

Comparative Evaluation Of Chest Radiographic Patterns of Pulmonary Tuberculosis among HIV Sero-Positive and HIV Sero-Negative Adults in Delta State

DO Isoje¹, OD Ogholoh^{2,3}, AI Nwajei^{2,3}, CO Ayara⁴, AO Ogbeide², JE Ikubor^{2,3}, AO Akhigbe⁵, VN Isitua²

Abstract

Introduction: Pulmonary tuberculosis (PTB) remains a major global health challenge, causing ill-health in nearly ten million people annually and ranking among the top ten causes of death worldwide. Sub-Saharan Africa contributes about one-quarter of the global burden, with Nigeria being a major contributor. The risk of developing PTB is significantly higher in individuals infected with Human Immunodeficiency Virus (HIV), and the chest radiographic patterns of PTB are known to be influenced by the degree of immunosuppression associated with HIV co-infection.

Objective: This study aimed to describe the chest radiographic patterns of PTB in HIV sero-positive patients and compare them with age and sex-matched HIV sero-negative adults in Delta State, Nigeria.

Method: This cross-sectional comparative study was conducted among 110 HIV sero-positive and 110 HIV sero-negative PTB patients. Diagnosis was based on positivity of sputum smear and Gene Xpert laboratory tests, together with chest radiographic findings. The data was

collected using researcher-administered questionnaires. Chest radiographs of all the participants were assessed for typical and atypical PTB patterns. Data analysis was performed using SPSS version 22.0 with statistical significance set at $p \leq 0.05$.

Results: The study findings showed that consolidation, fibrosis, and cavitations were more frequent among the HIV sero-negative patients, with consolidation being statistically significant (27.3% vs 43.6%, $p=0.011$). Conversely, HIV sero-positive patients had higher frequencies of hilar lymphadenopathy, pleural effusion, miliary opacities, and normal radiographs, with hilar lymphadenopathy (35.5% vs 21.8%, $p=0.025$) and miliary changes (11.8% vs 1.8%, $p=0.003$) being significant.

Conclusion: Atypical radiographic patterns were more common in HIV sero-positive patients, underscoring the role of immunosuppression in determining PTB presentation.

Key words: Chest Radiography, Pulmonary tuberculosis, HIV sero-positive, HIV sero-negative

Nigerian Research J Clin. Sci. 2025; 15(2): 30 - 40

¹Department of Radiology, Asaba Specialist Hospital, Asaba, Delta State.

²Department of Radiology, Delta State University Teaching Hospital, Oghara, Delta State.

³Department of Radiology, Delta State University, Abraka, Delta State.

⁴Department of Anatomy, Bingham University, Karu, Nasarawa State

⁵Department of Radiology, University of Benin Teaching Hospital, Benin City, Edo State.

Corresponding Author: Prof. Joyce Ikubor. Department of Radiology, Delta State University, Abraka, Delta State. Email: joyceikuborjune12@yahoo.com

Introduction

Pulmonary tuberculosis (PTB) remains a leading cause of morbidity and mortality globally, with sub-Saharan Africa and Nigeria carrying a significant burden. About a quarter of the global population are exposed to the disease with a relatively small proportion (5–10%) of the infected persons developing active disease during their lifetime.^{1,2} In Delta State, Nigeria, as in many resource-limited settings, the dual epidemic of PTB and Human Immunodeficiency Virus (HIV) poses major diagnostic challenges. HIV-related immunosuppression alters the classical chest radiographic patterns of PTB, often resulting in atypical presentations that delay diagnosis and treatment.^{3,4} Chest radiography, though widely available, may be limited by these variations. This study aimed to describe and compare the chest radiographic patterns of PTB in HIV sero-positive and sero-negative adults in Delta State, Nigeria.

Materials and Methods

This cross-sectional comparative analytical study was carried out in the Radiology Departments of the Delta State University Teaching Hospital, Oghara, and Central Hospital Warri, Delta State, Nigeria between October 2019 and September 2020. The sample size was determined as for a cross-sectional study using Fisher's statistical formula for population greater than 10,000 and a known prevalence rate of 6.8% for PTB-HIV coinfection.² The study participants who fulfilled the inclusion criteria were counseled and informed consent was obtained before their recruitment into this study. The participants who were eligible for the study were recruited consecutively until the sample size was reached.

The study population consisted of 110 HIV sero-positive as well as age and sex matched 110 HIV sero-negative newly diagnosed PTB patients. The diagnosis of PTB was based on the positivity of the sputum smear test, positivity of the Gene Xpert test, the Ade Dosumu⁵ case definition criteria and typical chest radiographic features of PTB for smear negative paucibacillary PTB patients. The major Ade Dosumu⁵ case definition criteria includes cough present for at least 6 weeks, sputum production for at least 6 weeks, chest wall pain for at least 6 weeks, fever lasting for at least 6 weeks, night sweat lasting for at least 6 weeks and weight loss greater than 10% of body weight; while the minor criteria include fatigue, headache, haemoptysis, dyspnoea, lassitude and anorexia. For the purpose of this study, the HIV sero-positive PTB patients and HIV sero-negative PTB patients were designated as Groups A and B respectively.

Ethical approval from the Health Research Ethics Committee of the two hospitals (EREC/PAN/2019/017/0309 and CHW/ECC VOL1/179) was sought before the commencement of the study. Furthermore, informed consent was obtained from the study participants prior to the commencement of the study. Identifiers were expunged from patients' information in order to maintain confidentiality. Data collection was via administered structured questionnaire that captured socio-demographic information of the participants and their clinical case definition criteria. Confirmed PTB patients were screened for HIV-1 and HIV-2 antibodies. Participants with smear and Gene Xpert positive PTB test results as well as those that met the case definition criteria⁵ were referred for chest

radiography. Posterior anterior chest radiographs were obtained. However, anteroposterior (AP) view was acquired for patients who were unable to stand, and lateral view for localization of lesions when necessary.

Chest radiographic findings of hilar adenopathy, pleural effusion, miliary opacities, fibrotic changes, consolidation, cavitations, loss of lung volume, and apical involvement were recorded. Consequently, chest radiographic findings (Figures 1-5) were categorized into two broad groups:

(1) Post primary pattern/typical PTB group: The findings are apical consolidation, fibrosis and volume loss with or without cavitations, (Figures 1, 2).⁶ Consolidations were seen as homogeneous or inhomogeneous opacities of soft tissue density in the affected lung zones (Figure 1). Cavitations were seen as round or oval transradiant areas with varying wall

thickness and devoid of lung markings, some with fluid level (Figure 3). Lung volume loss was seen as areas of increased density with crowded bronchovascular markings, overlying rib crowding and ipsilateral tracheal shift (Figure 2).

(2) Primary pattern/atypical PTB group: This includes features of hilar lymphadenopathy seen as lobulated hilar soft tissue opacity; pleural effusion seen as homogeneous opacity affecting part (Figure 1) or entire hemithorax (Figure 4) with a meniscus (depending on the volume); consolidation across multiple lung zones; cavitations (Figure 3); miliary opacities seen as widespread almost same size, pin-head opacities (Figure 5); and those without observable radiographic changes (normal radiographs) but with positive sputum and Gene Xpert TB tests.⁶

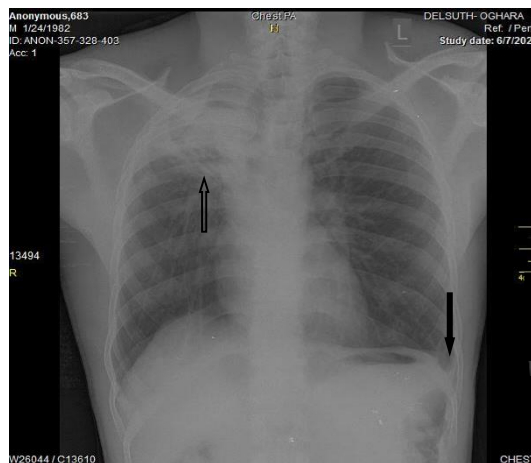


Figure 1: Posteroanterior chest radiograph of a 38-year old male HIV sero-negative PTB patient showing right upper lung zone consolidation with fibrocystic changes (white arrow) and loss of lung volume as evidenced by ipsilateral tracheal shift. There is also blunting of the left costophrenic angle possibly due to minimal pleural effusion. (black arrow).

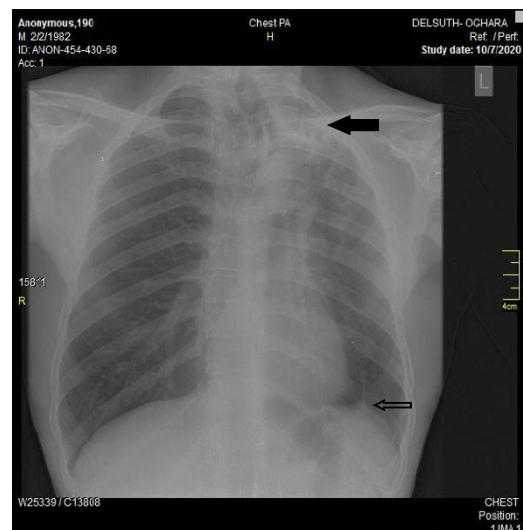


Figure 2: Posteroanterior chest radiograph of a 38-year old HIV sero-negative PTB patient showing left upper lobe volume reduction from fibrosis (black arrow), with ipsilateral tracheal deviation. There is tenting of the left hemidiaphragmatic outline caused by fibrotic strands (white arrow).

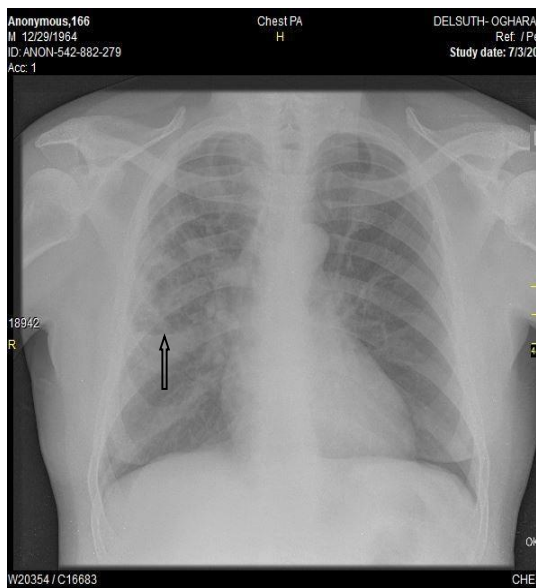


Figure 3: Posteroanterior chest radiograph of a 56-year-old male HIV sero-positive PTB patient showing a cavity in the right mid lung zone (arrow). There are also widespread inhomogeneous infiltrates in the right upper and mid lung zones.

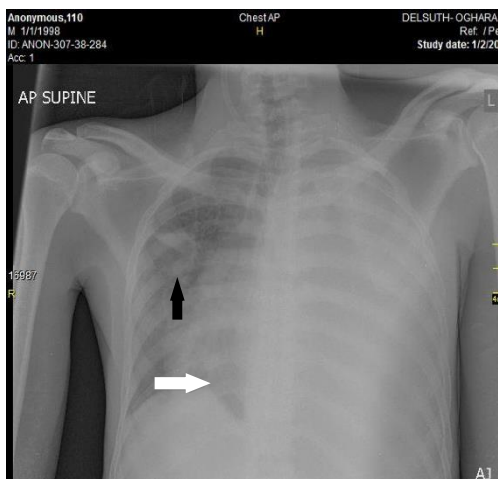


Figure 4: Posteroanterior chest radiograph of a 22-year-old male HIV sero-positive PTB patient showing complete homogenous opacification of the left hemithorax consistent with massive left pleural effusion. Contralateral shift of the mediastinum is noted. Inhomogeneous opacities are also seen in the right mid and upper lung zones. There is tenting of the right hemidiaphragmatic outline caused by fibrotic strands.

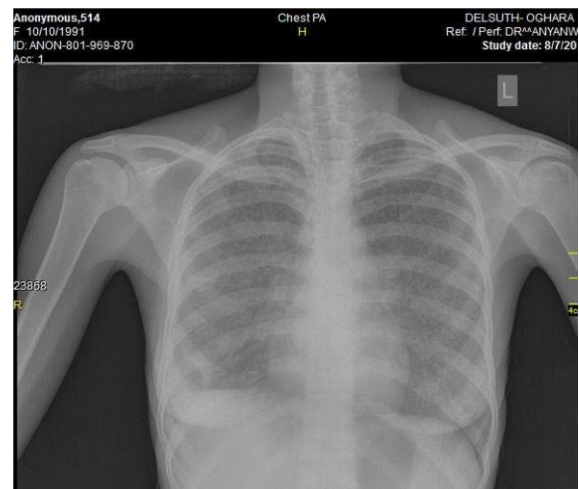


Figure 5: Posteroanterior chest radiograph of a 29-year-old female HIV sero-positive PTB patient showing widespread bilateral same-sized pin-head opacities suggestive of miliary pattern of PTB.

Data analysis

The data extracted from the filled questionnaires were entered into the spreadsheet. Data analysis was done using the statistical package for social sciences (SPSS) version 22.0 (IBM® 2016).

Results

The chest radiographs of one hundred and ten (110) HIV sero-positive PTB patients (Group A) and one hundred and ten (110) HIV seronegative PTB patients (Group B) were evaluated in this study. The age range of the patients in the HIV sero-positive group (Group A) was 18-77 years with a mean of 41.9 ± 13.4 years while that of the HIV seronegative group (Group B) was 18-80 years with a mean of 46.0 ± 18.5 years. The age group of 36-45 years had the highest frequency in group A while 26-35 years age group had the highest frequency in group B as shown in Table 1.

There were 47 (42.7%) females and 63 (57.3%) males in group A while group B

comprised of 54 (49.1%) females and 56 (50.9%) males as depicted in Table 1. There were more males than females in both groups with frequencies of 63 (57.3%) and 56 (50.9%) in the HIV sero-positive and HIV

sero-negative groups respectively. The difference in mean age and sex were not statistically significant ($p=0.06$ and $p=0.344$ respectively).

Table 1: Socio-demographic characteristics of the study population

		HIV +ve	HIV -ve	χ^2/t	df	p value
		N (%)	N (%)			
Age Group	18 – 25	17 (15.5)	16 (14.5)	5.483	6	0.484
	26 – 35	25 (22.7)	23 (20.9)			
	36 – 45	27 (24.5)	20 (18.2)			
	46 – 55	14 (12.7)	15 (13.6)			
	56 – 65	20 (18.2)	20 (18.2)			
	66 – 75	5 (4.5)	8 (7.3)			
	76 – 80	2 (1.8)	8 (7.3)			
Mean age		41.9 ± 13.4	46.0 ± 18.5	-1.887	218	0.060
Sex	Male	63 (57.3)	56 (50.9)	0.897	1	0.344
	Female	47 (42.7)	54 (49.1)			

Table 2 and Figure 6 show the chest radiographic findings in HIV sero-positive and HIV sero-negative patients with PTB. Atypical radiographic pattern of PTB were seen in the two groups but commoner in HIV-PTB co-infected group of patients which include hilar lymphadenopathy (35.5% vs 21.8%), pleural effusion (24.5% vs 20.0%), miliary changes (11.8% vs 1.8%), and normal chest radiographic findings (6.4% vs 4.5%) while the patients in group B on the other hand, had more of typical radiographic PTB pattern of fibrosis (26.4%

vs 16.4%), consolidation (43.6% vs 27.3%) and cavitations (20.9% vs 15.5%). Comparison of groups A and B showed statistically significant difference in the results of consolidation (27.3% vs 43.6%, $p=0.011$), hilar lymphadenopathy (35.5% vs 21.8%, $p=0.025$) and miliary changes (11.8% vs 1.8%, $p=0.003$) respectively as shown in Table 2. Seven and five subjects had normal chest radiographs in group A and group B respectively and this was not statistically significant.

Table 2: Chest radiographic findings in HIV Sero-positive and HIV Sero-negative patients with PTB.

Variable	Descriptor	Group A HIV +ve	Group B HIV -ve	Statistics		
		N (%)	N (%)	χ^2	df	p
Cavitation	Yes	17 (15.5)	23 (20.9)	1.1000	1	0.294
	No	93 (84.5)	87 (79.1)			
Consolidation	Yes	30 (27.3)	48 (43.6)	6.436	1	0.011*
	No	80 (72.7)	62 (56.4)			
Fibrosis	Yes	18 (16.4)	29 (26.4)	3.274	1	0.070
	No	92 (83.6)	81 (73.6)			
Pleural effusion	Yes	27 (24.5)	22 (20.0)	0.656	1	0.418
	No	83 (75.5)	88 (80.0)			
Hilar lymphadenopathy	Yes	39 (35.5)	24 (21.8)	5.005	1	0.025*
	No	71 (64.5)	86 (78.2)			
Miliary changes	Yes	13 (11.8)	2 (1.8)	8.657	1	0.003*
	No	97 (88.2)	108 (98.2)			
Normal	Yes	7 (6.4)	5 (4.5)	0.353	1	0.553
	No	103 (93.6)	105 (95.5)			

* Statistically significant | df=degree of freedom | χ^2 =chi-square

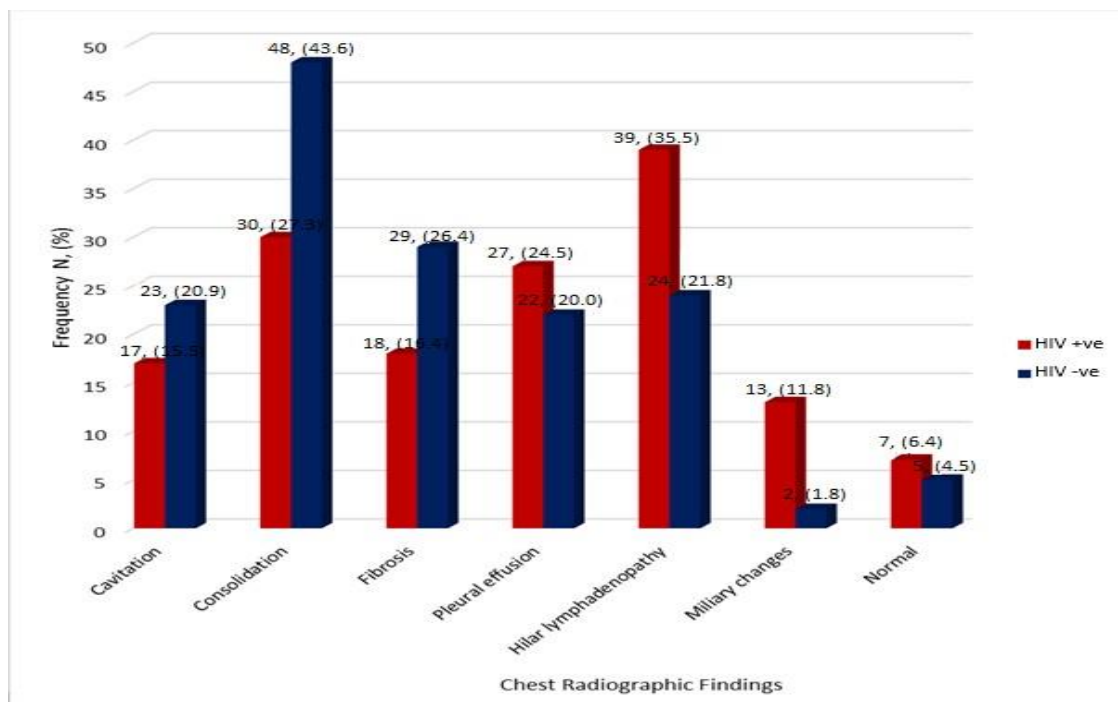


Figure 6: Comparison of chest radiographic findings between HIV sero-positive and HIV sero-negative PTB patients.

This study examined the chest radiographic patterns of PTB in HIV sero-positive and sero-negative adults in two health facilities in Delta State, Nigeria. The mean age of the HIV sero-positive and HIV sero-negative patients in this study are 41.9 years and 46 years respectively. These values are slightly higher compared to the mean age of less than 40 years previously reported in 2 studies carried out in Maiduguri, Nigeria and India by Ahidjo *et al*⁷ and Behera *et al*⁸ respectively. The higher mean ages seen in this study may be attributable to the higher upper age limits (85 years) used in the inclusion criteria in comparison with the lower upper age limits of the aforementioned studies.

The slight male preponderance of 1.2:1 seen in this study is similar to the male preponderance found in similar studies reported by Ahidjo *et al*⁷ in Maiduguri, Northern Nigeria and Ikuabe *et al*⁹ in Bayelsa, South South Nigeria. At variance to this is the report of female preponderance (female to male ratio of 1.2:1) by Affusim *et al*¹⁰ in Benin city. This variation may be due to the difference in the sampling method used in both studies.

There is a higher prevalence of PTB in the background of immunosuppression majorly from HIV/AIDS co-infection.¹ HIV increases the likelihood of reactivation, re-infection and progression of latent PTB infection to active disease. It has a 20-fold and 10-fold increase on the risk of latent PTB reactivation and development of active PTB disease respectively.³ The changing landscape of PTB as a result of various risk factors of which HIV infection has been reported to be the most important, has changed the spectrum of the clinical and radiological presentation of PTB.¹¹ The emergence of the HIV-TB syndemic has introduced a wide variation in the

clinicopathologic and radiologic manifestations of pulmonary tuberculosis depending on the degree of immunosuppression of the affected patient.¹² Before the advent of gene Xpert TB test, sputum smear microscopy for AAFB was the first-line diagnostic test for PTB patients but its diagnostic value has reduced significantly in the setting of paucibacillary tuberculosis as commonly seen in TB-HIV co-infection.¹² Chest radiographs have been found in many studies to play a major diagnostic role in patients with negative sputum smears.^{3,13,14}

Early in HIV infection, PTB present with the typical radiographic pattern of upper lobe opacities and cavities ($\pm$ fibrosis) as also seen in immuno-competent patients. The radiographic picture seen depends on the influence of the host immune system on the invading bacilli.⁶ This is because the cell mediated immune response is still potent enough to mount a granulomatous reaction.¹⁴ With progression of the disease or worsening immunosuppression, the less "typical" or atypical chest radiographic patterns are seen due to inadequate granulomatous reaction secondary to severe immunosuppression.⁶ These atypical chest radiographic features of PTB are mediastinal or hilar lymphadenopathy, miliary opacities, lobar consolidation in atypical locations, pleural effusion and normal findings.^{6,14} Marchie *et al*¹⁵ in a study done in Benin City, Nigeria, compared the level of immunosuppression from HIV with the chest radiographic patterns of PTB. In this study, "typical" pattern was defined as radiographic features in post primary tuberculosis which consists of apical consolidation, cavitations, fibrosis, volume loss and apical location of lesions while "atypical" patterns were referred to as radiographic features of primary tuberculosis consisting of broncho-

pulmonary infiltrates, miliary pulmonary infiltrates, lymphadenopathy and pleural effusion.

The chest radiographic patterns in HIV sero-positive and HIV seronegative subjects who were infected with pulmonary tuberculosis are presented in this study. The patients in the HIV sero-positive group in comparison with the HIV seronegative group had a statistically significant higher frequency of hilar lymphadenopathy (35.5% vs 21.8%) and pleural effusion (24.5% vs 20.0%). This is comparable to the finding of hilar lymphadenopathy (47.5% vs 14%) in a similar study conducted by Marchie *et al*¹⁵ in Benin City. The statistically significant higher frequency of hilar lymphadenopathy (35.5% vs 21.8%) and pleural effusion (24.5% vs 20.0%) found to be commoner in the HIV sero-positive group corroborates the prevalence of atypical chest radiographic pattern of PTB in the background of immunosuppression from HIV co-infection, and this is also in agreement with the findings of other researchers.^{8,9,15}

Miliary opacities were also found to be more common among the HIV sero-positive group in this study where a frequency of almost seven times that of the HIV seronegative group was recorded (11.8% vs 1.8%). This was statistically significant. This observation of miliary opacities as a common atypical chest radiographic presentation in the immunocompromised PTB patients agrees with those reported in previous studies.^{7, 16-17} The Angthong *et al*¹⁶ study in Thailand reported military opacities as the most frequent finding among the HIV seropositive PTB patients. The failure of containment of the mycobacterium infection in the face of immunosuppression may explain the higher frequency of miliary pattern of

presentation seen among the HIV seropositive group as reported in this study as well as widely documented by various authors.^{4, 7, 16-18}

Cavity formation, consolidation and fibrosis are radiographic features that were more common among the HIV sero-negative group in this study and is statistically significant. Cavity formation was commoner (15.5% vs 20.9%) among the HIV sero-negative group in this study. This is in agreement with the findings of similar studies by Affusimet *al*¹⁰ and Nwonwuet *al*.¹⁹ But in disagreement with the current and aforementioned studies is the finding of Ikuabe and colleagues⁹ in a similar study done in Yenogoa, Bayelsa State, Nigeria that reported a higher frequency of cavitations (30.6% vs 33.2%) among the HIV sero-positive group. The finding of higher incidence of cavity formation may be due to the higher CD4 count ($\geq 200\text{cell/mm}^3$) among the HIV-PTB co-infected patients which confers a relatively higher ability to invoke adequate immune response needed for cavity formation.¹⁸ Furthermore, the statistically significant higher frequency of consolidation and fibrosis recorded among the patients of the HIV sero-negative group in this study is in agreement with the studies carried out in India, Kampala, Uganda and Abakaliki, South-East Nigeria.^{8,12,19} These radiographic patterns seen in the HIV sero-negative/immunocompetent group can be attributed to the preserved ability to invoke immune response resulting in the radiographic findings of the typical (post-primary) patterns of PTB.

Normal chest radiographic findings were commoner in the immunosuppressed group (6.4% vs

4.5%) in this study, and this is in consonance with the finding of a similar

study by Ahidjo *et al.*⁷ The reason stated for this is the inability of these patients to mount adequate immune response to *M. Tuberculosis*.⁷ However, the 5 normal chest radiographs reported in the HIV sero-negative group of the index study were seen in elderly patients (all above 60 years), and this was deduced to be as a result of the inability of their senile-related weakened immune system to mount adequate response that will lead to chest radiograph findings.

Some authors have classified chest radiographic findings of PTB into primary (atypical) and post-primary (typical) on the basis of either recent or remote infection respectively.²⁰ This classification is true for individuals with intact immunity, as shown in the findings of the index study and corroborated by several other similar studies.^{9,14,15} Hilar lymphadenopathy, miliary opacities and pleural effusion classified as primary PTB or atypical findings are the frequent chest radiographic findings in adults with HIV-PTB co-infection. The typical findings of apical consolidation and fibrosis with or without cavitation which have been described as the main radiographic features of post-primary PTB

were reported more frequently in the immunocompetent group.^{6,15} From the foregoing, it can be stated that the time of onset of PTB infection i.e. recent (primary) or remote (post-primary) is more valuable in classifying chest radiographic features of PTB into typical and atypical patterns among immunocompetent patients while the level of immunosuppression is a more valuable index of classification among HIV-PTB co-infected patients.

Conclusion

Chest radiographic features of PTB vary significantly between HIV sero-positive and sero-negative patients, with atypical manifestations being more common in the former group and classical manifestations being more common in the latter, which is a direct response to the effects of immunosuppression, thereby underscoring the role of immunosuppression in determining PTB presentation. This implies that the diagnosis of PTB in HIV-infected patients is dependent not only on the radiographic appearances alone but in combination of clinical and laboratory approaches which should be adopted for a timely and accurate diagnosis.

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