immunosuppressive medication or having co-existing immunosuppressive diseases, such as diabetes or chronic kidney disease.
- ✓ Patients on long-term steroid therapy or immunosuppressant therapy.

Methods

A total number of 150 cases of HIV-TB coinfection were enrolled in our study. According to NACO guidelines, serological status of HIV was determined using 3 recombinant enzyme-linked immunoassay (ELISA) methods. Positive results from all three procedures were considered diagnostic of HIV infection. PTB (Pulmonary Tuberculosis) cases were diagnosed among HIV seropositive patients based on clinical history,

physical examination (general & systemic), sputum smear investigation for AFB using Ziehl-Neelson and fluorescent staining methods according to guidelines, and radiologically by chest X-ray and CT scan of the thorax. Extra-pulmonary TB was diagnosed using tests such as FNAC or excisional biopsy, pleural fluid analysis for AFB, ADA, glucose, protein, and cytology, ascitic fluid analysis for ADA, cytology, CSF analysis, lumbar puncture, histopathological study of diseases, tissue biopsy, culture of specimen for M. tuberculosis, and CT Scan of the brain and abdomen. Routine baseline investigations like complete hemogram, ESR, blood glucose levels, serum electrolytes, LFT and RFT were conducted on all the patients. Lateral view of chest X-ray, USG of the abdomen, CT scan and USG of the thorax were performed on select cases as needed to establish the diagnosis.

Statistical Analysis

All relevant data were collected in the proforma designed for the study and subsequently recorded in a Master Chart in the Microsoft Excel Program 2010. Data analysis was done with the help of a computer using SPSS version 16.0 statistical software. The statistical approaches used in the current study were the cross tabs process, descriptive statistics, frequencies and percentages, and ANOVA-analysis of various two-way tests. $p<0.05$ was considered significant.

Ethical Considerations

The Institutional Ethics Committee (Ethics Committee approval number: IEC/IRB:17/12 dated 12 Oct 2013) of the "VSS Medical College & Hospital" Burla, India approved the study and informed consent was obtained from the patients before the study.

Results

In our study, 150 HIV-TB coinfected patients were studied, including both pulmonary and extra-pulmonary TB cases. Most cases in the study's population were in the age range of 31 to 40 years (40 % men & 4 % women), followed by 21 to 30 years (16 % men & 6 % women). Most males were in the age range of 31 to 40 years, while most females were in the 21 to 30-year range (40 % & 6 %, respectively) (Figure 1). The age of the study subjects ranged from 15-65 years. The mean age was 36.32±9.93. 68.27% of male patients were aged 26.82 (35.83-9.01) to 44.84 (35.83 + 9.01) years. Similarly, 68.27% of female patients were aged 25.12 (38.56-13.44) to 52 (38.56 + 13.44) years

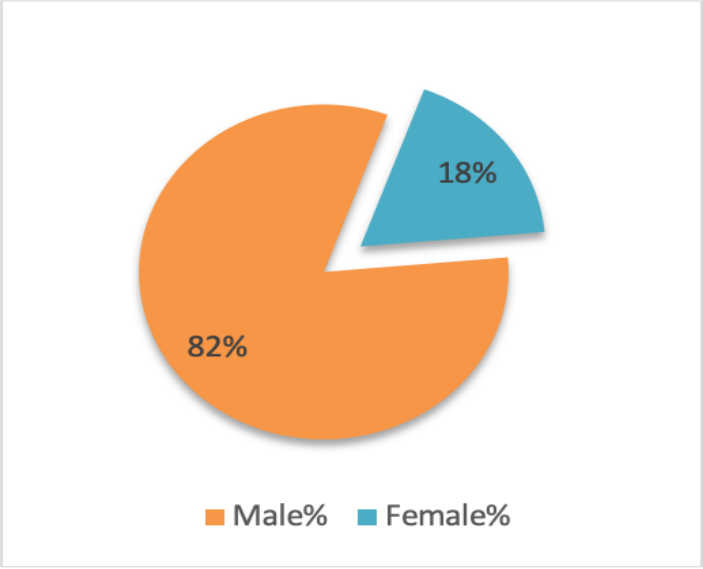


Figure 1: Sex distribution of TB patients

The most common vocations in the research group were drivers (36%), housewives (16%), farmers (11%), labourers (10%), businessmen (8%), hotel workers (4%), storekeepers (3%), private company workers (3%), weavers (2%), factory workers (2%), mechanics (1%), and printing press workers (1%). The most often reported constitutional ailment was weight loss (69%), followed by fever (67%) and anorexia (57%). The most common presenting symptom of the respiratory symptoms identified was cough (50%), followed by chestpain (29%), expectoration (14%), dyspnea (12%), and hemoptysis (2%).

At 7% frequency, gastrointestinal symptoms such as nausea/vomiting, constipation, diarrhoea, jaundice, and abdominal distension were noted. Neurological symptoms such as headache and tingling/numbness were reported at a similar rate (3% each). Physical examination showed BMI <18.5kg/m^2 in 42%, pallor in 51%, lymphadenopathy in 29%, oral

candidiasis in 19%, tachypnea in 13%, icterus in 4% and pedal oedema in 3% (Figure 2).

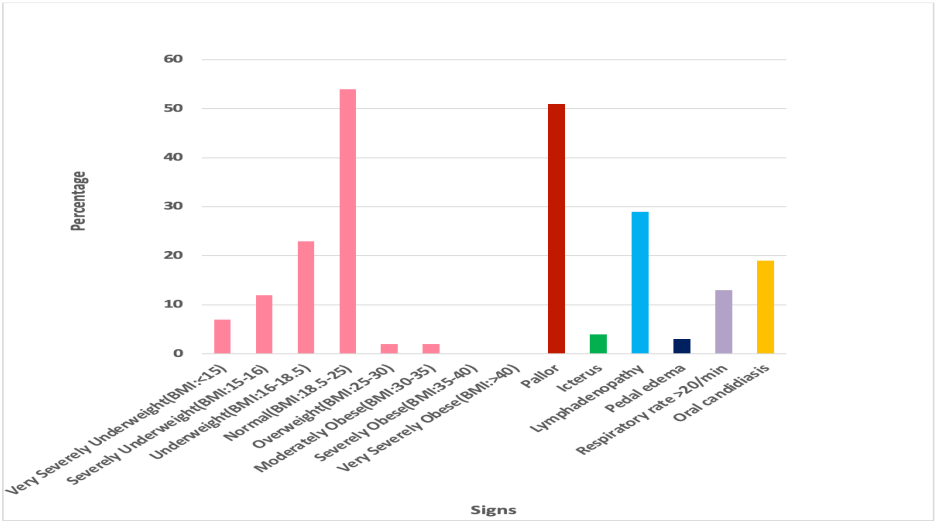
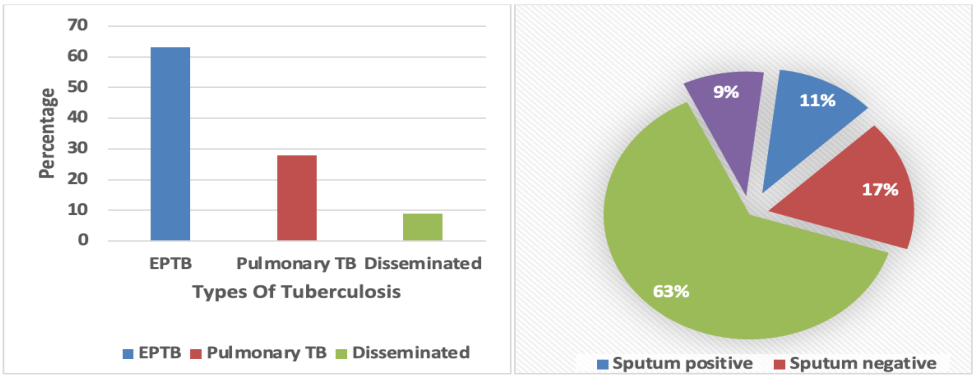


Figure 2: Physical signs of TB patients

Among the patients studied, extra-pulmonary TB was observed in 63%, pulmonary TB was observed in 28% (sputum +ve PTB in 17% and sputum –ve PTB in 11%), and disseminated TB was observed in 9% of the cases (Figure 3).



(a) (b)

Figure 3: (a) Types of tuberculosis; (b) Distribution of types of tuberculosis

Among the patients with extra-pulmonary TB, TB lymphadenitis was found in 40%, pleural effusion in 29%, CNS TB in 5%, abdominal TB in 14%, bone and joint TB in 3% and cold abscess in 1%. Tuberculin negativity i.e induration of <5mm was seen in 33% of the patients and tuberculin positivity i.e. induration of ≥5mm was seen in 67% of patients (Figure 4).

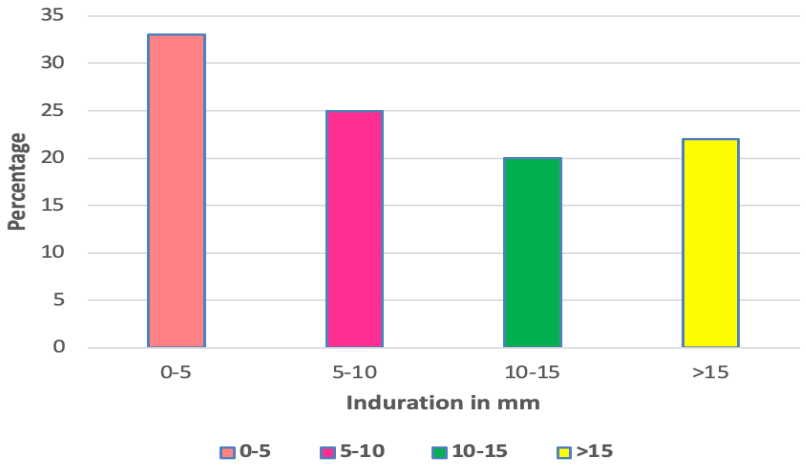


Figure 4: Tuberculin negativity and positivity in TB patients

Among the total patient population, upper zone infiltrations were observed in 4%, mid and lower zone infiltrations were observed in 12%, consolidations were seen in 7%, fibro-cavitary lesions were seen in 4%, bilateral infiltrative lesions + miliary lesions were seen in 3% patients. Regarding extra-pulmonary lesions, pleural effusion was found in 21%, pneumothorax was seen in 1%, and mediastinal/hilar lymphadenopathy was seen in 8%. The chest X-ray was normal in 40% of the cases (Figure 5).

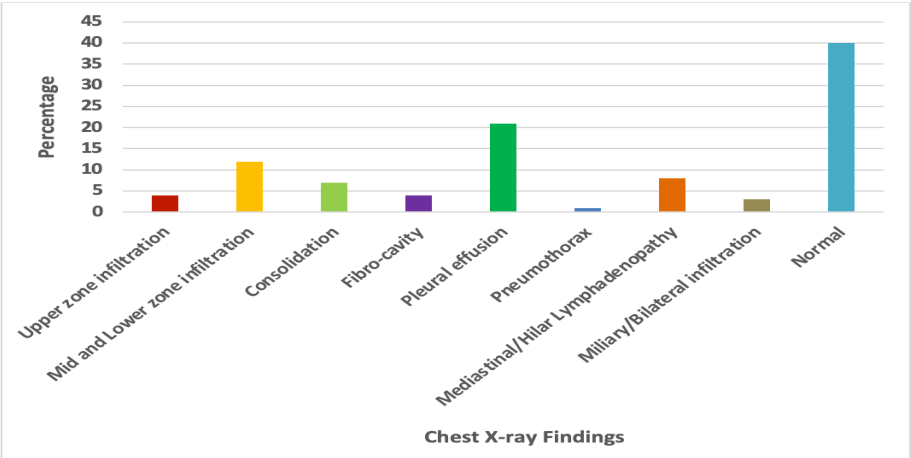


Figure 5: Chest x-ray findings

60% of patients with upper zone lesions exhibited sputum +ve PTB, while 40% had sputum -ve PTB. However, 78.8% of patients with mid/lower zone lesions showed –ve PTB and 21.1% showed sputum +ve PTB. Furthermore, 84.6% of patients with multiple zone lesions had sputum –ve PTB and 15.4% had sputum +ve PTB (Figure 6,7). This is statistically significant with $p<0.001$(HS).

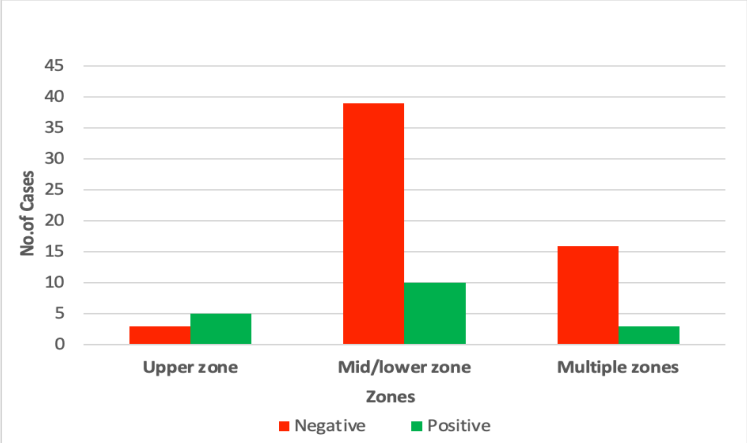


Figure 6: Correlation between sputum smear AFB status and zonal distribution of lesions in x-ray of chest

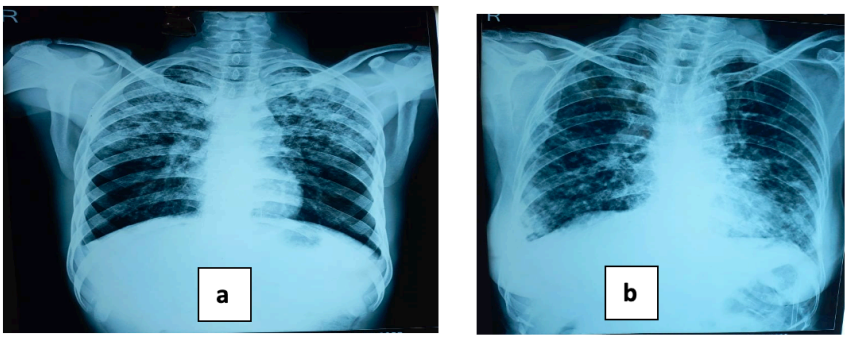


Figure 7a: A Chest X-ray of a male patient with PLHA and sputum +ve pulmonary tuberculosis showing bilateral upper and mid zone infiltrations; 7b: A Chest X-ray of a female patient with PLHA and pulmonary tuberculosis shows bilateral infiltration covering the right upper, mid and lower zone along with the left mid and lower zone.

Discussion

In our study group, 82% of the participants were males and 18% were females. This is analogous to Beena and Pai's[10] investigation, where 68.9% were males, while 31% were females. NACO report also showed 61% males and 39% females [11]. This is like the study by Rajasekaran *et al.* [12].

Males in our study had an average age of 35.83 years, while females had an average age of 38.56. This is like the study done by Rajasekaran *et al.* [12], in which 84.6% of patients were between the ages of 21 and 40, and NACO report also showed that around 83% of patients were between the ages of 15 and 49 [11]. This indicates the disease's prevalence in the sexually active age range.

The most prevalent occupation was drivers (36%) followed by housewives (16%), farmers (11%), labourers (10%), businessmen (8%), hotel workers (4%), students (3%), employees of private companies (3%), factory workers (2%), weavers (2%), mechanics (1%), and printing press workers (1%), indicating the coinfection affected people from a variety of occupational groups. This is comparable to the studies of Purohit *et al.* [13], Thanasekaran *et al.* [14], and Piramanayagam *et al.* [15], in which truck drivers were the most prevalent occupation seen. According to a NACO survey, some HIV patients were long-distance truck drivers and migrant workers who work alone. According to Mohanty *et al.* [16], 36.8% of patients worked as manual workers. Zuber *et al.* [17] also identified a similar occupational profile. The present study showed that in all the married females, both husband and wife were affected except for one who had received blood transfusions during a prior pregnancy. This result was like that of Swaminathan *et al.* [18], who found that in the case of married females, except in one instance, both the husband and wife were impacted. The percentage distribution of occupations is thus found to vary among research, partly due to variations in employment trends and the method used to choose the patients.

In our study group, weight loss was the most prevalent constitutional symptom (69%) and was followed by fever (67%) and anorexia (57%). This is in comparison with the Beena and Pai [10] study, which found 100% anorexia and 100% weight loss. Fever was comparable to that reported by Deivanayagam *et al.* [19] and Jaryal *et al.* [20]. Cough was the most prevalent respiratory symptom in our study. Still, its prevalence (50%) was significantly lower than that in studies by Deivanayagam *et al.* [19] (85.4%), Swaminathan *et*

al. [18] (97%), and Beena and Pai [10] (100%). Compared to their research, the other respiratory symptoms, such as haemoptysis (2%), expectoration (14%), and chest pain (29%), were also significantly fewer. This might be because our study had more extra-pulmonary tuberculosis cases than pulmonary cases of HIV +ve patients with TB. As compared to Beena and Pai [10] (48.3%), Swaminathan *et al.* [18] (18%), and Deivanayagam *et al.* [19] (11.5%) studies, hemoptysis (2%) was also much lower in our study. This might be because there are not many fibro cavitary lesions among the few, who already have pulmonary tuberculosis.

The most prevalent indicator observed in our study was pallor (51%). Our investigation found that 42% of the cases were underweight, as measured by a BMI of 18.5kg/m^2, comparable to Swaminathan *et al.* [18] (47%). Respiratory distress was observed in 13% of cases compared to 42.94% in Deivanayagam *et al.* [19] due to fewer pulmonary TB cases in our study. Lymphadenopathy was found in 29% of cases, which is comparable and the same as that of Swaminathan *et al.* [18] (29%). This is because extra-pulmonary tuberculosis was more prevalent in our study, with TB Lymphadenitis being the most common.

In our study, extra-pulmonary tuberculosis was the most frequent, accounting for 63% of cases. However, 28% had pulmonary tuberculosis, whereas 9% had disseminated tuberculosis (Figures 3 and 4). This is comparable to that of Jaryal *et al.* [20] study; they found 54.6% cases of extra-pulmonary tuberculosis, 28% of pulmonary tuberculosis and disseminated tuberculosis was 17.4%. Other studies by Kumar *et al.* [21] and Deivanayagam *et al.* [19] had a significantly higher proportion of pulmonary tuberculosis.

Sputum positivity (12%) in our study was comparable to Deivanayagam *et al.* [19] (15%) and Kumar *et al.* [21] (21.4%) studies. However, it was significantly lower than in the investigations of Swaminathan *et al.* [18] (72%) and Zuber *et al.* [17] (49.33%). Sputum culture was also used in these two studies. Our study's low sputum positivity could be attributed to reduced cases of pulmonary tuberculosis and a shortage of cavitary lesions.

Pleural effusions (21%) and infiltrative lesions (16%) were the most prevalent X-ray findings, whereas mediastinal/hilar lymphadenopathy was found in 8% of cases (Figure 6). This could be explained by our study's increased number of extra-pulmonary tuberculosis cases. This is not comparable to all the other studies, which reveal a higher proportion of infiltrative lesions in HIV-linked TB. Upper zone infiltrations were identified in 4% of cases, mid and lower zone infiltrations in 12% of patients, and miliary/extensive lesions in 3%. Deivanayagam *et al.* [19] showed a similar pattern and frequency of distribution.

Our investigations observed consolidation in 7% of patients and fibro-cavitary lesions in 4%, whereas the chest X-ray was normal in 40% of the patients.The radiological symptoms in our study were diverse and heterogeneous. This is because most of our patients had extra-pulmonary TB, and the degree of immunosuppression influences the appearance of tuberculosis on X-rays.

TB lymphadenitis was found in 40% of cases of isolated extra-pulmonary tuberculosis, followed by pleural effusion in 29%, abdominal tuberculosis in 22%, CNS TB in 5%, bone and joint TB in 3%, and cold abscess(left psoas abscess) in 1%. Our investigation's most typical extra pulmonary TB manifestations were lymphadenopathy and pleural effusion. These results concur with research from Deivanayagam *et al.* [19] and Kumar *et al.* [21]. In our study, the higher percentages are due to the number of extra-pulmonary TB among all the cases of HIV-associated TB.

In the present study, 67% of the patients reported tuberculin positivity (>5mm induration with TU), of which 25% had induration in the 5-9mm range, 20% in the 10-15mm range, and 22% had induration >15mm. 32% of the patients had tuberculin negativity (Figure 5). This data deviates from the consensus and contrasts sharply with that of Kumar *et al.*[21], who found tuberculin negativity in 85.7% of patients. This could be attributed to the individuals in our study receiving early and rapid diagnosis and having less immunosuppression overall.

Conclusion

The converging dual epidemics of tuberculosis HIV and TB are a major public health challenge. Tuberculosis is the primary cause of death in HIV-infected patients, and HIV infection increases the likelihood of developing active TB in those infected with *M. tuberculosis.* The treatment of HIV-TB coinfection is complicated, with a high pill burden, overlapping drug toxicities, and the possibility of immune reconstitution inflammatory syndrome. The major challenges are to contain the infection to the lowest, increase awareness and counselling, and maintain a high index of clinical suspicion for early diagnosis and treatment. This study identifies trends in HIV-TB coinfection in demographics, clinical manifestations, radiological patterns, zonal distribution, and microbiological profile. The study reveals a skewed sex ratio of HIV affection in western Odisha, with a higher percentage of male seropositivity than females. Symptoms include fever, pallor, TB lymphadenitis, and pleural effusion. Tuberculin sensitivity is higher in this study, possibly due to a larger patient population and early diagnosis. The study found that the early stages

of the disease showed typical radiological manifestations of upper zone affection and fibro cavitary lesions, while atypical manifestations occurred later. Many patients had normal chest X-rays, emphasizing the need for early diagnosis and timely treatment.

Strengths and Limitations

1) The small size of the sample population.
2) CD4 counts, though available for all patients, could not be followed at regular intervals to assess the prognosis due to various inconveniences.
3) Response to therapy and patient follow-up were not considered in all cases.

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