# A MULTI-CENTRE STUDY: CHEST RADIOGRAPHIC FINDINGS IN ADULT PATIENTS WITH HIV/PTB CO-INFECTION AND THEIR CD4+ COUNT.

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***Abstract-***
**INTRODUCTION: Tuberculosis (PTB) is a major global health problem, one-fourth of the world's population is infected with the disease. The radiographic findings are atypical in the immuno-compromised and resemble the primary type.**
**AIM: To determine the relationship between Chest radiographic findings of patients diagnosed with HIV/PTB co-infection and their $CD4^+$ count.**
**METHODS: A cross-sectional, descriptive plain chest radiographic evaluation of pulmonary tuberculosis in patients with HIV/AIDS and their $CD4^+$ count levels.**
**RESULTS: Nineteen subjects with HIV/PTB co-infection had normal chest X-ray findings (CXR). There were more females with CD4+ count < 200/mms$^3$ (44 versus 33 for male to female values) while CD4+ count of > 200/mm$^3$ showed more males (20 versus 15 for male to female values). Lobar pneumonia, miliary, cystic changes, fibrosis, and effusion were seen more in HIV/PTB subjects with CD4+ count < 200/mm$^3$ with p- values of < 0.001, 0.016, 0.10, 0.003, and 0.016 respectively. Atypical CXR findings were seen in more subjects with a CD4+ count of <200mm$^3$ (35) versus a CD4+ count of > 200mm$^3$ (2) with a p-value of 0.001. The typical CXR findings were seen more in subjects with CD4+ counts of > 200/mm$^3$ (27) versus those with CD4+ counts of < 200mm$^3$ (9).**
**CONCLUSION: Patients with HIV/PTB co-infection have a significant chance of manifesting atypical CXR findings like lymphadenopathy than typical CXR findings like volume loss, cavities, or lobar pneumonia.**

***Keywords*: CXR findings, CD4+ count, HIV/PTB co-infection, male-to-female values, radiographic.**

## INTRODUCTION

Tuberculosis (TB) is an infectious bacterial disease caused by closely related gram-positive, acid and alcohol-fast bacteria known as the *Mycobacterium tuberculosis* complex. It most commonly affects the lungs resulting in pulmonary tuberculosis. TB is transmitted from person to person via inhalation of droplets (aerosols) containing a critical dose of bacilli from the throat and lungs of patients with active pulmonary tuberculosis and importantly those with cavities. Once in the lungs, the bacilli are internalized through phagocytosis by the resident macrophages of the lungs. In healthy subjects, infection with *M. tuberculosis* often causes no symptoms since the person's immune system acts to wall off the bacteria.[1.2] Pulmonary tuberculosis is classified as primary or post-primary tuberculosis. The radiographic findings are atypical in the immuno-compromised and resemble the primary type. Atypical distribution of the disease entails the involvement of the anterior segment of the upper lobe, the basal segments of the lower lobe, the right middle lobe, and the lingular segments. Other atypical patterns are diffuse lung infiltrates, mid-zone predilection, bilateral lung involvement, interstitial nodules, pleural effusion, mediastinal or hilar lymphadenopathy, and normal radiograph of the lung.[3] The human immunodeficiency virus (HIV) infection continues to modify the radiographic pattern of pulmonary tuberculosis (PTB). Various strains, new mutants, and super-infection patterns of the HIV virus may cause PTB to be radiographically present in unusual and undocumented ways.[4] There is also an increase in the prevalence and transmission of multidrug-resistant (MDR) and totally drug-resistant *Mycobacterium tuberculosis* strains worldwide.[5,6] Therefore, the current pattern of manifestations of PTB in the face of the ever-evolving dynamics of the HIV virus and the increasing transmission of MDR pulmonary TB should be known. New strains and recombinant forms of the HIV virus may alter the radiographic picture of pulmonary tuberculosis in an entirely new manner.[4] A systematic review and meta-analysis study by Onyedum and colleagues[5] equally revealed high prevalence rates of drug-resistant PTB in Nigeria. According to the study, newly diagnosed patients with PTB and previously treated patients with PTB had prevalence rates of 32% and 53% respectively. It is also reported that there is an increase in the prevalence and transmission of multidrug-resistant and totally drug-resistant MTB strains worldwide.[6]
Tuberculosis is a major global health problem, one fourth of the world's population is infected with the disease.[7] In 2018, there were 10 million new TB cases: 5.8 million among men, 3.2 million among women, and one million among children worldwide. People living with HIV/AIDS accounted for 9% of the total.[7] In 2017, there were also 1.6 million deaths from pulmonary tuberculosis including 0.3 million deaths among people living with HIV.[8] In 2017, the lifetime risk of pulmonary tuberculosis was 17-23 times greater in people living with HIV than in those without HIV infection.[9] The presentation of TB in HIV-negative patients conforms with the known clinical features and investigation findings of TB infection.[10] However, in patients with HIV and reduced immunity, there is a rise in extra-pulmonary forms of tuberculosis.[10]

Globally in 2017, the largest number of new TB cases were recorded in South-East Asia (4,440,000) while 2,480,000 new cases were recorded in Africa.[11] Nigeria currently ranks seventh in the world and second in Africa among the 30 countries with the highest burden of TB, TB/HIV, and multidrug-resistant TB.[12] According to WHO, as of 2016, only 15% of the total burden of the disease was notified.[13] Between 2000 and 2014, an estimated 43 million lives were saved through TB diagnosis and treatment.[14] Globally, TB prevalence is falling at about 3% per year.[15] The global rate of TB case reduction needs to accelerate to 4-5% by 2020 in order to keep the END TB Strategy on track.[16]

**AIM**

To determine the relationship between chest radiographic findings of patients diagnosed with HIV/PTB co-infection and their $CD4^+$ count.

**METHODS**

The study was a cross-sectional, descriptive plain radiographic evaluation of the chest findings of pulmonary tuberculosis in patients with HIV/AIDS and their $CD4^+$ count levels. Institutional consent and authorization for the study were obtained from the various study centers following which ethical clearance was obtained from the Research and Ethics Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi. A detailed explanation of the study was given and written informed consent was obtained from each patient. All patient information and data obtained were treated with the utmost confidentiality. Patients' names were coded. The research assistants were healthcare providers in the different hospitals who freely volunteered to assist in the study. The researchers had a detailed and one-on-one explanation of the study with each one of them. They were educated on obtaining written and informed consent and on how to fill out the sociodemographic part of the questionnaire.

The study population was adults of 18 years and above referred from the PTB/DOTS clinics to the Radiology departments on account of laboratory diagnosis of pulmonary tuberculosis and who had not started HAART medication. The exclusion criteria were patients less than 18 years of age, those who did not give consent, and HIV patients who were currently on HAART medication. Using the consecutive sampling method, eligible participants were recruited until the sample size of 112 was reached. Patients were recruited into the study from the PTB/DOTS clinics of the various study centers. The researchers and the research assistants administered the sociodemographic part of the data and obtained the patient's clinical history. This information was entered into the datasheet. The chest radiographs were interpreted under the supervision of a consultant radiologist and the findings were entered into the study data sheet.

Chest radiographs were taken with the patient standing erect facing the standing bucky of an x-ray machine, arms akimbo or hugging the bucky. The chin was extended and centered on the middle of the top of the cassette. The chest was placed against the cassette. The median sagittal plane was adjusted at right angles to the middle of the cassette. The X-ray beam centered around the $5^{th}$ -$6^{th}$ thoracic vertebra passes through the chest in a posteroanterior direction. For an average patient, the manual method used about 60-70kV and 10-12mAs for a single PA exposure. When the digitizer was used, about 60-70kV and 12-16 mAs were used. A film focus distance of 120cm was used. All exposures were taken at full arrested inspiration.

Laboratory diagnosis of PTB was done using the National TB guidelines.[17] Tests were carried out in the laboratory facilities of the various hospitals. All suspected PTB patients had two sputum samples for Ziehl-Neelson staining and one sample for GeneXpert analysis done. Samples were collected in sterile dry containers. The first sputum sample was collected on the spot. The second sputum sample was an early morning sputum, collected without brushing the mouth or drinking water. Any of these samples were used for the GeneXpert analysis.

HIV screening was done using a serial algorithm. The first line screening was done using Determine ELISA kit®. A second-line test using Unigold ELISA kit® when positive was regarded as confirmatory. When there are conflicting results, a third ELISA kit® (the start pack) was used as a tie-breaker. CD4+ count was determined using the flow technique.[18] Twenty milliliters of the patient's blood was collected using an EDTA bottle, mixed with 20mls of Partec antibody, incubated in the dark for 15 minutes, and then attached to the Partec Cyflow counter for an automated CD4+ count.[4]

The data was entered and cross-checked by two other independent persons. The IBM Statistical Package for Social Sciences (SPSS) Statistics version 20.0 (USA; 2015) for Windows software was used for data analysis. Frequency distribution and two-way tables were used to summarize the data. Chi-square($X^2$) was used to determine the strength of the association between independent and dependent variables. Using mean and standard deviation, descriptive statistics were done for variables like $CD4^+$ count. A test of significance with a p-value of less than 0.05 was considered significant. Logistic regression was carried out.

**RESULTS**

There were 59 females (53.7%) and 53 males (42.3.7%). **Table 1** The highest age specific prevalence was seen in those aged 31-40 years and 41-50 years with values of (23.6%) each. The 81-90 years age group had the least number of subjects with 4 patients (1.6%); 1 female (0.4%) and 3 males (1.2%). **Figure 1**

The average $CD4^+$ count was higher in females than males; 171.01 ± 158.48 (mean ± SD) and 167.60 ± 95.08 (mean ± SD) respectively. The minimum and maximum $CD4^+$ count values, 15 cells/$mm^3$ and 961 cells/$mm^3$ respectively were noted in the females. With females having an average higher count than males. In the female group, those whose $CD4^+$ count was less than 200 cells/$mm^3$ were more, 44 (39.3%) compared to those whose $CD4^+$ count was greater than 200 cells/$mm^3$, 15 (13.45). In the males, 33 subjects (29.4%) had $CD4^+$ count values less than 200 cells/$mm^3$, while 20 (17.8%) had $CD4^+$ count values greater than 200 cells/$mm^3$. **Table 2**

Of the 19 subjects (17%) with normal chest radiographs, 18 subjects (16.1%) had $CD4^+$ count < 200cells/$mm^3$ compared to 1 subject (0.9%) with $CD4^+$ count > 200cells/$mm^3$. This difference was significant with a p-value = 0.006. Opacities were seen more frequently in those with $CD4^+$ count less than 200 cells/$mm^3$, 50 subjects (44.6%) compared with 33 subjects (29.5%) with $CD4^+$

count > 200 cells/mm$^3$. This was significant with a p-value of 0.001. There was a significant difference in the presence of reticular opacities between those with CD4$^+$ count < 200 cells/mm$^3$ seen in 6 subjects (5.4%) and those with CD4$^+$ count > 200 cells/mm$^3$ seen in 8 subjects (7.1%), the p-value was 0.004. In the right upper lung zone, opacities were more among those with CD4$^+$ count greater than 200 cells/mm3, 9 subjects (8%), compared to 6 subjects (5.4%) with CD4$^+$ count less than 200 cells/mm3, with a p-value <0.001. Similarly in the left upper zone, there was a statistically significant difference (Chi-square = 30.16, p-value < 0.001) in the presence of opacities seen in 12 subjects (10.7%) of those with CD4+ count greater than 200 cells/mm3 compared to 4 subjects (3.6%) whose CD4$^+$ count was less than 200 cells/mm$^3$. **Table 3**

In those with lobar pneumonia, subjects with CD4$^+$ count greater than 200 cells/mm$^3$ were significantly higher in number, 12 subjects (10.7%), compared to those whose CD4$^+$ count was less than 200 cells/mm$^3$, 5 subjects (4.5%), with a p-value < 0.001. Of all the subjects with miliary opacities, 11 patients (9.8%) had CD4$^+$ count less than 200 cells/mm$^3$. None of those whose CD4$^+$ count value was higher than 200 cell/mm$^3$ had miliary opacities (p-value = 0.016). Based on the presence of cystic changes in the lungs, the two CD4$^+$ count groups had an equal number of cystic changes 15 (13.4%) respectively. This similarity in the presence of cystic change is statistically significant with a p-value equal to 0.010. Subjects with CD4$^+$ count higher than 200 cells/mm$^3$ showed a slightly higher frequency of fibrosis, 13 subjects (11.6%) compared to those with CD4$^+$ count less than 200 cells/mm$^3$ who numbered 10 (8.9%), the p-value was 0.003. Those with pleural effusion showed that those with CD4$^+$count less than 200cells/mm$^3$ were 31 subjects (27.7%) compared to those with CD4$^+$ count greater than 200cells/ mms$^3$, 6 subjects (5.4%.). This was significant with a p-value of 0.016. Pleural effusion was seen more on the left side, especially in those with CD4$^+$ count less than 200cells/mm$^3$, 21 subjects (18.8%) compared with CD4 count greater than 200cells/mm$^3$ with 1 subject(0.9%), with a p-value of 0.003. The presence of volume loss showed a statistically significant difference between the two CD4$^+$ count groups, the p-value was 0.009. This was seen in 12 subjects (10.7%) with CD4$^+$ count greater than 200 cells/mm$^3$ and in 10 subjects (8.9%) with CD4$^+$ count less than 200 cells/mm$^3$ **Table 4**

Out of a total of 10 subjects (8.9%) who had cavitary lesions, 9 (8%) were seen in the subjects with CD4$^+$ count greater than 200 cells/mm$^3$, in comparison to only 1 subject (0.9%) with CD4$^+$ count greater than 200 cells/mm$^3$. This difference was statistically significant with a p-value < 0.001. The distribution of thick-walled cavities between the two CD4$^+$ count groups was significant, (p-value = 0.002), and it was seen only in those with CD4$^+$ count greater than 200 cells/mm$^3$ 5 subjects (4.5%). Thin-walled cavities were also seen only in those with CD4$^+$ count greater than 200 cells/mm$^3$, with a p-value of 0.008, 4 subjects (3.6%). The distribution of cavities in the right and left mid-zone between the two CD4$^+$ count groups was significant, with p-values of < 0.001 and 0.008 respectively. **Table 5**

On the other hand, in those with HIV/PTB co-infection, the atypical pattern was seen in 37 subjects (14.8%) while the typical pattern was seen in 36 subjects (14.4%). There was no significant relationship between the patient group (PTB only or HIV/PTB co-infection) and the presence of a typical or atypical pattern, the p-value was 0.084. **Table 6**

There was a significant relationship between patient CD4$^+$ count classification and the presence of typical or atypical post-primary PTB pattern, the p-value was < 0.001. In those with a CD4$^+$ count of less than 200 cells/mm$^3$, 35 subjects (31.5%) had an atypical pattern, and 9 (8%) had typical patterns. On the other hand, among those with CD4$^+$ count greater than 200 cells/mm$^3$, 27 subjects (24.1%) had typical post-primary patterns while only 2 subjects (1.7%) showed atypical patterns. **Table 7**

In the group with HIV/PTB co-infection, only lymphadenopathy had an Odd's ratio greater than 1, (OR = 3.115, p-value = 0.007). The rest of the findings; opacities, bronchopneumonia, cystic change, fibrosis, cavities, thick-walled cavity, thin-walled cavity, and volume loss had OR less than 1 (0.323, 0.550, 0.529, 0.480, 0.267, 0.275, 0.263, 0.308) and p-value = 0.001, 0.028, 0.021, 0.013, 0.001, 0.013, 0.020, < 0.001) respectively. HIV/PTB co-infection is, therefore, a strong risk factor for the development of lymphadenopathy. **Table 8**

**Table 1:** Showing the sex distribution and percentages of subjects in the study population**.**

| S/N | SEX | DISTRIBUTION (%) |
|---|---|---|
| 1. | MALE | 53 (47.3%) |
| 2. | FEMALE | 59 (52.7%) |
| | TOTAL | 112 (100%) |

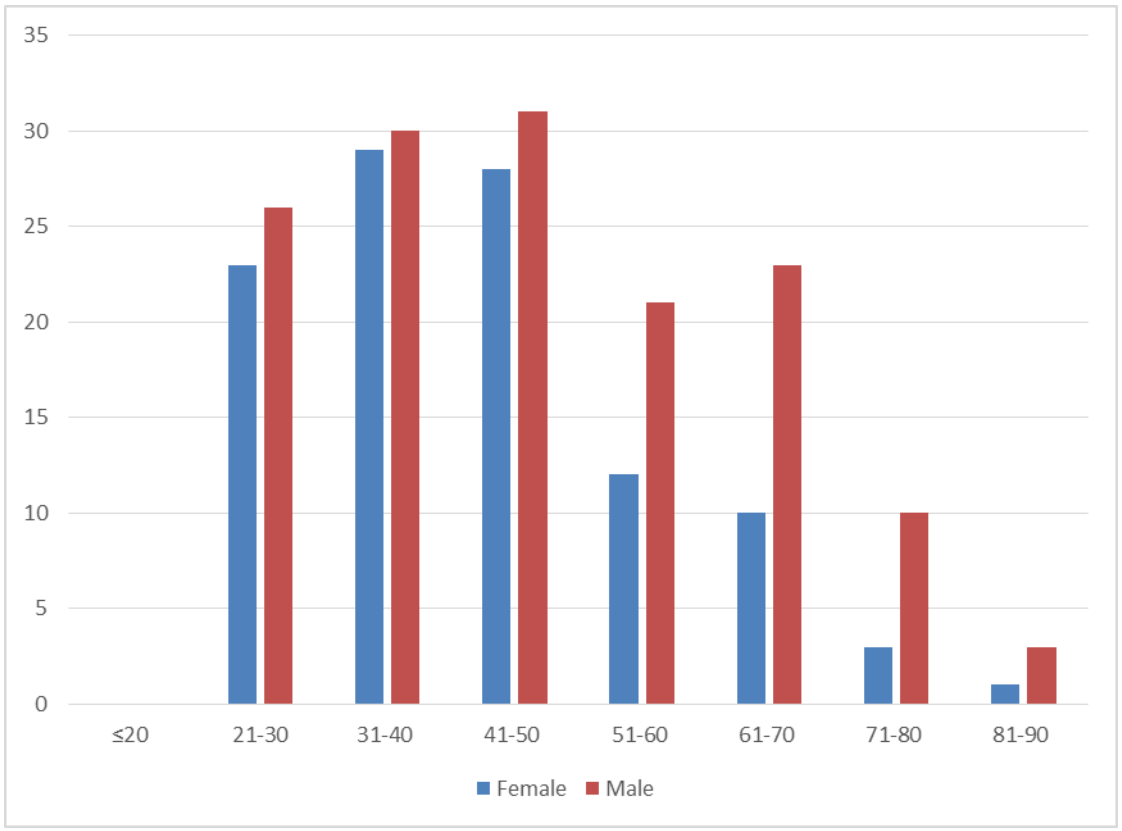


**Figure 1:** Bar chart showing the distribution of age ranges in males and females in the study population

**Table 2**: Mean values of $CD4^+$ counts and $CD4^+$ classification among male and female patients with HIV/PTB co-infection (Normal distribution)

| **$CD4^+$ counts** | **Gender** | | **Total** |
|---|---|---|---|
| | **Male (N=53)** | **Female (N=59)** | |
| Mean ±STD | 167.60± 95.08 | 171.01± 158.48 | 169.40± 131.76 |
| Minimum | 24 | 15 | |
| Maximum | 433 | 961 | |
| **$CD4^+$ Classification** | | | |
| <200 cells/$mm^3$ | 33 (29.4) | 44 (39.3) | 77 (68.7) |
| >200 cells/$mm^3$ | 20 (17.8) | 15 (13.4) | 35 (31.3) |
| **TOTAL** | **53 (47.3)** | **59 (52.7)** | **112 (100)** |

**Table 3:** Chi-square analysis showing the relationship between types of chest opacity, zonal distribution, and $CD4^+$ count in patients with HIV/PTB co-infection.

| CXR findings | Total Freq (%) (n=112) | $CD4^+$ classification | | $\chi^2$ value | p-value |
|---|---|---|---|---|---|
| | | <200 cells/mm$^3$ | >200 cells/mm$^3$ | | |
| **Normal** | 19 (17.0) | 18 (16.1) | 1 (0.9) | 7.192 | 0.006* |
| **Opacities** | 83 (74.1) | 50 (44.6) | 33 (29.5) | 10.802 | 0.001* |
| Alveolar/Nodular | 33 (29.5) | 22 (19.6) | 11 (9.8) | | |
| Interstitial/Reticular | 14 (12.5) | 6 (5.4) | 8 (7.1) | 13.418 | 0.004* |
| Reticulonodular | 36 (32.1) | 22 (19.6) | 14 (12.5) | | |
| **Right lung** | | | | | |
| Lower zone | 2 (1.8) | 2 (1.8) | 0 | | |
| Mid zone | 5 (4.5) | 4 (3.6) | 1 (0.9) | | |
| Mid + lower zone | 7 (6.2) | 7 (6.2) | 0 | | |
| Upper zone | 15 (13.4) | 6 (5.4) | 9 (8.0) | 35.191 | <0.001* |
| Upper + lower | 1 (0.9) | 1 (0.9) | 0 | | |
| Upper + mid zones | 16 (14.3) | 3 (2.7) | 13 (11.6) | | |
| U + M + L zones | 25 (22.3) | 22 (19.6) | 3 (2.7) | | |
| **Left lung** | | | | | |
| Lower zone | 3 (2.7) | 2 (1.8) | 1 (0.9) | | |
| Mid zone | 3 (2.7) | 3 (2.7) | 0 | | |
| Mid + lower zone | 7 (6.3) | 6 (5.4) | 1 (0.9) | | |
| Upper zone | 16 (14.3) | 4 (3.6) | 12 (10.7) | 30.163 | <0.001* |
| Upper + lower | 1 (0.9) | 1 (0.9) | 0 | | |
| Upper + mid-zone | 7 (6.3) | 2 (1.8) | 5 (4.5) | | |
| U + M + L zones | 23 (20.5) | 22 (19.6) | 1 (0.9) | | |

**Table 4:** Chi-square analysis showing the relationship between specific chest findings and $CD4^+$ classification in patients with HIV/PTB co-infection.

| CXR findings | Total Freq (%) (n=112) | $CD4^+$ classification | | $\chi^2$ value | p-value |
|---|---|---|---|---|---|
| | | <200 cells/mm$^3$ | >200 cells/mm$^3$ | | |
| Bronchopneumonia | 66 (58.9) | 45 (40.2) | 21 (18.7) | 0.024 | 0.877 |
| Lobar pneumonia | 17 (15.2) | 5 (4.5) | 12 (10.7) | 14.436 | <0.001* |
| Nodularity | 55 (49.1) | 35 (31.3) | 20 (17.9) | 1.686 | 0.194 |
| Miliary | 11 (9.8) | 11 (9.8) | 0 | 5.544 | 0.016* |
| Cystic change | 30 (26.8) | 15 (13.4) | 15 (13.4) | 6.705 | 0.010* |
| Fibrosis | 23 (20.5) | 10 (8.9) | 13 (11.6) | 8.933 | 0.003* |
| Lymph Node | 20 (17.9) | 16 (14.3) | 4 (3.6) | 1.434 | 0.231 |
| Pleural Effusion | 37 (33.0) | 31 (27.7) | 6 (5.4) | 5.812 | 0.016* |

| | | | | | |
|---|---|---|---|---|---|
| Effusion right side | 18 (16.1) | 14 (12.5) | 4 (3.6) | 0.813 | 0.367 |
| Effusion left side | 22 (19.6) | 21 (18.8) | 1 (0.9) | 9.087 | 0.003* |
| Apical Cap | 13 (11.6) | 6 (5.4) | 7 (6.3) | 3.495 | 0.107 |
| Volume loss | 22 (19.6) | 10 (8.9) | 12 (10.7) | 6.915 | 0.009* |

**Table 5:** Chi-square analysis showing the relationship between lung cavities and $CD4^+$ classification in patients with HIV/PTB co-infection.

| **Chest X-ray radiographic findings** | **Total Freq (%) (n=112)** | **$CD4^+$ classification** | | **$X^2$ value** | **p-value** |
|---|---|---|---|---|---|
| | | **<200 cells/mm$^3$** | **>200 cells/mm$^3$** | | |
| **Cavity** | 10 (8.9) | 1 (0.9) | 9 (8.0) | 17.640 | <0.001* |
| Thick-walled Cavity | 5 (4.5) | 0 | 5 (4.5) | 11.514 | 0.002* |
| Thin-walled Cavity | 4 (3.6) | 0 | 4 (3.6) | 9.125 | 0.008* |
| **Right Lung cavities** | | | | | |
| Mid-zone | 1 (0.9) | 0 | 1 (0.9) | 16.426 | <0.001* |
| Upper zone | 6 (5.4) | 0 | 6 (5.4) | | |
| **Left Lung cavities** | | | | | |
| Mid-zone | 1 (0.9) | 0 | 1 (0.9) | 9.125 | 0.008* |
| Upper zone | 3 (2.7) | 0 | 3 (2.7) | | |
| **Number of Cavities** | | | | | |
| One | 6 (5.4) | 0 | 6 (5.4) | | |
| Two | 2 (1.8) | 0 | 2 (1.8) | | |
| Three | 1 (0.9) | 0 | 1 (0.9) | | |

**Table 6:** Chi-square analysis showing the relationship between post-primary PTB pattern and patient HIV infection status.

| **Post-primary PTB** | **Total Freq (%) (n=250)** | **Patient status** | | **$X^2$ value** | **p-value** |
|---|---|---|---|---|---|
| | | **PTB alone** | **HIV/TB co-infection** | | |
| Atypical | 83 (33.20) | 46 (18.4) | 37 (14.8) | | |
| Typical | 96 (38.40) | 60 (24) | 36 (14.4) | 5.016 | 0.084 |

**Table 7:** Chi-square analysis showing the relationship between post-primary PTB pattern and $CD4^+$ count in HIV/PTB co-infected patients.

| Post-primary PTB pattern | Total Freq (%) (n=112) | CD4 classification (%) | | $\chi^2$ value | p-value |
|---|---|---|---|---|---|
| | | < 200 cells/$mm^3$ | >200 cells/$mm^3$ | | |
| Atypical | 37 (33.0) | 35 (31.25) | 2 (1.7) | | |
| Typical | 36 (32.1) | 9 (8.0) | 27 (24.1) | 48.145 | <0.001* |

**Table 8:** Bivariate Logistic regression analysis showing the association between the patients with HIV/PTB co-infection and the development of significant abnormal chest radiographic findings.

| Findings (HIV/PTB co-infection) *(n=112)* | OR | Std. Error | *P-value* | (95% CI) | |
|---|---|---|---|---|---|
| | | | | Lower | Upper |
| **Opacities** | 0.323 | 0.114 | 0.001* | 0.161 | 0.647 |
| **Bronchopneumonia** | 0.550 | 0.149 | 0.028* | 0.323 | 0.936 |
| **Cystic change** | 0.529 | 0.145 | 0.021* | 0.308 | 0.907 |
| **Fibrosis** | 0.480 | 0.141 | 0.013* | 0.269 | 0.854 |
| **Cavities** | 0.267 | 0.102 | 0.001* | 0.126 | 0.566 |
| Thick-walled | 0.275 | 0.142 | 0.013* | 0.099 | 0.760 |
| Thin-walled | 0.263 | 0.150 | 0.020* | 0.086 | 0.807 |
| **Lymph Node** | 3.115 | 1.321 | 0.007* | 1.357 | 7.152 |
| **Volume loss** | 0.308 | 0.090 | <0.001* | 0.173 | 0.548 |

**Note:**
For Outcome variables, absent= reference is recorded as 0
OR = Odds ratio, * = significant p-value

**DISCUSSION**

Chest radiography remains a cornerstone in the assessment of various pulmonary pathologies in both adults and children. It is sensitive but not specific in the detection of pulmonary tuberculosis. It is widely employed and relatively cheap.

The highest age-specific prevalences were in the age groups 31-40 years and 41-50years age brackets who were affected equally, 59 subjects (23.6%) respectively. This agrees with studies by Ojiezeh et al[19] in Ekiti and Adetunji et al[20] in Oyo State that found PTB most prevalent in those aged between 25 and 40 years and 31-40 years respectively but is contrary to a national study by Ogbo et al[21] where the highest TB burden was found in those aged 50-69 years. In this study, the high disease burden in young adults could be attributed to the improvement in case reporting and the migration of young adults to over-crowded urban areas which is a known risk factor for PTB. The difference between the lower age-specific prevalence of PTB in our study when compared to the higher prevalence in the above national study, could be as a result of the rising disease prevalence in young adults over the decades.

This study showed that females had a higher CD4+ count, 171.01 ± 158 (mean ± SD) than males, 167.60 ±95.08 (mean ± SD). Also, 77 patients (68.7%) had a CD4+ count of less than 200 cells/$mm^3$ while 35 patients (31.3%) had a CD4+ count of more than 200 cells/$mm^3$. This is similar to findings made by other authors.[22, 23, 24] This finding of higher CD4+ count in females may be linked to the immuno-modulatory sex steroid hormones such as estrogen and progesterone, behavioral and epidemiologic risk factors, socioeconomic disparities, and differences in gene expression.[25]

In our study subjects, the atypical pattern was found slightly higher, 37 patients (14.8%) than the typical pattern, 36 patients (14.4%). This was not statistically significant, the p-value was 0.084. This is similar to findings in the study by Lau et al[26] and Tahir et

al[27] both of which showed higher percentages of atypical patterns in patients with HIV/PTB co-infection. Clinical manifestations of PTB occur most in settings of immunosuppression in HIV/PTB co-infection.

The presence of normal chest radiographs was significantly higher in patients with CD4+ count < 200 cells/mm$^3$ compared to those with higher values ($X^2$= 7.192, p-value = 0.006). However, chest computed tomography (CT) scans may be able to detect radiographic abnormalities in some of these patients. There were also significant differences in abnormal chest opacities between patients with CD4$^+$ count < 200 cells/mm$^3$ and those with CD4+ count > 200 cells/mm3, ($X^2$ = 10.802, p-value = 0.001). Other authors including Olufemi et al[28] and Affusim et al[22] reported similar findings. Atypical or primary PTB pattern in those with low CD4+ count is due to marked immunosuppression as such patients do not have an adequate level of immunity to mount a strong inflammatory reaction against the disease.

Patients with CD4+ count > 200 cells/mm$^3$ had significantly more upper zone distribution of opacities for the right and left lungs, (p- value <0.001 and < 0.001 respectively) compared to those with CD4+ count < 200 cells/mm$^3$. Marchie et al[29] in their study of 200 subjects reported similar findings. Contrary to our findings, Rosemeri et al[30] in a study involving 87 subjects did not find a significant distribution of radiographic patterns with respect to CD4+ count. This may be due to the smaller sample size used in their study.

Patients with CD4+ count > 200 cells/mm$^3$ had more lobar pneumonia compared to those with CD4+ count < 200 cells/mm$^3$, [12 (10.7%) versus 5 (4.5%) respectively, p-value < 0.001] while those with CD4+ count < 200cells/mm$^3$ had more bronchopneumonia. This may be because those with higher immunity are able to contain the infection to a lobe while in those with reduced immunity, the infection is not confined within a single lobe. This is similar to that reported by Marchie et al.[29] Conversely, Akinbanmi et al[31] in their study of 106 patients with HIV infection in Lagos, did not find any significant relationship between patient CD4+ count level and the presence of either lobar or bronchopneumonia.

All those with miliary patterns in this study had a CD4+ count of less than 200 cells/mm$^3$. This is statistically significant with a p-value of 0.016. The haematogenous spread is a reflection of an overwhelmed immune system in an uncontrolled TB infection. The diagnosis on chest radiography can be challenging since not all cases, especially in the early stage, will present with the classical conspicuous miliary nodules.[32] Marchie et al[29] reported a miliary pattern in 3 patients (7%) with CD4+ count < 200 cells/mm$^3$ while those with CD4+ count > 200 cells/mm$^3$, had 2 patients (25%) with the miliary pattern. Cystic changes were significantly noted with equal frequency, with 15 patients in both CD4+ count groups in our study. Those with CD4+ count > 200 cells/mm3, had a slightly higher frequency of subjects with lung volume loss, cavities, and fibrosis.

In Malaysia, Kooi et al[33] studied 80 HIV-positive patients with PTB, 62 (77.5%) had CD4+ count of fewer than 200 cells/mm$^3$ of which 61 (98.4%) had atypical post-primary CXR pattern. They also reported six patients (33.3%) out of eighteen (22.5%) with CD4+ count greater than 200 cells/mm$^3$ showing atypical chest patterns. Ahmadi et al[34] in Iran documented that atypical patterns including miliary pattern, hilar and mediastinal lymphadenopathies were more common in the HIV seropositive group.

The study by Olufemi et al[28] in Ilorin, Nigeria involving 127 patients found that 79 persons (79.15%) showed atypical patterns at CD4+ count less than 200 cell/mm$^3$ while 25 (75.8%) had an atypical pattern at CD4+ count greater than 200 cells/mm$^3$, with a p-value of 0.02. In Benin Nigeria, Marchie et al[29] studied 200 patients with HIV/PTB co-infection and 100 HIV-negative PTB controls. They found 111 subjects (86.72%) with chest radiographs showing atypical chest X-ray patterns at CD4+ count < 200 cells/mm$^3$ as against 31 (43.1%) with CD4+ count > 200 cells/mm$^3$. This was statistically significant, p < 0.001. Similarly, Keiper et al[35] found a direct association between the atypical pattern of post-primary PTB with falling CD4+ count. He documented an incidence of 80.77% for atypical chest findings in patients with CD4+ count less than 200cells/mm$^3$ compared to 11% in those with CD4+ count greater than 200cells/mm$^3$, (p<0.001). He also recorded the mean CD4+ count of the study group with an atypical pattern as 0.069 x10$^9$ cells/mm$^3$ (n=22) and that of those with the typical post-primary PTB pattern as 0.323 x 10$^9$ cells/mm$^3$ (n=13) respectively. All the above findings are similar to that reported in this study. These researchers have clearly shown that there is a strong positive relationship between falling CD4+ lymphocyte count and atypical chest radiographic patterns.[28, 29, 33- 35]

Typical post-primary pulmonary tuberculosis pattern was also associated with higher CD4+ count > 200 counts/mm$^3$ with values of 24.1% in this study. Guilherme et al[36] in Brazil showed that patients with CD4+ count greater than 200 cells/ml had more typical post-primary chest pattern (63.6%), compared to those whose CD4+ count was less than 200 cells µ/L two (7.4%), p=0.02). Kooi et al[74] recorded (66.7% versus 1.61%) while Olufemi et al[28] recorded (18.2% versus 8.1%, p=0.02) for typical PTB chest pattern at CD4+ count greater and less than 200 cells µ/L respectively. In this study, the values recorded are closest to that reported by Olufemi et al[28]. The concordance in the findings between this study and that reported by other researchers is probably due to similarities in the methodology.

Apart from normal chest radiographs, other atypical CXR patterns of PTB, also show a direct relationship with falling CD4+ lymphocyte count. Studies have found that patients with HIV/AIDS co-infected with pulmonary tuberculosis show more atypical chest X-ray pattern (CXR) patterns compared to patients with PTB- only. This is objectively considered according to the degree of immuno-suppression as expressed by patient CD4+ count.[28, 29, 33, 34, 35]

Other studies also show comparable results at CD4$^+$ count of less than 200 cells µ/L for atypical and typical chest TB patterns respectively. A study involving 58 subjects by Woo et al[37] in Korea recorded eighteen subjects (33%) versus 37 subjects (67%) for atypical and typical CXR patterns respectively. Similarly, a Pakistani study of 150 patients with PTB by Rao et al[38] showed that the atypical pattern was 63 (42%) while the typical chest pattern was 87 (58%). The reverse was the case in our study with atypical versus typical chest patterns in CD4$^+$ count < 200 counts/mm$^3$ of 35 subjects (31.3%) versus 9 subjects (8.0%) respectively. The variations in findings may be due to differences in the sample criteria of the methodology.

The odds or chances of the development of lung cavity and volume loss in HIV/PTB co-infection were least compared with the rest of the other findings. This is due to the fact that tuberculosis-induced metalloproteases (MMP) concentrations are suppressed by HIV infection.[39] Metalloproteases (MMP) are a family of zinc-dependent proteases expressed mostly in diseased tissues that are undergoing repair and remodeling.[40] This process leads ultimately to cavity formation, alveolar destruction, and volume loss.

## CONCLUSION

The study showed that patients with PTB had very high chances of developing lymphadenopathy and fewer chances for the development of all the other abnormal chest radiographic findings like cavities, volume loss, etc. Many of the chest radiographic findings showed a significant relationship with the patient's $CD4^+$ count value. **LIMITATIONS:** In apparently normal radiographs, very small abnormalities could have been missed in the hidden areas of the lung. **RECOMMENDATIONS:** The high age-specific prevalence of pulmonary tuberculosis amongst the young adults in this study shows that the disease is still very present and active in this environment. This implies that further advocacy on HIV and PTB prevention and control across all levels of health care, health agencies, and governments is required.

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