Determination of the Effect of Highly Active Antiretroviral Therapy on Radiographic Features of Pulmonary Tuberculosis in HIV Infected Patients

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ABSTRACT

Background: The chest radiographic appearances of HIV-seropositive patients presenting with pulmonary tuberculosis (PTB) are diverse, creating difficulty in diagnosis and treatment. Determination of the effect of highly active antiretroviral therapy (HAART) on radiographic features of pulmonary tuberculosis among HIV infected patients was investigated in order to find out the pattern in our environment and to provide an empirical approach for early diagnosis and treatment of patients. **Aim:** The aim of this study is to determine the effect of HAART on radiographic features of pulmonary tuberculosis in HIV-infected patients. **Materials and Methods:** A cross sectional study of 60 consecutively confirmed HIV- seropositive patients who had been diagnosed of the infection for at least six months before the commencement of this study, aged between 19 and 50 years (Mean ± SD: 32.9 ± 7.15) comprising 22 males and 38 females with newly diagnosed sputum smear positive PTB was conducted at the infectious disease clinic of the University of Maiduguri Teaching Hospital, between March 2010 and February 2011. The subjects were HIV/PTB patients on HAART for at least 6 months before presenting with PTB (32) and HIV/PTB but Antiretroviral (ARV)-naïve who were already confirmed HIV positive for at least 6 months before presenting with PTB (28). Posterior-anterior (PA) and lateral chest radiographs were obtained with film screen at 50-70 kVp in majority of the patients. CD4 + lymphocyte counts were obtained for all the patients. The chest radiographic images were evaluated for the presence of either typical or atypical patterns of PTB. Apical opacities with or without cavitations was considered typical while atypical patterns included miliary, lower or mid-zone consolidation, reticulonodular opacities, pleural effusion, hilar adenopathy and normal radiograph. **Results:** Majority (78.6%) of HIV/PTB patients on HAART with CD4 counts of ≥ 200 cells/μl had typical pattern of PTB whereas atypical pattern of PTB was significantly seen in HIV/PTB ARV naïve patients with majority of this group of patients (62.5%) had CD4 count of <200 cells/μl (P = 0.001). **Conclusion:** Majority (78.6%) of HIV/PTB patients on HAART had typical pattern of PTB whereas atypical pattern of PTB was significantly seen in HIV/PTB ARV naïve patients (62.5%) (P = 0.001). We concluded that radiographic patterns of PTB in HIV varied over a spectrum and are related to HIV disease stage and HAART treatment.

Key words: Chest radiograph, highly active antiretroviral therapy, human immunodeficiency virus, pulmonary tuberculosis

Introduction

The recent increase in the prevalence of tuberculosis (TB) globally and particularly in Africa has been attributed to the increase in number of human immunodeficiency virus (HIV) - infected patients.[1,2] Reports from different parts of the world, including Nigeria have demonstrated the rising incidence of TB especially pulmonary TB in HIV - infected patients as well as a high rate of HIV in patients suffering from tuberculosis.[3] Co-infection with HIV and *M. tuberculosis* has profound implications for the course of both diseases. HIV - induced immunodeficiency is thought to lead to reactivation of latent infection with *M. tuberculosis* and may the main factor behind the resurgence of tuberculosis and the high rates of primary or recent tuberculosis due to inability to control the initial infection.

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The course of human immunodeficiency virus (HIV) infection has been profoundly modified by the introduction of protease inhibitor - containing combination therapy, also known as highly active antiretroviral therapy (HAART). In industrialized countries, a strong decline in the incidence of acquired immunodeficiency syndrome (AIDS)-related conditions and mortality of HIV-infected persons has been recorded since the widespread clinical use of this therapy.[4,5] It has been shown that the use of HAART significantly reduces the risk of developing active TB among HIV-infected persons.[6,7]

The chest radiograph of pulmonary TB in HIV - infected patients, who receive HAART, reflects more frequently the "classic" post-primary pattern, including cavitary consolidation in the upper lobes. A series of studies suggest that the radiographic appearance of pulmonary TB in HIV-infected patients varies with degree of immunosuppression.[6,7] Highly active antiretroviral therapy may significantly increase the CD4 lymphocytes number and function in a significant proportion of HIV–infected patients. Moreover there is accumulating evidence that this therapy may reduce the risk of developing HIV–associated TB, although this continues to occur also in HIV–infected patients who are on HAART.[7,8]

Conventional chest X-ray and high resolution computerized tomography of the chest are the commonest radiological methods of investigation that could be used to determine the effect of HAART on radiographic features of pulmonary TB in HIV-infected patients.[9,10]

However, we decided to make use of conventional chest X-ray to carry out this study, because it is readily available, affordable, and more importantly delivers less radiation dose to patients when compared to computerized tomography and they can be reproduced in most hospitals in developing countries.[9]

The aim of this study was to determine the effect of HAART on radiographic features of pulmonary tuberculosis in HIV-infected patients.

Materials and Methods

This study was carried out at the University of Maiduguri Teaching Hospital, Maiduguri, Nigeria between March 2010 and February 2011. Maiduguri is the capital of Borno State in north-eastern Nigeria with a population of about 0.7 million.

A total of 60 consecutive patients with pulmonary tuberculosis, and who were positive for HIV antibodies as detected by enzyme - linked immunosorbent assay (ELISA) and confirmed by immunocomb 11 (IMMUNOCOMBFIRM), who must have been diagnosed positive for HIV antibodies for at least six months duration before presenting at the infectious diseases (ID) clinic of University of Maiduguri Teaching Hospital, Maiduguri where they were diagnosed positive for pulmonary tuberculosis and who also fulfilled the inclusion criteria were recruited into a prospective cross-sectional study after obtaining an informed written consent.

Inclusion criteria

I Adult patients (>15 years) with confirmed HIV–infection for at least 6 months duration before they were diagnosed with pulmonary TB. Pulmonary TB is diagnosed by the presence of (a) and one other criteria listed below;
- Presence of AFB in the sputum.
- Clinical features (cough >3 weeks, night sweat, fever, and weight loss)
- Chest X-ray features suggestive of pulmonary TB.
- Positive mantoux reaction.

II Adult Patients who had commenced HAART for at least 6 months before presenting with features of pulmonary TB as in 1 above.

Exclusion criteria

- Patients on immunosuppressive drug therapy
- Patients on anti TB therapy for more than one month
- Patients who declined consent to participate in the study
- Patients with diabetes mellitus, chronic renal failure, nephrotic syndrome, sickle cell disease and widespread malignancies.

On entering the study after satisfying the inclusion criteria, a questionnaire was administered to each patient and details regarding demographic data, CD4 T-lymphocyte count and radiographic patterns were documented.

Posterior anterior (PA) and lateral chest radiographs were obtained with film screen at 50-70 kVp in majority of the patients.

The obtained chest radiographic images were reviewed by 3 consultant radiologists to arrive at consensus diagnosis. Where there were uncertainties in the imaging findings the cases were not included in the study.

For descriptive purposes, both lung fields were divided in to 3 zones by two horizontal lines through the anterior ends of the second and fourth anterior ribs.[11] Findings were classified as consolidation, cavitations, reticular changes, nodular opacities, reticulo-nodular opacities, mediastinal/hilar–adenopathy, pleural effusion, lung collapse and miliary pattern. Where all such features were absent the radiograph was classified as normal. Furthermore, the Chest radiograph patterns of pulmonary TB were classified as typical when there is apical opacities with or without cavitations, and they were classified as atypical if reticular changes and cavities were present predominantly in the lower zones, and if intra-thoracic adenopathy, and miliary disease was present, or if the chest radiograph was normal.[9]

Statistical methods

The data obtained were entered into a computer to generate a computerized database for subsequent analysis using SPSS version 11.0. Values were expressed as mean ± standard deviation (M ± SD). Chi-square and Student *t*-test were used to analyse the data. A $P < 0.05$ was considered significant. Tables and diagrams were used for illustration as and when appropriate.

Outcome measures

1. CD4 + cell counts
2. Chest Radiographic patterns

Ethical consideration

All aspects of the study were reviewed and authorized by the ethical committee of the University of Maiduguri Teaching Hospital before initiation. Patients had freedom to decline consent for, or opt out of the study at any stage without any consequences.

Results

Sixty patients who had been confirmed HIV positive for at least six months duration and newly diagnosed with positive sputum AFB smear were studied. Of these, 32 (53.3%) were on HAART for at least 6 months before presenting with PTB and 28 (46.7%) were not on HAART because they absconded after they were confirmed HIV positive and only returned to the clinic when they developed pulmonary complication (PTB). This prospective, cross sectional study was carried out between March 2010 and February 2011. All the patients had plain PA and lateral chest radiographs and $CD4^+$ T-lymphocyte count determination. Thirty eight (63.3%) patients were females and 22 (36%), were males. Their ages ranged between 19 and 50 years (Mean ± SD: 32.9 ± 7.15).

Table 1 shows the frequency of HIV/PTB in the different age groups and sexes. The most prone sex and age groups occurred in females between 25 and 34 years.

Figure 1 shows the frequency of HIV/PTB in the different marital status groups. Married men and women were the majority in the study representing 61.7%.

Figure 2 shows the distribution of occupation of the patients. Significant numbers of patients were made up of either house wives or students, representing 25% and 23.3%, respectively.

Table 2 shows extent and distribution of consolidation in HIV/PTB patients on HAART and HIV/PTB ARV- naïve patients in the study. Of note is that more of the patients with HIV/PTB on HAART had consolidation in their upper zones when compared with HIV/PTB ARV- naïve ($P = 0.01$). The lobar pattern of consolidation was less commonly seen among HIV/PTB ARV-naïve patients than HIV/PTB patients on HAART ($P = 0.04$). Also left sided consolidation tended to occur frequently among HIV/PTB on HAART compared to HIV/PTB ARV- naïve patient ($P = 0.03$).

Table 1: Age and sex distribution of the patients studied

Age (years)	Sex		Total (%)
	Male	Female	
15-19	-	1	1 (1.7)
20-24	-	1	1 (1.7)
25-29	3	16	19 (31.7)
30-34	7	9	16 (26.7)
35-39	5	4	9 (15)
40-44	3	6	9 (15)
45-49	3	-	3 (5)
≥50	1	1	2 (3.3)
Total	22	38	60 (100)

Table 2: Consolidation in HIV/PTB on HAART and HIV/PTB Arv-naïve

Characteristics	HIV/PTB ARV naïve (%)	HIV/PTB on HAART(%)	Total (%)	*P* value
Consolidation				
Zonal distribution				
Upper zone	1 (3.6)	24 (75)	36 (60)	0.011*
Mid zone	4 (14.3)	0 (0)	1 (1.7)	0.47
Lower zone	7 (25)	2 (6.3)	6 (10)	0.27
Mid/Lower zone	5 (17.9)	5 (15.6)	12 (20)	0.37
Extentof consolidation				
Patchy	7 (25)	2 (6.3)	7 (11.7)	0.24
Segmental	10 (35.7)	4 (12.5)	11 (18.3)	0.18
Lobar	2 (7.1)	20 (62.5)	30 (50)	0.038*
Entire lung	14 (50)	5 (15.6)	7 (11.7)	0.43
Side of consolidation				
Right	6 (21.4)	10 (31.3)	24 (40)	0.19
Left	4 (14.3)	14 (43.8)	20 (33.3)	0.026*
Bilateral		7 (21.9)	11 (18.3)	0.52

*Significant at *P*=0.05. HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy

Table 3 shows the cavitation pattern in the HIV/PTB patients on HAART and HIV/PTB ARV- naïve patients. Significantly, more of HIV/PTB patients on HAART had cavitary lesions when compared to HIV/PTB ARV-naïve ($P = 0.03$). However, the trend towards the zonal location, side of affectation, wall thickness or presence of air-fluid level in the cavities in the two groups of patients were not statistically significant.

Table 4 shows the distribution of reticular, nodular, reticulonodular, miliary changes and loss of volume among HIV/PTB patients on HAART and HIV/PTB ARV- naïve patients. PTB/HIV patients on HAART had significantly more reticular changes in the upper zone than HIV/PTB ARV-naïve ($P = 0.02$).There was no statistically significant difference in the appearance of nodular opacities in the two groups of patients ($P > 0.05$). HIV/PTB patients on

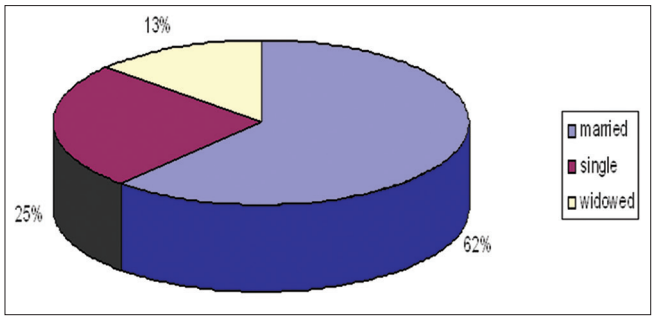

Figure 1: Distribution of marital status among the patients studied

Table 3: Cavitations in HIV/PTB on HAART and HIV/PTB Arv-naïve

Characteristics	HIV/PTB ARV-naïve (%)	HIV/PTB on HAART (%)	Total (%)	*P* value
Cavities present	7 (25)	7 (53.1)	24 (40)	0.027*
Upper zone	5 (71.4)	15 (88.2)	20 (33.3)	0.55
Mid zone	0 (0)	1 (5.9)	1 (1.7)	1.0
Lower zone	2 (28.6)	1 (5.9)	3 (5)	0.19
Right	3 (42.9)	10 (58.8)	13 (21.7)	0.66
Left	2 (28.6)	4 (23.5)	6 (10)	1.0
Bilateral	2 (28.6)	3 (17.6)	5 (8.3)	0.4
No of cavities				
0	21 (75)	15 (46.9)	36 (60)	0.027*
1	1 (14.3)	3 (17.6)	4 (6.7)	1.0
2-4	1 (14.3)	2 (11.8)	3 (5)	1.0
5-8	3 (42.9)	10 (58.8)	13 (21.7)	0.66
>8	2 (28.6)	2 (11.8)	4 (6.7)	0.55
Thin wall (<2mm)	1 (14.3)	4 (23.5)	5 (8.3)	0.4
Thick wall (≥2mm)	6 (85.7)	13 (76.5)	19 (31.7)	0.1
Air-fluid level	2 (28.6)	6 (35.3)	8 (13.3)	1.0

*Significant at *P*=0.05. HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy

HAART showed less reticulonodular opacities compared to PTB/HIV ARV-naïve patients, and this was commonly noted bilaterally ($P = 0.005$).

Similarly, there was significant difference in the appearance of normal chest radiographs in HIV/PTB ARV- naïve compared to HIV/PTB on HAART with the former subjects being the majority ($P = 0.038$). The prevalence of other features such as lung collapse and miliary disease all occurred with a very low frequency [Table 4].

Table 5 shows Adenopathy in HIV/PTB on HAART and HIV/PTB Arv-naïve patients. Adenopathy was more common in HIV/PTB ARV-naïve patient compared to HIV/PTB patients on HAART ($P = 0.00$). The hilar adenopathy was commonly unilateral on the right but this was not statistically significant ($P > 0.05$). Only two cases of mediastinal adenopathy (paratracheal) were seen in this study [Table 5].

Table 6 Pleural fluid collection among HIV/PTB patients on HAART and HIV/PTB ARV-naïve. Pleural effusion was more

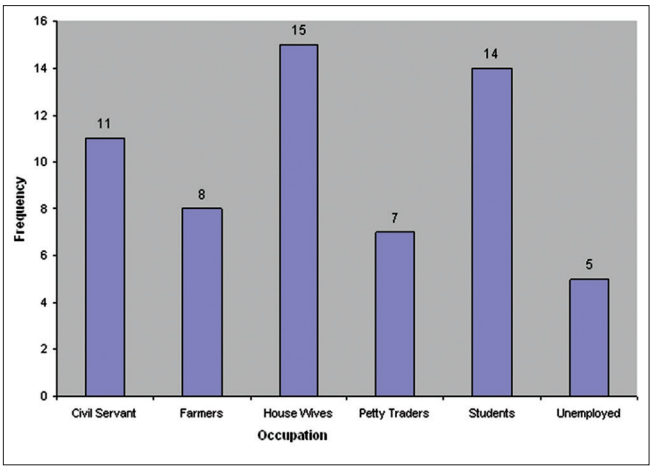

Figure 2: Distribution of occupation among the subjects studied

common among HIV/PTB ARV- naïve patients and were found on the right in both group of patients but the differences were not statistically significant ($P > 0.05$) [Table 6].

Table 7 summarises the chest X-ray pattern, and it shows that typical radiological presentations were more in HIV/PTB on HAART patients ($P = 0.001$) about 62.5% of cases had typical pattern while atypical pattern were seen more among HIV/PTB ARV-naïve patient (78.6%).

A total of 68.7% of HIV/PTB on HAART patients had a CD4 counts of ≥200 as against 39.3% of ARV-naïve HIV/PTB patients ($P = 0.00$). Also 60.7% of HIV/PTB ARV-naïve patients had CD4 counts less than 200 cells/μl. as against 31.3% of HIV/PTB on HAART patients ($P = 0.00$). Figures 3-8 are some of the chest radiographic findings in the patients studied.

Discussion

The age distribution among HIV-associated PTB patients reported by other Nigerian workers,[9,10] and Hsieh *et al.*,[12] in Taiwan, is similar to this study. This corroborates the fact that HIV is more common in people in their reproductive and sexually active age groups.

The male:female ratio reported by authors in other parts of the world[13] and Nigeria[9,10,14,15] either found a male preponderance or an even sex distribution. This is in contrast to the female preponderance in this case. The reason for this could be either due to polygamy, early marriages, and freedom to remarry after divorce or death of a spouse which is the order of the day in this part of the country. A remote possibility could be that more women may be presenting to the hospital than men.

Majority of the patients were low income earners as most of them were house wives, students, civil servants and farmers. The rest of the patients were petty traders or unemployed and therefore belong to low socioeconomic stratum of the society.

Table 4: Reticular/Nodular/Reticulonodular changes in HIV/PTB on HAART and HIV/PTB ARV-naïve

Characteristics	HIV/PTB ARV-naïve (%)	HIV/PTB on HAART (%)	Total (%)	*P* value
Reticular changes				
Upper zone	5 (17.9)	15 (46.9)	20 (33.3)	0.017*
Mid zone	1 (3.6)	3 (9.4)	4 (6.7)	0.36
Lower zone	6 (21.4)	0 (0)	6 (10)	0.008*
Mid/Lower zone	7 (25)	2 (6.3)	9 (15)	0.4
Entire Lung	2 (7.1)	1 (3.1)	3 (5)	0.5
Right	10 (35.7)	15 (46.9)	25 (41.7)	0.4
Left	4 (14.3)	4 (12.5)	8 (13.3)	1.0
Bilateral	7 (25)	2 (6.3)	9 (15)	0.42
Nodular changes				
Upper zone	1 (3.6)	3 (9.4)	4 (6.7)	0.4
Mid zone	0 (0)	1 (3.1)	1 (1.7)	0.4
Lower zone	2 (7.1)	0 (0)	2 (3.3)	0.5
Right	2 (7.1)	2 (6.3)	4 (6.7)	0.2
Left	1 (3.6)	2 (6.3)	4 (6.7)	1.0
Reticulo-nodular opacities				
Upper zone	0 (0)	2 (6.3)	2 (3.3)	0.2
Mid zone	0 (0)	1 (3.1)	1 (1.7)	0.2
Mid/Lower zone	2 (7.1)	2 (6.3)	4 (6.7)	0.5
Lower zone	5 (17.9)	6 (18.8)	11 (18.3)	0.6
Entire lung	3 (10.7)	5 (15.6)	8 (13.3)	0.6
Right	6 (21.4)	3 (9.4)	9 (15)	0.3
Left	4 (14.3)	1 (3.1)	5 (8.3)	0.2
Bilateral	4 (14.3)	12 (37.5)	16 (26.7)	0.005*
Miliary disease	2 (7.1)	0 (0)	2 (3.3)	0.00*
Loss of volume	2 (7.1)	3 (9.4)	5 (8.3)	0.6
Normal	8 (28.6)	2 (6.3)	10 (16.7)	0.038*

*Significant at *P*=0.05. HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy; ARV – Antiretroviral

Table 5: Adenopathy in HIV/PTB on HAART and HIV/PTB ARV-naïve patients

Characteristic	HIV/PTB Arv naïve (%)	HIV/PTB on HAART (%)	Total (%)	*P* value
M/adenopathy	2 (7.1)	0 (0)	2 (3.3)	0.2
H/adenopathy				
Right	7 (25)	2 (6.3)	9 (15)	0.47
Left	3 (10.7)	0 (0)	3 (5)	0.096
Bilateral	2 (7.1)	0 (0)	2 (3.3)	0.2
T/adenopathy	14 (50)	2 (6.25)	16 (26.7)	0.00*

*Significant at *P*=0.05. M – Mediastinalm; H – Hilar; T – Total; HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy; ARV – Antiretroviral

This, coupled with poverty, ignorance and disease further assist the spread of HIV/PTB in these patients.

The work of Kolawole *et al*.,[16] in Ibadan Nigeria in 1975 shows that, the upper lobes were the most affected and there were also adults with the childhood pattern, the reason for which was said to be most probably due to failure of the localization of the primary intrapulmonary parenchyma lesions with

Table 6: Pleural fluid collection HIV/PTB on HAART and HIV/PTB ARV-naïve

Characteristics	HIV/PTB ARV-naïve (%)	HIV/PTB on HAART (%)	Total (%)	*P* value
Pleural effusion				
Mild	3 (10.7)	2 (6.3)	5 (8.3)	0.5
Moderate	2 (7.1)	1 (3.1)	3 (5)	0.5
Severe	1 (3.6)	1 (3.1)	2 (3.3)	0.7
Total	6 (21.4)	4 (12.5)	10 (16.7)	0.49
Site of effusion				
Right	5 (83.3)	3 (75)	8 (13.3)	0.3
Left	1 (16.7)	1 (25)	2 (3.3)	0.7

HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy; ARV – Antiretroviral

Table 7: Summary report of patient's radiographic pattern of presentation

CXR presentations	HIV/PTB on HAART (%)	HIV/PTB ARV-naïve (%)
Typical	20 (62.5)	6 (21.4)
Atypical	12 (37.5)	22 (78.6)
Total	32 (100)	28 (100)

P=0.001. HIV – Human immunodeficiency virus; PTB – Pulmonary complication; HAART – Highly active antiretroviral therapy; ARV – Antiretroviral

subsequent hematogenous spread. The Ibadan study was carried out before the era of HIV infections suggesting that in the Nigerian population, other factors could account for atypical radiological features as seen in HIV related PTB. Braun,[17] Solomon and Robinowitz[18] concluded that the high incidence of diabetes mellitus, malnutrition and other infections as well as environmental socioeconomic factors could account for the severity of PTB. However Bussi Rizzi *et al*. in 2003[19] concluded that chest imaging of pulmonary TB in HIV–infected patients who received HAART, reflects more frequently the "classic" post primary pattern and a primary pattern was significantly more frequent in HIV/PTB ARV naïve compared with HIV/PTB on HAART. This study is in agreement with the above workers and the reason for these findings is probably due the partial restoration of cell mediated immunity that can be induced by HAART.

The work of Lawn *et al*.,[20] *in* 1999 described low frequencies of bronchopulmonary spread, less consolidation, apical involvement, volume loss and pleural thickening in HIV/PTB ARV- naïve patients. The paucity of consolidation in HIV/PTB ARV- naïve patients when compared to HIV/PTB on HAART in this study is in conformity with the above workers. It is likely that the observed difference was due to a reflection of the decreased cell-mediated immunity in ARV- naïve patients. Obajimi *et al*.,[21] reported more radiographic changes in the left, which is in agreement with this study. Generally, from the anatomic point of view, the left lung has only two lobes, upper and lower with lingular representing the middle lobe on the right. Spread of disease from the lingular to the upper zone was much easier. This coupled with the fact that patients on

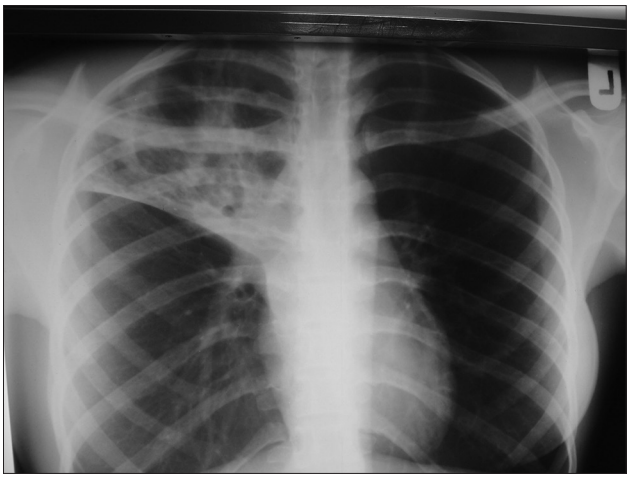

Figure 3: PA chest radiograph of HIV/PTB on HAART patient showing a fairly homogenous opacity with background cavitatory changes in the right upper zone bounded inferiorly by elevated transverse fissure. There is obliteration of the right mediastinal outline

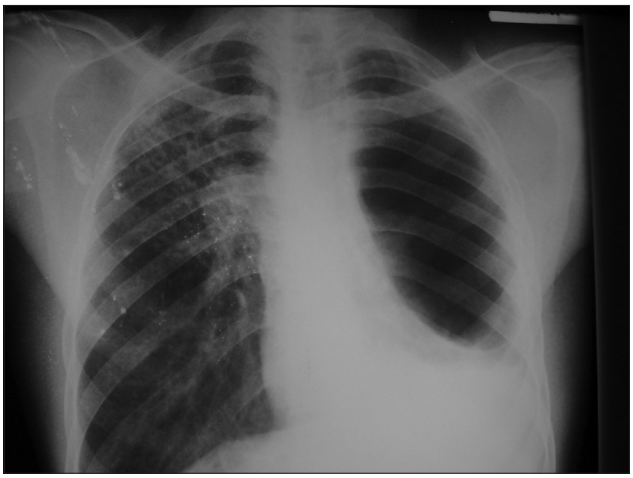

Figure 5: PA chest radiograph of HIV/PTB on HAART patient showing streaky opacities in the right upper zone. The right hilum is full with lobulated outline representing adenopathy. There is a homogenous opacity in the left lower zone obliterating both diaphragmatic and cardiac outline with tracking along the lateral chest wall. These appearances are in keeping with right upper zone fibrosis with right hilar adenopathy and left pleural fluid collection

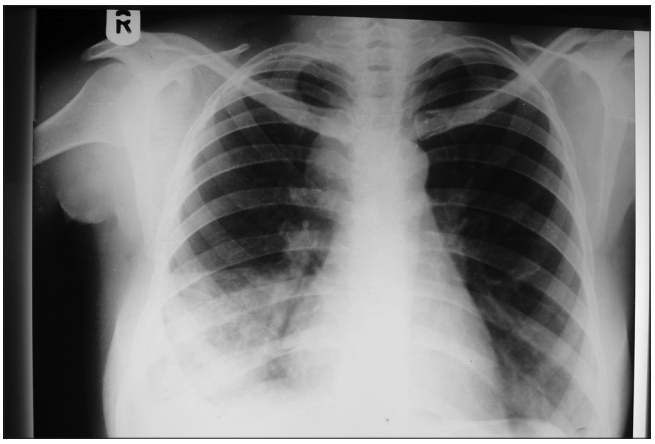

Figure 4: PA chest radiograph of HIV/PTB ARV-naïve patient showing a fairly homogenous opacity in the right lower zone obliterating the adjacent diaphragmatic outline in keeping with consolidation. There is widening of the right superior mediastinum with lobulated outline suggesting mediastinal adenopathy.Right axillary fullness with lobulated outline and curvilinear calcification was also noted suggestive of axillary adenopathy

Figure 6: PA chest radiograph of HIV/PTB ARV-naïve patient showing marked right hilar fullness with lobulated outline representing hilar adenopathy. Reticulonodular changes are also seen in the remaining lung fields bilaterally but worse on the left

HAART have higher immunity in most cases than ARV- naïve patients may account for such findings in the study.

Cavity formation is the end result of granuloma formation and necrosis with subsequent liquefaction and drainage of caseous material in to the bronchial tree, and occurs only in the presence of reasonably intact specific delayed type of hypersensitivity. Extra cellular growth of tubercle bacilli is greatest in the liquefied material in cavity lesions. PTB in patients with advanced HIV immunosuppresion is characterized by diffuse infiltrates, a high tissue burden of mycobacteria in the lung, a poorly formed or absent granuloma formation and a lower frequency of cavitary disease.[22-24] The work of Agua *et al*.,[25] found cavitations to occur less frequently as the CD4 count declined. This is in agreement with this study which shows highly significant percentage of HIV/PTB on HAART to have pulmonary cavitation compared to HIV/PTB ARV- naïve patient. Furthermore, Kolawole *et al*.,[16] and Ahidjo *et al*.,[26] concluded that multiple cavitations are a common finding in pulmonary tuberculosis and occur predominantly in the upper lobes.

The highly significant wide spread bilateral reticulonodular opacities among HIV/PTB patients on HAART to the best of our knowledge it has not been reported. Woodring *et al*.,[27] was of the opinion that, in an area of high PTB prevalence, atypical chest radiographic presentation of PTB is common and is a specific clinical predictor of advanced HIV infection. This is not in any way different from the work of Choyke

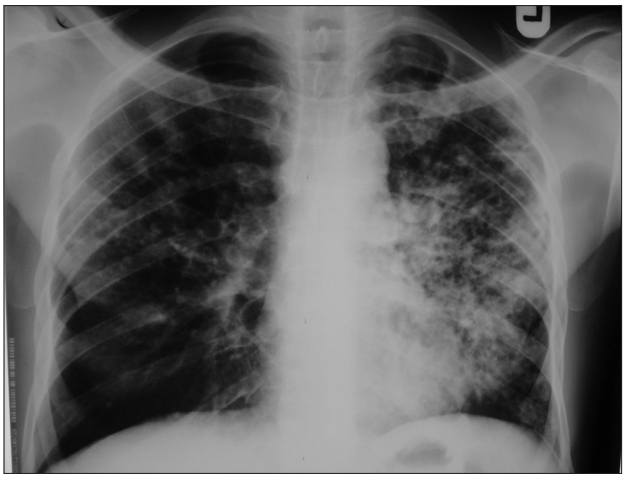

Figure 7: P.A chest radiograph of HIV/PTB ARV-naïve patient showing widespread reticulonodular opacities with background cystic changes in both lung fields worse on the left

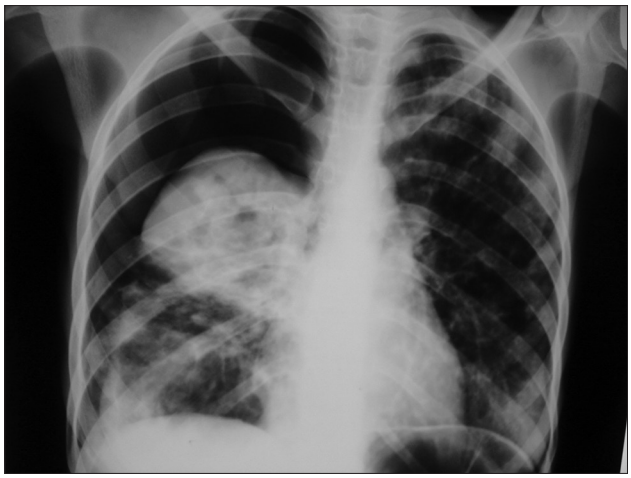

Figure 8: PA chest radiograph of HIV/PTB on HAART patient, showing an area of increased transradiancy devoid of lung markings in the right upper and mid zones in keeping with pneumothorax. A homogenous opacity in the right hilar and perihilar region obliterating the adjacent mediastinal outline representing a collapsed lung is noted. Patchy and streaky changes are seen in the remaining lung fields bilaterally but worse on the left. Patient is markedly wasted

et al.,[28] who found out that, the pattern associated with primary TB include hilar and mediastinal adenopathy, pleural effusion, miliary disease, pulmonary opacities in the anterior segment of the upper lobes or middle and lower lobes and normal chest radiograph. The atypical chest radiographic findings among the HIV/PTB ARV naïve patients in this study are in conformity with the findings by the above workers in which the consensus was that CXR findings in patients with HIV/PTB co-infection are more atypical than those with only PTB.

Lymphadenopathies have been reported by other workers as an unusual mode of presentation of PTB in adults.[29,30] Although these studies were carried out before the era of HIV, the trend has changed as evidenced by the work of other authors such as Ahidjo *et al*.,[31] who concluded that there is a rise in the prevalence of lymphadenopathy among pulmonary tuberculosis patients when compared to a previous study done in the pre-HIV era in Nigeria. In the study by Ahidjo *et al.*,[31] it was reported that 32.7% had hilar adenopathy out of which 12.9% was left sided. Atalabi *et al.*,[32] also recorded high incidence of lymphadenopathy on chest radiograph among antiretroviral therapy naïve human immune-deficiency virus positive children in a paediatric care program in Ibadan. In this present study there was more lymphadenopathy recorded among HIV/PTB ARV-naïve compared to HIV/PTB on HAART. In this study right hilar adenopathy was more common than left for HIV/PTB ARV-naïve and HIV/PTB Patients on HAART, but the difference was not statistically significant. The higher percentage of adenopathy in HIV/PTB ARV-naïve in this study is in keeping with the work of Aguwa *et al.*,[25] who reported 55.2% in Enugu, Nigeria and is also similar with workers in Cape Town, South Africa[33] who concluded that adenopathy is the best predictor of low CD4 + Lymphocyte count.

Also, studies in Rwanda,[24] Zambia[34] and South Africa[33] show that, significantly more hilar lymphadenopathy and less cavitations and upper lobe involvement were noted among HIV/PTB patients which is in agreement with our study.

In another report, Pitchenic and Rubinson[35] described a typical radiographic pattern in only one (6%) of 17 AIDS patients. This study reported much higher percentage than the above workers, probably because the immune status of the patients in our study is higher than that of the patients in the above study.

The high percentage of normal chest radiographs in HIV/PTB ARV-naïve compared to HIV/PTB on HAART agrees with the work of Ahidjo *et al.*,[36] and Given *et al.*,[37] in which they concluded that absence of changes in chest radiograph does not exclude the diagnosis of PTB. Normal chest radiograph probably reflects the inability of the immunocompromised patient to generate a granulomatous inflammatory response.

There was no significant difference in the appearance of pleural fluid collection between HIV/PTB on HAART and HIV/PTB ARV-naïve patients. This is higher than the 9% reported by kolawole *et al.*[16] The above study was carried out before the era of HIV which may account for the low values. The differences may be due to immune status of the patients or racial variations in host response to *M tuberculosis*. Some studies established that pleural effusion, though regarded as a marker of early clinical HIV-disease[33,38] occurred even when the lymphocyte counts are low and its presence was less helpful for prediction of HIV stage of disease.[8]

It is interesting to note that, no significant difference was observed in the occurrence of lung collapse and miliary pattern for HIV/PTB ARV-naïve and HIV/PTB Patients on

HAART, respectively. These findings are in agreement with other workers.[25,39]

A series of studies[40,41] suggest that the radiographic appearance of PTB in HIV-infected patients varies with the degree of immunosuppression. Patients with CD4 lymphocyte count above 200cells/mm, more commonly have the post primary pattern of TB, including cavitary consolidation in the upper lobe and infrequently lymphadenopathy. A CD4 lymphocyte count below 200cells/mm is usually associated with a primary TB pattern including adenopathy, pleural effusion, and areas of non-cavitary consolidation, more frequent in the middle-lower lobes but often randomly distributed in the lung.

Conclusion

The chest radiograph remains a useful diagnostic modality for PTB in HIV-positive patients. HIV-infected patients with pulmonary TB, receiving HAART, had a post-primary pattern more frequently than those not receiving this treatment. This observation is consistent with the partial restoration of cell-mediated immunity that can be induced by HAART.

Limitation

The study was a cross-sectional study and hence did not involve the follow-up of patients to see the various radiological changes that might occur with treatment.

Recommendation

Chest-x-ray should be carried out on all patients with suspected HIV-related PTB while bearing in mind that a normal chest radiograph does not rule out PTB.

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