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Pattern and Distribution of HIV associated Pulmonary Tuberculosis Lesion on Chest Radiograph in Nigeria

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Abstract

We compared the pattern and distribution of pulmonary lesion on chest radiograph of HIV patients with CD4 count < or ≥200cells/µl and HIV-1RNA viral load < or ≥ $\log 10^5$. Of the 133 patients consecutively recruited, 84 (63.2%) had CD4 count <200 cells/µl. Patients with CD4 count <200 cells/µl had consolidation (15.5% vs 28. P = 0.054) and streaky changes 39.3% vs 55.9%, P = 0.049) less often. Pulmonary lesions involving upper and middle radiological zones were less common in cohort with CD4 count < 200cells/µl (11.9% vs 30.5%, P = 0.006), conversely middle and lower zone involvement were most often seen in them (27.4% vs 15.3%, P = 0.008). Patients with HIV-1 RNA viral load $\geq 10^5$copies/ml had nodular lesions less often (31.7% vs 55.1%, p = 0.038) and more often had hilar or mediastinal lymphadenopathy (22.0% vs 7.3%, P = 0.012). Lower zone involvement was predominantly seen in cohort with HIV-1 RNA viral load $\geq 10^5$copies/ml (19.5% vs 0.01%, p = 0.000). Our study demonstrates association between HIV disease stage with pattern and distribution of certain tuberculosis lesion on chest radiograph. Knowledge of immunological and virological parameters is important to clinicians and radiologist when evaluating CXR findings in HIV-infected patients.

Keywords: Human immunodeficiency virus, Pulmonary tuberculosis lesion,

1 Introduction

The global burden of tuberculosis is frightening with the reported one third of the 33 million HIV population worldwide are estimated to be infected with mycobacterium tuberculosis [1]. The challenge caused by tuberculosis is enormous and presently at it worst in sub-Saharan Africa as 85% of the estimated 700 000 HIV-infected people with

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active tuberculosis (TB) live in this region [2,3]. Rapid and accurate diagnosis of tuberculosis especially in those co-infected with HIV infection is therefore expedient in order to substantially reduce morbidity and mortality. Although sputum smear microscopy for acid-fast bacilli (AFB) is the first-line diagnostic test for evaluating these patients, with overwhelmingly reported evidences that HIV-infected patients with pulmonary TB are less often smear positive, chest radiography (CXR) is valuable and recommended in establishing cases of tuberculosis especially in those with negative sputum smears [4-6].

Radiological manifestations of tuberculosis in HIV-infected patients are known to vary according to the degree of immunosuppression based on CD4 count level [7-10]. To our knowledge no studies have specifically described the radiological abnormalities in patients with viral load >100 000 copies/ml, an indication of severe infection with high risk of mortality.

We therefore carried out a cross-sectional study of patients that presented at the infectious diseases clinic at university of Maiduguri teaching hospital with HIV-TB co-infection. We describe the pattern of radiological lesion and its distribution in HIV sero-positive patients with tuberculosis; and we correlate chest radiographic findings with CD4 count and plasma HIV-1 RNA level.

2 Materials and Methods

This cross-sectional analytic study was conducted on HIV positive patients at diagnosis of pulmonary tuberculosis at the University of Maiduguri Teaching Hospital, Maiduguri, North eastern Nigeria. Patients with radiological evidence of active pulmonary tuberculosis were recruited into the study either at assessment for possible commencement of antiretroviral drugs (ART) or at diagnosis of pulmonary tuberculosis while already on ART. The diagnosis of pulmonary tuberculosis (PTB) was based on WHO recommendation for the diagnosis of PTB that includes; one sputum smear positive for acid fast bacilli (AFB) and radiographic abnormalities consistent with active PTB for sputum positive PTB and symptoms suggestive of PTB and three negative smears for AFB and radiographic abnormalities consistent with active PTB for sputum negative PTB as sputum negative for AFB does not exclude PTB especially when clinical symptoms and radiological features are consistent of the diagnosis. Patient without radiological evidence of TB, extra pulmonary TB or those that had treatment for TB for more than a week at current diagnosis or TB treatment in the past were excluded from analysis. Standard posterior anterior chest radiograph were obtained with film-screen at 90-140KVp in all patients, the radiographs were reported by radiologist without their knowledge of enrollment into the study. Sample for CD4+ T cell count was collected within a week of diagnosis of PTB between 9:00-10:00am and assayed within 6 hours of collection of whole blood using standardized flow cytometric Cyflow machine (manufactured by Cytec, Partec, Germany 2005). Plasma HIV RNA levels were measured using freshly frozen specimen separated within 6 hours of phlebotomy utilizing the Amplicor HIV-1 Monitor Test, version 1.5 Manufactured by Roche® Germany, with a minimum cut off value of 200 copies per ml. Data were analyzed using SPSS version 16 for windows, we used chi square or Fishers exact test for proportions. To compare proportions, we calculated risk ratios (RRs) with 95% confidence intervals. All tests were two-tailed and we considered p values less than 0.05 statistically significant.

Ethical consideration: Permission to conduct this study was granted by the ethics and research committee of the University of Maiduguri Teaching Hospital.

3 Results

This cross-sectional analytic cohort study consecutively recruited 143 participants with active pulmonary TB and consistent radiographic features, consisting of 77 (53.9%) females and 66 (46.1%) males. Females with mean ages± stddev (min – max) of 32.19±7.98 (19 – 60) were significantly younger than their male counterpart that had 39.85 ± 7.87 (21 – 62) ($p<0.05$). The participants were stratified into two; based on defined immunological parameter i.e. CD4 count of < or ≥ 200cells/µl and virological parameter, HIV -1 RNA viral load < or ≥ 100,000 copies/ml. As shown in Table 1, the CD4 count and viral load parameters between the stratified cohorts were comparable. Table 2 compares radiographic findings after stratification by CD4 count <200 cells/µl and CD4 count ≥ 200cells/µl. Of the 133 patients, 84 (63.2%) had CD4 count <200 cells/µl. Patients with CD4 count <200 cells/µl had consolidation (15.5% vs 28.8%, RR 0.42, 95% CI 0.18 – 1.10, P = 0.054) and streaky changes 39.3% vs 55.9%, RR 0.49, 95% CI 0.24 – 1.06, P = 0.049) less often, though it fails to reach statistical significance. Appearance of pulmonary lesions on the upper and middle radiological zones tended to be less common in those with CD4 count < 200cells/µl (11.9% vs 30.5%, RR 0.31,95% CI 0.12, P = 0.006), conversely middle and lower zone involvement were most often seen in them (27.4% vs 15.3%, RR 1.85, 95% CI 0.83 – 5.40, P = 0.008).

Table 3 depicts radiographic findings after stratification of participants by HIV-1 RNA viral load ≥100,000copies/ml and <100,000copies/ml. Patients with HIV-1 RNA viral load ≥100,000copies/ml had nodular lesions less often (31.7% vs 55.1%, RR 0.46, 95% CI 0.20 – 1.03, p = 0.038) and more often had hilar or mediastinal lymphadenopathy (22.0% vs 7.3% , RR 3.55, 95% CI 0.14 – 11.20, P = 0.012) and features suggestive of consolidation (34.2% vs 14.7%, RR 3.01, 95% CI 12.1 – 7.54, P = 0.008). Lower zone involvement was predominantly seen in cohort with HIV-1 RNA viral load ≥100,000copies/ml (19.5% vs 0.01, RR 12.71, 95% CI 3.12 -57.9, p = 0.000).

Table 1: Age, CD4 count and HIV-1 RNA Viral load parameters of studied participants

	Proportion (%)	Mean ± std dev (95%CI)	Statistical significance
Sex, females (%)	53.9		
Age		35.63±8.78(34.03 – 37.23)	0.000
Females	53.9	32.19±7.98(30.21 – 34.16)	
Males	46.1	39.85±7.87(37.68 – 42.02)	
CD4 Count			
All participants		238.80±197.88(206.43 – 271.17)	0.000
<200	63.2	109.84±48.57(99..42 – 120.25)	
≥200	36.8	423.65±183.98(99.42 – 120.25)	
HIV-1 RNA viral load			
All participants		5.34±5.84(4.99 – 5.53)	0.000
≥100,000 (≥ $Log10^5$)	27.3	5.80±6.05 (5.38 – 6.00)	
<100,000 (< $Log\ 10^5$)	72.7	4.32±4.47(4.16 – 4.43)	

Table 2: Chest radiographic finding in HIV-seropositive patients according to AIDS status

	CD4 count level			
	<200cells/µl	≥200 cells/µl	Risk ratio	p-value
Radiographic lesion	no = 84	no = 59		
Nodular lesion	41(48.8)	36(61.0)	0.58(0.29-1.26)	0.149
Cavity	29(34.5)	27(45.8)	0.59(0.30 -1.31)	0.175
Plueral Plaque				
Fungal ball				
Streaky changes	33(39.3)	33(55.9)	0.49(0.24- 1.06)	0.049
Consolidation	13(15.5)	17(28.8)	0.42(0.18–1.10)	0.054
Plueral effusion	09(10.7)	04(06.8)	1.30(0.43–6.76)	0.420
Hilar adenopathy	10(11.9)	07(11.9)	0.87(0.32 –3.16)	0.994
Distributionof lesion				
Upper zone	10(11.9)	18(30.5)	0.31(0.12 –0.79)	0.006
Middle/lowerzone	23(27.4)	09(15.3)	1.85(0.83 –5.40)	0.008
Lower zone	07(08.3)	02(03.4)	1.71(0.47 –18.81)	0.231
Hemithorax	03(03.6)	04(06.8)	0.40(0.09 – 2.83)	0.381
Bilateral lungfield	13(15.5)	17(28.8)	0.42(0.18 – 1.10)	0.054

NB: (There may be more than one abnormality for the same patient).

Table 3: Chest radiographic finding in HIV-sero positive patients according to viral load

	Viral load (≥100,000copies/ml)	Viral load (<100,000copis/ml)	Risk ratio	p-value
Radiographic lesion	no = 41	no = 109		
Nodular lesion	13(31.7)	60(55.1)	0.46(0.20 – 1.03)	0.38
Cavity	14(34.2)	44(40.4)	0.77(0.34 – 1.73)	0.486
Plueral Plaque				
Fungal ball				
Streaky changes	16(39.0)	52(47.6)	0.70(0.32 – 1.55)	0.341
Consolidation	14(34.2)	16(14.7)	3.01(1.21 – 7.54)	0.008
Plueral effusion	06(14.6)	08(07.3)	1.87(0.61 – 7.53)	0.171
Hilar adenopathy	09(22.0)	08(07.3)	3.55(0.14 – 11.20)	0.012
Distributionof lesion				
Upper zone	09(22.0)	19(17.4)	1.23(0.50 – 3.51)	0.527
Middle/lower zone	11(26.8)	31(28.4)	0.80(0.38 – 2.21)	0.845
Lower zone	08(19.5)	01(0.01)	12.71(3.12 – 57.9)	0.000
Hemithorax	01(02.4)	06(0.06)	0.37(0.02 – 3.87)	0.439
Bilateral lung field	08(19.5)	19(17.4)	1.06(0.03 – 0.95)	0.767

NB: (There may be more than one abnormality for the same patient).

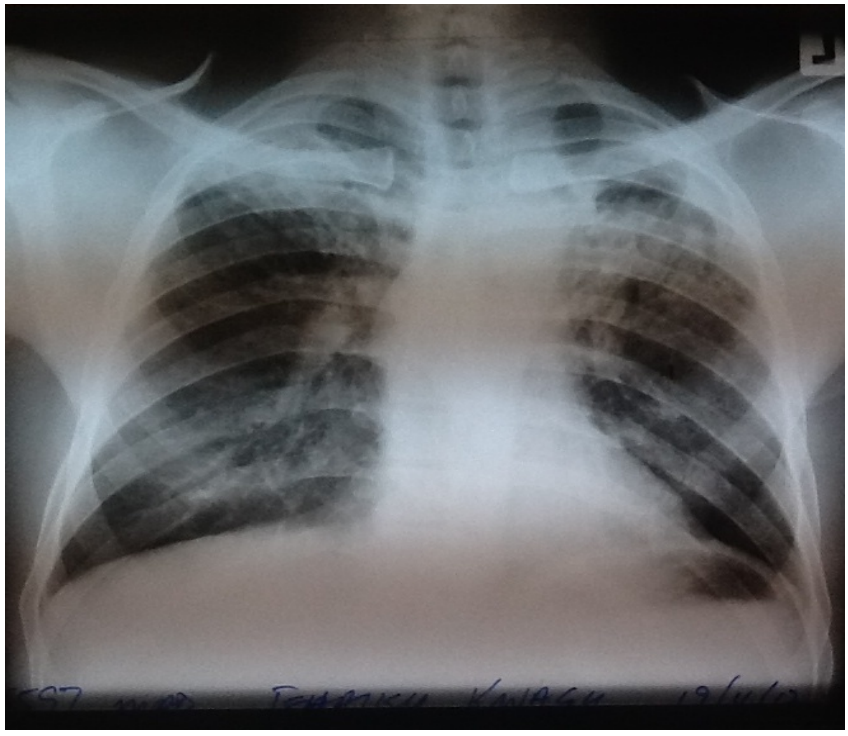

Figure 1: PA chest radiograph of 34 year old patient showing widespread recticulonodular opacities in both upper and the right lower zones (19/11/12).

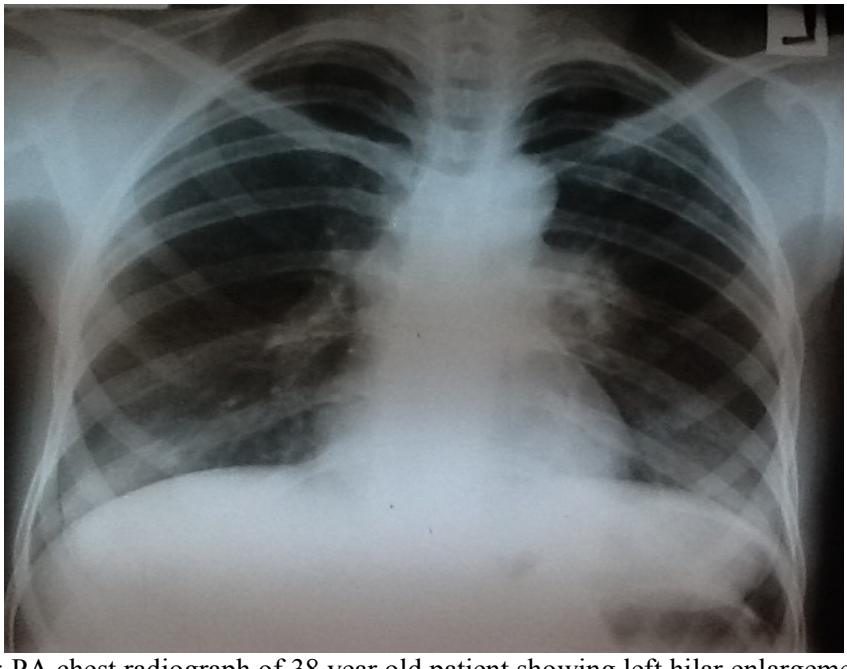

Figure 2: PA chest radiograph of 38 year old patient showing left hilar enlargement (CD4 count = 22cells/µl, VL = 32,688 copies/ml.

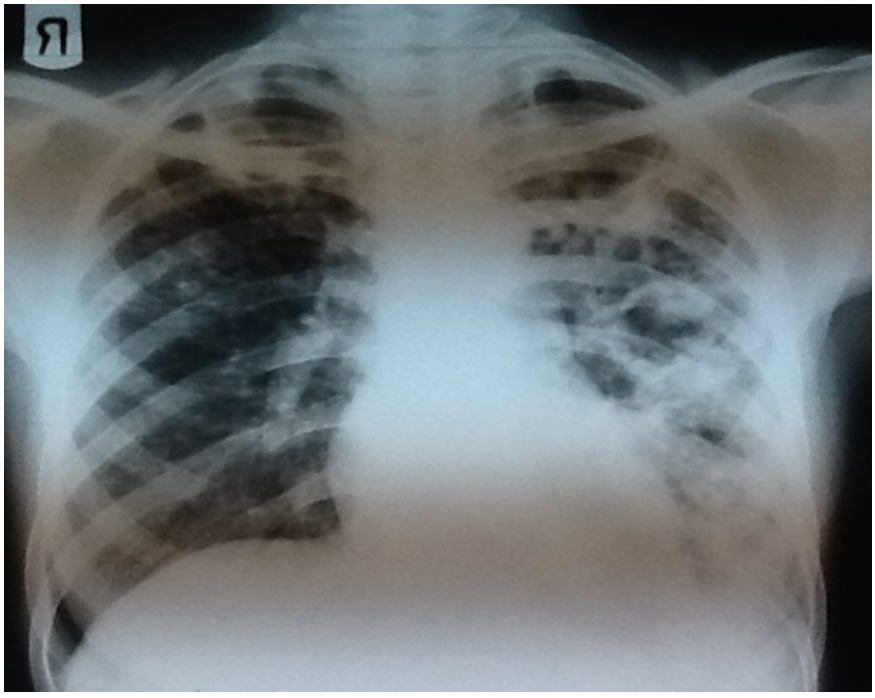

Figure 3: PA chest radiograph of 48 year old patient showing fibrocavitatory lesion in entire left lung field and right upper zone (CD4 Count = 468cells/µl, VL = 200 copies/ml).

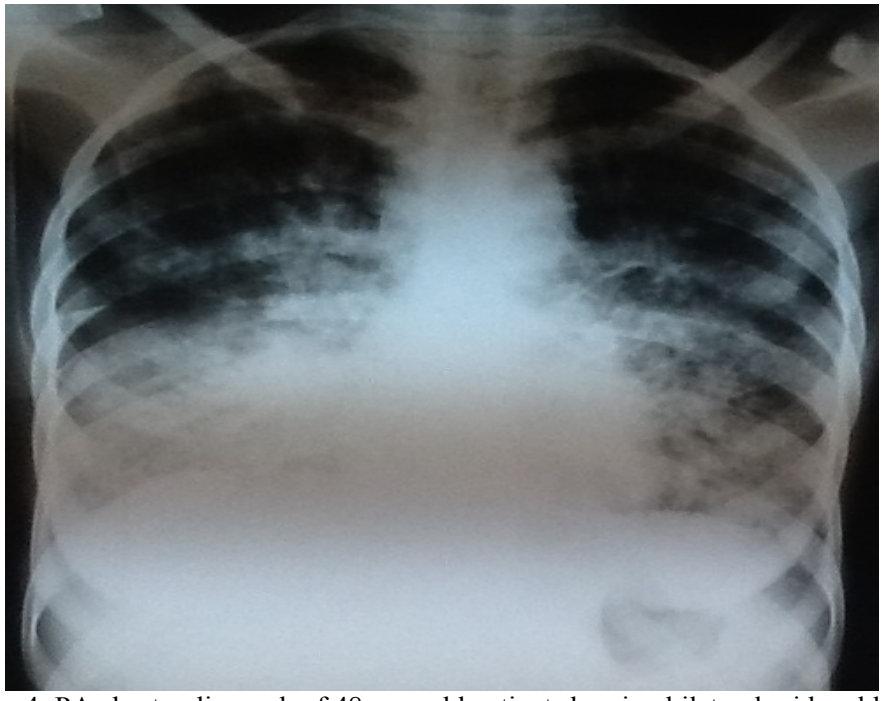

Figure 4: PA chest radiograph of 48 year old patient showing bilateral mid and lower zones non homogeous opacities. VL = 242,152 copies/ml

4 Discussion

The result of this study shows that the pattern and distribution of HIV-related pulmonary tuberculosis lesion on chest radiograph are heterogonous. The association between certain radiographic features and immunosuppression as reflected by CD4 count and viral load, may be attributable to the role played by intact cellular immunity or otherwise and different pathogenic mechanisms of TB among persons with HIV infection. In this report, high viral load $\geq \log10^5$ copies/ml an indication of advanced disease was associated with intrathoracicadenopathy, a common feature of primary TB. Similar to report by [11] but in sharp contrast to [12-14] we did not observe association between level of CD4 count a marker of immunity and adenopathy. Hilar or mediasternaladenopathy has been noted to be more common among those with HIV-related TB than among HIV-uninfected TB, among those with HIV infection, adenopathy was more common in patients with advanced disease[12,15]. Additionally, adenopathy was observed most commonly on chest radiolgraphs of individuals with primary multi drug-resistance TB [16]. This link may suggest that individuals with advanced disease are at greater risk of developing progressive primary TB.

Cavity lesion was common in our cohort, reports from studies conducted in other African countries [4,12,17-19] shows cavities is a common radiological feature observed among HIV-TB co infected patients. While cavities may be seen in primary TB, they usually represent a manifestation of reactivated TB, and their formation requires an adequate delayed hypersensitivity response. This may imply that in Africa, a substantial part of the burden of HIV-related tuberculosis is likely due to reactivation of latent infection and progression of chronic disease, perhaps as result of immunodeficiency. Further more, although several data suggest that radiographic pattern of reactivated TB are more commonly seen in HIV-infected patients with intact cell mediated immunity, the absence of association between cavities and near intact immunity CD4 Count ≥200cells/µl in our study may suggest persistence of cavity lesions with progression of HIV infection. Nodular lesions on chest radiographs were observed to be more frequent with lower HIV-RNA viral load, while streaky changes and features of consolidation was seen more frequent with higher CD4 counts. Studies have documented higher preponderances of infiltrate with higher CD4 counts.

Although pleural effusions due to TB have been reported to occur across wide range of CD4 count with higher incidence in those with intact immunity, we did not observe a remarkable difference in the frequency of pleural effusion as a function of CD4 count or viral load parameters similar to previous reports[11,12],. Our finding is in contrast to a study in Brazil [7] that documented pleural effusion to be associated with CD4 count <200cells/µl. On the other hand, workers that reported pleural effusion predominantly in patients with CD4 count ≥200cells/µl argue that pleural effusion in HIV positive patients is due to hypersensitive reaction in the pleura, occurring in patients with relatively intact immunity [13].

We report that lesions involving the upper zone was most often observed among patient with relatively intact immune system (CD4 count ≥200 cells/µl) as commonly observed in HIV negative individuals with PTB. Our finding was corroborated by other workers. The middle and lower lung zone involvement were most commonly seen in cohort with CD4 count <200cells/µl, in agreement with report from USA, Brazil and Cote divoire [7,20,21]

5 Conclusion/Limitations

Our study demonstrates association between HIV disease stage with pattern and distribution of certain tuberculosis lesion on chest radiograph. Knowledge of immunological and virological parameters is important to clinicians and radiologist when evaluating CXR findings in HIV-infected patients.

This report has some limitations, mixed respiratory infections may influence the pattern of abnormalities seen on chest radiographs. Howevever this is a known challenge for radiologists evaluating films from immunocompromised patients. Our study was limited in size and large studies of patients across a range of CD4 count, including patients with greater frequency of non-TB opportunistic infections, are needed in order to determine what features distinguishes TB from other opportunistic infections. Other pulmonary conditions such as occupational lung diseases, sarcoidosis and chronic obstructive airway diseases that could mimic features of PTB on chest radiograph were not controlled for in this study. Lastly, the time lag between onset of symptoms and patients presentation could affect the radiological findings.

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