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Comparison of chest radiographic findings among HIV positive and negative adults with smear positive Pulmonary Tuberculosis in Dar-es-salaam

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Abstract

Background
Chest X-ray radiography is a widely available and cheap imaging modality used for identification of pulmonary tuberculosis (PTB) in suspected patients. Knowledge of discriminatory features of PTB among HIV infected patient is of utmost importance to improve tuberculosis case detection and consequently reduce morbidity and mortality associated with TB among HIV infected individuals. We aimed to describe chest radiographic findings among PTB patients and their association with HIV co-infection and CD4 levels among HIV positive patients.

Methodology
A total of 170 newly diagnosed consented smear positive PTB patients underwent postero-anterior Chest radiographs (PA - CXR) and HIV testing. Determination of CD4 count was performed among HIV positive patients. The radiographs were interpreted using glossary of terms for thoracic radiology by two independent radiologists who were blinded to HIV diagnosis.

Results
Study participants included 100 (58.9%) males and 70 (41.1%) females. Among these 54 (31.8%) had HIV/PTB co-infection. The pattern of radiographic findings among patients with PTB/HIV compared to PTB only were: pulmonary cavities 44.4% vs 61.2%, (p=0.04), alveolar consolidation 64.9% vs 81.7%, (p=0.04), upper zone consolidation 40.7% vs 57.8%, (p=0.039), middle zone consolidation 25.9% vs 44.8%, (p=0.019) and typical PTB 40.7% vs 57.8%, (p=0.039), respectively. Therefore, lesions were less likely to be observed among PTB/HIV compared to PTB only and the differences were statistically significant. When compared to PTB patients only HIV/PTB co-infected patients had more nodules on the left lung field 85.2% vs 60.9% (p=0.023); on each left lung zone upper 59.3% vs 34.4% (p=0.028); mid 77.8% vs 54.7% (p-value=0.039); lower 66.7% vs 34.4% (p=0.005) and miliary nodules 44.4% vs 15.6% (p=0.003), respectively. HIV/PTB co-infected patients with CD4 $\geq$ 200 cells/µL had more mid zone consolidation (42.9% vs 15.2%, p=0.024).

Conclusion
The commonest chest radiographic findings in HIV/PTB co-infected patients were pulmonary cavities and alveolar consolidation are associated with HIV negative status. HIV/PTB co-infected patients with severe immunosuppression had mid zone consolidation. Patients with severe immunosuppression showed less chest radiographic findings. HIV/PTB co-infection was highly associated with mid and lower zone pulmonary nodules and miliary nodules.

Key words: PTB, HIV, CXR

Introduction

Pulmonary tuberculosis (PTB) and Human Immunodeficiency virus (HIV) co-infection is a global health problem posing tuberculosis (TB) diagnostic challenge at public health perspective (1, 2). HIV infection predisposes to tuberculosis and immunodeficiency leads to PTB reactivation and progression to active TB disease (3, 4). PTB is an opportunistic infection in HIV and is associated with increased mortality among AIDS patients (5). Also PTB leads to treatment challenges among HIV/AIDS patients(6).. PTB/ HIV co-infection has been observed between 30% and 39% among PTB patients (7, 8).

Chest radiograph (CXR) is a cost effective imaging modality for screening of active PTB (9). Chest radiographic findings seen among PTB patients are either primary or post primary PTB. Primary PTB present with either normal chest radiograph, intrathoracic lymphadenopathy including hilar or mediastinal lymphadenopathy(10-12); with or without parenchymal disease including interstitial nodules, miliary nodules, lobar opacities in the lower and mid lung zones(13, 14), or pleural effusion (15, 16). They have significantly lesser apical involvement (17), with lesions localized in mid or lower zones (18). Post-primary PTB chest radiographs present with infiltration of the upper lung zone, with or without cavitation(10, 19); or consolidation, fibrosis, cavitations and apical locations (20).

However in one study HIV/PTB co-infected patients had significant mixed presentation than HIV negative patients(14).Again HIV/PTB co-infection was not associated with higher prevalence of miliary nodules (21, 22); and pleural effusion (13, 22).

Occurrence of chest radiographic findings is affected by HIV status and degree of immune suppression (23). HIV/PTB co-infected patients when compared to HIV negative PTB patients frequently present with primary PTB (24-27). However;

HIV/PTB co-infected or severely immunosuppressed patients do not necessarily present with a normal chest radiograph (15, 28) or pleural effusion (13, 29).

Throughout review of literature there are discrepancies in the occurrence of chest radiographic patterns among PTB patients with respect to HIV status and CD4 levels among HIV-positive patients. There is no prior study in Tanzania to address chest radiographic patterns and their association with HIV status and CD4 levels. Such a study would contribute towards tuberculosis elimination efforts particularly through prompt diagnosis of TB among HIV co-infected population in Tanzania.

The aim of the study was to determine chest radiographic patterns and their association with CD4 levels among HIV positive and HIV negative adults with smear positive PTB attending TB clinic at Mwananyamala referral hospital.

Methodology

This was cross- sectional hospital-based study conducted among TB clinic attendees from Mwananyamala referral hospital from July to December, 2011. The study consecutively included all consenting adult patients with confirmed pulmonary tuberculosis through positive sputum smears by Auramine staining Fluorescence Microscopy. The smear negative, follow up, previously treated and on treatment PTB patients were excluded from the study. Recruited patients were subjected to postero-anterior chest radiographs (CXR) acquired by a radiographer through a high KV technique chest radiography using PHILIPS HD 30 system (Best, Eindhoven, The Netherlands). CXR films were interpreted by two independent radiologists. Radiologists were double-blinded for PTB diagnosis and HIV serostatus. Fleischner Society; glossary of terms for thoracic imaging was used to define chest radiographic findings (30). Chest radiographic findings reading checklist was used during CXR films interpretation. The findings were recorded when the two radiologists had matched interpretations. In addition, HIV status of the patient was determined by rapid testing strategy with Bioline then Determine and Unigold for confirmation, and

CD4+T cell enumeration was done using FACS calibur machine (Becton Dickinson, USA) for CD4 determination among HIV/PTB co-infected.

Collected data was recorded on structured questionnaires, data was coded and entered into SPSS version 20 for analysis. Data cleaning was done by consistence checks. Frequency distribution and two way tables were used to summarize the data. Chi-square ($X^{2)}$ and Fisher's exact tests were used to determine the association between independent and dependent categorical variables. P value of < 0.05 was considered statistically significant. Ethical clearance was obtained from MUHAS Senate Research and Publications Committee. Both verbal and written informed consent was administered to patients before interview and chest radiograph. HIV counselling was done before HIV testing and CD4 determination among HIV/PTB co-infected patients. HIV immunosuppressed patients were later referred to Anti-retroviral therapy (ART) clinic for further management. All the information gathered were kept confidential by use of code numbers.

Results

Between July to December, 2011 a total of 170 newly diagnosed smear positive PTB patients were recruited for the study. There were 100 (58.8%) males and 70 (41.1%) females. Fifty-four (31.8 %) had HIV/PTB co-infection. HIV/PTB co-infection was significantly more in females ($p < 0.001$) and in widowed ($p = 0.036$)**. (Table 1)**

PTB only patients significantly presented with pulmonary cavities than HIV/PTB (61.2% vs 44.5% p = 0.04). Distribution of pulmonary consolidation in upper (57.8% vs 40.1% p = 0.039) and middle lung zones (44.8% vs 25.9%, p = 0.019) was significantly more frequent among PTB only patients compared to HIV/PTB co-infected patients. (**Table 2)**

Table 1: Socio-demographic characteristics distribution of the study population by HIV status among adults with AFB sputum smear positive Pulmonary Tuberculosis.

	HIV STATUS		p-value
	POSITIVE	NEGATIVE	
	N=54	N=116	
Socio-demographic characteristic	N (%)	N (%)	
Age group	54 (31.8)	116 (68.2)	
18 to 25 years	7 (20.0)	28 (80.0)	0.139
26 to 35 years	17 (29.8)	40 (70.2)	
More than 35 years	30 (38.5)	48 (61.5)	
SEX			
Male	18 (18.0)	82 (82.0)	0.000
Female	36 (51.4)	34 (48.6)	
Marital status			
Never married	18 (27.7)	47 (72.3)	0.036
Married	21 (26.9)	57 (73.1)	
Divorced	9 (52.9)	8 (47.1)	
Widowed	6 (60.0)	4 (40.0)	

HIV/PTB co-infected patients compared to PTB only had CXRs with higher left lung nodules (p = 0.023), bilateral lung nodules (p = 0.004), left upper zone nodules (p = 0.028), left mid zone nodules (p = 0.039), left lower zone nodules (p = 0.005) and miliary nodules (p = 0.003) (**Table 2**)

HIV/PTB co-infected patients had minimum, maximum and mean CD4 counts of 14 cells/μL, 864 cells/μL and 225.70 cells/μL, respectively with standard deviation of 204.257.

HIV/PTB co-infected patients with CD4 levels < 200 cells/μL had CXRs with lesser mid zone consolidation (p = 0.024) compared to those with CD4 levels ≥ 200 cells/μL. (**Table 3**)

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Table 2: Chest radiographic findings by HIV status among adults with AFB sputum smear positive Pulmonary Tuberculosis.

	HIV STATUS			
Radiographic pattern	**POSITIVE**	**NEGATIVE**	**TOTAL**	**P-value**
	N=54	**N=116**	**N=170**	
Radiographic pattern	**N** (%)	**N** (%)	**N (%)**	
Pulmonary parenchyma lesion	54 (100)	116 (100)	170 (100)	-
Consolidation	37 (68.5)	93 (80.2)	130 (76.5)	0.095
Nodules	27 (50.0)	64 (55.2)	91 (53.5)	0.529
Cavities	24 (44.4)	71 (61.2)	95 (55.9)	0.040
Intrathoracic lymphadenopathy	32 (59.3)	65 (56.0)	97 (57.1)	0.693
Pleural effusion	15 (27.8)	38 (32.8)	53 (31.2)	0.514
Pulmonary consolidation distribution	**N=54**	**N=116**	**N=170**	
	N (%)	**N** (%)	**N (%)**	
Upper zone	22 (40.7)	67 (57.8)	89 (52.4)	0.039
Mid zone	14 (25.9)	52 (44.8)	66 (38.8)	0.019
Lower zone	18 (33.3)	42 (36.2)	60 (35.3)	0.715
Position of pulmonary nodules	**N=27**	**N=64**	**N=91**	
	N (%)	**N** (%)	**N** (%)	
Right Lung	23 (85.2)	49 (76.6)	72 (79.1)	0.355
Left Lung	23 (85.2)	39 (60.9)	62 (68.1)	0.023
Bilateral lung fields	19 (70.4)	24 (37.5)	43 (47.3)	0.004
Right upper zone	15 (55.6)	24 (37.5)	39 (42.9)	0.112
Right mid zone	20 (74.1)	36 (56.3)	56 (61.5)	0.110
Right lower zone	15 (55.6)	26 (40.6)	41 (45.1)	0.191
Left upper zone	16 (59.3)	22 (34.4)	38 (41.8)	0.028
Left mid zone	21 (77.8)	35 (54.7)	56 (61.5)	0.039
Left lower zone	18 (66.7)	22 (34.4)	40 (44.0)	0.005
Milliary nodules	12 (44.4)	10 (15.6)	22 (24.2)	0.003

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Table 3: CD4 levels distribution and Chest radiographic findings by CD4 levels among adults with AFB sputum smear positive PTB/HIV co-infection.

	CD4 LEVEL (µmol/l)			P-value
	≥ 200 (%)	< 200 (%)	TOTAL (%)	
	N=21	N=33	N=54	
	N (%)	N (%)	N (%)	
HIV positive	21 (38.9)	33 (61.1)	54 (100)	
Radiographic pattern				
Consolidation	15 (71.4)	22 (66.7)	37 (68.5)	0.713
Pulmonary nodules	9 (42.9)	18 (54.5)	27 (50.0)	0.402
Cavity	11 (52.4)	13 (39.4)	24 (44.4)	0.349
Intrathoracic lymphadenopathy	11 (54.4)	21 (63.6)	32 (59.3)	0.412
Pleural effusion	5 (23.8)	10 (30.3)	15 (27.8)	0.422
Pulmonary consolidation distribution				
Upper zone	8 (38.1)	14 (42.4)	22 (40.7)	0.489
Mid zone	9 (42.9)	5 (15.2)	14 (25.9)	0.024
Lower zone	8 (38.1)	10 (30.3)	18 (33.3)	0.554
Position of pulmonary nodules	N=9 N (%)	N=18 N (%)	N=27 N (%)	
Right Lung	9 (100)	14 (77.8)	23 (85.2)	0.125
Left Lung	6 (66.7)	17 (94.4)	23 (85.2)	0.055
Bilateral lung fields	6 (66.7)	13 (72.2)	19 (70.4)	0.766
Milliary nodules	4 (44.4)	8 (44.4)	12 (44.4)	0.660

Discussion

Study findings depicts estimate of extent of chest radiographic abnormalities in newly diagnosed smear positive patients with pulmonary tuberculosis. Among the study population 54 (31.8%) were HIV/PTB co-infected. This is slightly similar to 30% reported in a study done in prison setting in Ivory Coast (31). Also 31.8% PTB/HIV co-infection rate is lower than previously reported findings of 33.7% in Tanzania (8); 38.5% in Oman (7); and 50.7% in Nigeria. The differences in present study compared to previous studies may be attributed to large sample sizes in the previous studies (8, 32), inclusion of on treatment PTB patients (7); and tertiary hospital setting (32).

Females were significantly more HIV/PTB co-infected than males ($p< 0.001$). This is similar to previous studies done at similar settings (33, 34). The reason could be due to having a positive contact or a partner with HIV infection (33, 34).

This study found HIV co-infection among PTB patients was significantly associated with more left and bilateral pulmonary nodules on chest radiography. Again, HIV co-infection among PTB patients was significantly associated with distribution of pulmonary nodules more in the left upper, mid and lower zones and miliary nodules on chest radiography.

Distribution of pulmonary nodules in upper zone (primary PTB), mid and lower zone (post-primary PTB) reveal mixed chest radiographic presentation in HIV/PTB co-infection. This is in contrary with previous studies whereby HIV/PTB co-infection was significantly associated with primary PTB nodules (18, 35); and significantly less upper zone infiltrations seen among HIV/PTB co-infected patients (35-37).

Above observed differences may be due to study setting and inclusion criteria used. The present study was done at the TB clinic, involved strictly adult patients with

smear positive PTB which was different from inclusion of culture positive PTB patients in previous studies (18, 35, 38).

In the present study left and bilateral pulmonary nodules and miliary nodules signify diffuse pulmonary spread of tubercle bacilli among HIV/PTB co-infected patients than in PTB only patients (13, 15, 38). This is due to immunosuppression which causes increased risk of haematogenous spread of primary PTB among HIV patients (20). Higher prevalence of miliary nodules among HIV positive patients with pulmonary tuberculosis has also been observed in previous studies (14, 39).

In this study there was no association between pulmonary nodules and miliary nodules with level of CD4 counts among HIV/PTB co-infected patients. This lack of association is due to random distribution of nodules throughout the lung as observed in previous study (40), which is contrary to significant prevalence of pulmonary nodules among HIV/PTB co-infected patients observed in other studies (15, 27, 29). The differences could be use of culture from bronchoalveolar lavage in PTB diagnosis (15, 29) and inclusion of late stage AIDS patients only (15, 27, 29)
This study found that HIV co-infection among PTB patients was significantly associated with lesser alveolar consolidation, lesser upper and mid-zone consolidation. This may be due to immune system inability of mounting a complete immune response to an antigen in HIV positive patients (38).

HIV/PTB co-infected patients with CD4 counts $\geq$ 200 cells/µL compared to patients with CD4 levels < 200 cells/µL had CXRs findings with significantly higher mid zone consolidation (p=0.024). This shows presence of primary PTB among HIV/PTB co-infected patients which is also seen in immune-competent individuals. This is different from previous studies in which presence of primary PTB radiographic findings among HIV/PTB co-infected patients was associated with CD4 levels < 200µmol/l (15, 41). The differences could be due to differences in HIV testing

methodologies such as use of ELISA and Western blot (15, 41); and study setting such as hospital (15, 41) and adult HIV clinic (15, 41).

In this study it was found that PTB/HIV co-infected patients had CXRs with significantly lesser pulmonary cavities than in PTB only patients which is similar to previous studies (22, 35, 42). This is due to inadequate immune response in HIV positive patients(38).

There was lack of significant association of pulmonary cavities in HIV/PTB co-infected patients with CD4 levels, this may be due to chance variation of pulmonary cavities with CD4 levels contrary to significant association of pulmonary cavities with CD4 counts $\geq$ 200 cells/μLin previous studies (27, 37).

The finding that intra-thoracic lymphadenopathy, pleural effusion and their distribution were not associated with either HIV/PTB co-infection or CD4 levels may be due to chance variation.

Study limitations

Radiographic findings observed might have been influenced by mixed respiratory infections, PCP or lung tumor. However, strict use of symptom screening questionnaire was used to reduce these. Lastly; limited number of HIV/PTB co-infected patients might have led to absence of association of radiographic patterns with severe immunosuppression.

Conclusion

All patients with smear positive pulmonary tuberculosis have abnormal chest radiographs. This study demonstrates that pulmonary cavitation and consolidation are highly associated with negative HIV status. HIV positive patient with smear positive pulmonary tuberculosis are more likely to have left or bilateral pulmonary nodules. Also, HIV positive sero-status is associated more with miliary nodules and

left upper, mid and lower zone nodules. Right mid zone consolidation in HIV patients was associated with CD4 counts of equal or more than 200 cells/μL. There was no radiographic pattern which was significantly associated with severe immunosuppression.

Recommendations

Patients with chest radiographs presenting with pulmonary nodules should be evaluated for pulmonary tuberculosis and HIV. There is a need of more studies focusing on radiographic patterns among HIV positive and HIV negative patients with or without PTB symptoms using large community-based sample in order to get findings which will reflect to the general population.

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Conflict of interest

The authors declare to have no financial or personal relationship(s) that may have inappropriately influenced in writing this article.

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