British Journal of Medicine & Medical Research
4(35): 5474-5483, 2014

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Chest Radiographic Patterns of Smear Positive Tuberculosis in Relation to HIV: A Cross-Sectional Study in a Population with a High Burden of HIV and Tuberculosis

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Authors' contributions

Author AG conceived, designed, analyzed and written the manuscript. Author SG participated in the protocol design, statistical analysis and draft manuscript writing. Author TS designed the protocol, analyzed the data and contributed to the draft manuscript. Author JI contribute to the data management, analysis and draft manuscript. All authors read and approved the final manuscript.

Original Research Article

Received 1st October 2013
Accepted 18th February 2014
Published 30th July 2014

ABSTRACT

Aim: The purpose of this study was to investigate the chest radiographic patterns of smear positive pulmonary tuberculosis patients in relation to HIV co-infection.
Study Deign: Cross-sectional descriptive study
Place and Duration of the Study: The study was conducted at Gondar University hospital between May 2004–December 2007.
Methodology: We studied chest radiographs of 207 (128 HIV negative and 79 HIV positive) consecutive sputum smear positive pulmonary tuberculosis patients according to the standard classification. Mean and percentages/ proportions were used for descriptive analysis. Chi square test was used to measure association.
Results: The prevalence of HIV in patients with smear positive pulmonary tuberculosis was 38.2%. The most common chest radiographic patterns were fibronodular (83.1%), cavity (60.4%), lobar consolidation (49.8%), and brochopnemonic consolidation (9.2%). Lymphadenopthy and pleural effusion were more common in HIV co infected patients

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(p<0.01). Cavities, upper lobe disease and increased mean number of lung lobes involved were more prominent in HIV negative patients (P<0.05). Despite a higher rate of patients with far advanced CXR patterns in HIV negative TBC patients compared to HIV positive (p<0.026), there was no significant difference in the radiographic, sputum smear conversion or clinical response in terms of increased body mass index after 8 weeks of anti TBC treatment between HIV negative and HIV positive patients.

Conclusion: Post primary pulmonary tuberculosis was the commonest chest radiographic pattern at presentation in both HIV positive and HIV negative patients, but atypical chest radiographic presentations were associated with co-infection. It was more common for HIV negative tuberculosis patients to have a radiologically far advanced pattern which did not correspond to the clinical and radiological response. This may prompt a need for revision of the current radiological classification.

Keywords: Pulmonary tuberculosis; sputum smear positive tuberculosis; chest radiography; HIV co infection.

1. BACKGROUND

Tuberculosis (TBC) is a curable global health problem and it is a leading killer among HIV infected individuals. According to the 2013 WHO report there are 8.6 million incident and 12 million prevalent cases globally. For Ethiopia, WHO estimates, the prevalence, incidence and mortality of 224, 247 and 18 per 100,000 respectively for 2012 [1].

Radiologic manifestations of pulmonary TBC depend on several host factors including prior exposure to TBC, age, and underlying immune status. In immune competent persons, radiographic manifestations classified as primary and post primary. The hall mark of primary TBC is lymphadenopthy (LAP) occurring in 83%-96% of pediatric cases. The right para-tracheal and hilar LAPs are the most common sites, though combinations of the two, bilateral hilar and mediastinal LAP may also occur [2-4].

Post primary TBC present as an opacity in the upper lobe and apical segment of the lower lobe (92%). The remaining 8% has unusual presentations such as an isolated lower lobe disease, hilar LAP, miliary TBC, tuberculoma, pleural effusion and normal chest radiograph (CXR) findings [2-4].

In a previous study in Ethiopia, HIV positive patients, compared to HIV negatives, were less likely to have a cavity but more likely to have pleural effusion, miliary and interstitial patterns or a normal CXR [5].

While the recommended method of diagnosis of pulmonary tuberculosis in high endemic areas is sputum smear microscopic examination, CXR provides useful information in the detection of TBC and assessment of response to treatment in particular in patients with HIV and in sputum smear negative disease. Therefore, the objective of this study was thus to describe the CXR patterns of pulmonary TBC patients in relation to HIV co-infection.

2. METHODS

The study was conducted at the outpatient clinic of Gondar University Teaching Hospital which is the only referral hospital in the North West Ethiopia serving as a referral hospital for the catchment area of over 5 million populations.

A cross sectional hospital based descriptive study was utilized as a study design.

All patients were recruited from the out patients TBC treatment and follow up clinic. Those with sputum smear positive pulmonary TBC above the age of 15years and having a base line chest radiograph (CXR) were included as the study subjects. We studied consecutive baseline CXRs taken before initiation of anti TB treatment, between May 2004–December 2007. All participants provided informed consent prior to enrollment. Those subjects who were critically sick and admitted, those who were transferred out to peripheral health facility and those who didn't have CXR at base line were not included in the study.

The study protocol was reviewed and approved by institutional ethical review board (IRB) of the University of Gondar (UOG).

We also collected the follow up CXR taken after 8 weeks of anti TB treatment but we got follow up CXR only for 162 of study subjects. Follow up CXR was not found for 45 patients for various reasons like; default, transfer out, lost CXR or that CXR was not done.

Diagnosis and treatment of smear positive pulmonary TBC was performed according to the WHO based national guideline for directly observed treatment short course (DOTS) treatment of SSP pulmonary TBC. Though CXR is not a mandatory baseline investigation according to the guide line, in the teaching referral Hospital, most patients got CXR concomitantly with or prior to sputum test.

All patients were offered pre and post HIV test counseling at the VCT (voluntary counseling and testing) clinic as part of the hospital routine. All the tested HIV positive patients were linked to the chronic HIV care clinic.

Baseline characteristics such as clinical symptoms, CXR findings, body mass index (BMI), and Erythrocyte sedimentation rate (ESR) were recorded. CXRs were analyzed by a consultant radiologist who was blinded to the HIV status of the patient. CXRs were interpreted after assessment of the quality. CXRs were considered acceptable when they had proper identification, well centered, inspiratory film, with optimal penetration and exposure. CXRs were acceptable when there is no technical fault which could significantly affect the diagnostic information.

The extent of disease on the CXR was classified according to the commonly used guidelines from the American Thoracic Society (6) as normal, minimal, moderately or far advanced TBC. Radiographic response after 8 weeks of Anti TBC treatment was recorded as either normal, regress, stable or progress [6]. Normal and regression compared to the initial CXR findings were considered as positive responses where as stable and progression of findings were considered as unfavorable response.

Furthermore, the following CXR patterns were recorded: Lobar pneumonic consolidation, bronchopneumonic consolidation, and fibro-nodular lesion, cavitary lesion including diameter, hilar/para-tracheal LAP, miliary pattern, pleural lesion /effusion, presence of atypical patterns and the location of radiographic abnormalities.

Data was analyzed using EPI info 2000 and we used proportions/percentages, means, and median used for descriptive analysis. Chi square test was used to measure association and 95% CI and P values<0.05 was used to determine level of significance.

3. RESULTS

During the study period we included 207 SSP TBC patients who had baseline CXR and consented to be included in the study. Out of the 207 patients included, 53.1% were male and 46.9% were females and the mean age was 27.7±9.5 years. The prevalence of HIV in the study subjects was 38.2% (79/207) and the baseline characteristics in relation to HIV co-infection are presented in (Table 1).

CXR grading of the extent of involvement showed that 25.6% were classified minimal TBC (31.6% vs 21.9%, p=0.026), 43.5% to be moderately advanced TBC (45.6% vs. 42.2%), and 30.9% to be far advanced TBC (22.8% vs 35.9%, p=0.026) in HIV positives and HIV negatives patients respectively.

Table 1. Baseline characteristics of smear positive pulmonary TB patients in relation to HIV status

Variable	HIV Negatives n- 128	HIV positives n-79	Total N=207
Sex			
male	71(64.5%)	39(35.5%)	110(53.1%)
Female	57(58.8%)	40(41.2%)	97(46.9%)
Age group			
15-24	71(55.5%)	20(25.3%)	91(44%)
25-34	38(29.7%)	31(39.2%)	69(33.3%)
35-44	11(8.6%)	19(24.1%)	30(14.5%)
>45	8(6.3%)	9(11.4%)	17(8.2%)
Mean age (±SD)	25.26(±8.67)	31.34(±9.4)***	27.7(±9.5)
Clinical presentation			
Cough	128(100%)	78(98.7%)	206(99.5%)
Haemoptysis	36(28.1%)	19(24.1%)	55(26.6%)
Fever	119(93%)	77(97.5%)	196(94.7%)
Weight loss	119(93%)	76(96.2%)	195(94.2%)

*Data is presented as mean±SD. *p=0.08, **p<0.01, ***p<0.001*

The most common radiographic manifestation, in this study were fibronodular lesion (85.2% vs 79.9%), followed by Cavitary lesion (71.1% vs 43%), and lobar pneumonic consolidation (44.5% vs 58.2%), bronchopneumonia consolidation (9.4% vs 8.9%), LAP (8.6% vs 19%) and pleural effusion (9.4% vs 15.2%) in HIV negative and HIV positive patients respectively (Table 2).

There were 125 patients with Cavitary lesions (60.4%) out of which 22.4% of presented with multiple cavities. The mean cavity diameter was 4.1cm±1.2cm.

The most common locations of lesions in both co-infected and HIV negative TBC patients were the LUL (61% vs 69.8%) and RUL (59.7% vs 69%) in HIV positive and HIV negative patients respectively (Table 3).

Table 2. Proportion of radiographic presentation in relation to HIV co-infection among smear positive tuberculosis (TB) patients (N=207)

Radiographic patterns	HIV negative (128) n (%)	HIV positive (79) n (%)	Observation (207) n (%)	p-value
Fibro nodular	109(85.2)	63(79.9)	172(83.1)	.31
Cavity	91(71.1)	34(43)	125(60.4)	<.001
Lobar pneumonia	57(44.5)	46(58.2)	103(49.8)	.056
Broncho Pneumonia	12(9.4)	7(8.9)	19(9.2)	0.9
Hilar & mediastinal LAP	11(8.6)	15(19)	26(12.6)	.028
Pleural effusion	12(9.4)	12(15.2)	24(11.6)	.27
Miliary	3(2.3)	2(2.5)	5(2.4)	.93
Normal	0	1	1	
Over all presentation				
Typical Pulmonary TBC	123(96.1)	66(83.5)	189(91.3)	
Atypical Pulmonary TBC	5(3.9)	13(16.5)	18(8.7)	.004
CXR grading				
Minimal	28(21.9)	24(30.4)	52(25.1)	.026
Moderately advanced	54(42.2)	36(45.6)	90(43.5)	
Far advanced	46(35.9)	18(22.8)	64(30.9)	

Table 3. Treatment response 8 weeks after initiation of treatment (N=162)

Clinical response	Week 0 (207)		Week 8 (162)	
	HIV negative N=128	HIV positive N=79	HIV negative N=100	HIV positive N=62
ESR	63+/-24	81+/-21	32+/-25***	60+/-24***
BMI	16.8+/-2.4	16.2+/-2	18+/-3***	17.5+/-2***
Sputum conversion	0	0	87.6%***	85.1%***
Radiographic response				
Normal			2(2.0%)	2(3.2%)
Regress			91(91%)	51(82.3%)
Stable			6(6%)	8(12.9%)
progress			1(1%)	1(1.6%)
Location of the lesion				
Right upper lobe	89(69.5%)	48(60.8%)	62(62%)	36(58.1%)
Right middle lobe	24(18.8%)	12(15.2%)	11(11%)	10(16.1%)
Right lower lobe	20(15.6%)	10(12.7%)	8(8%)	7(11.3%)
Left upper lobe	90(70.3%)	49(62.0%)	63(63%)	35(56.5%)
Left lower lobe	31(24.2%)	15(19%)	14(14%)	7(11.3%)
Pleural effusion	13(10.2%)	13(16.5%)	7(7%)	13(21%)**
Hilar/mediastinal Lymphadenopthy	11(8.6%)	15(19%)*	4(4%)	7(11.3%)

**p<0.05, **p<0.01 (between TB/HIV- and TB/HIV+). The radiological response is evaluated semi-quantitatively comparing chest x-ray from treatment initiation and eight weeks after treatment, blinded for HIV status. ***p<0.001 for ESR, BMI, sputum smear conversion and radiological improvement from week 0 to week 8 for both co-infected and HIV-negative TB patients*

Eight weeks after anti TBC treatment, BMI increased and ESR was reduced in both HIV positive and HIV negative patients, and sputum for AFB became negative in 85.1% in HIV positive and 87.6% in HIV negative patients. But no statistical difference noted between the two. Concerning the CXR response after 8 weeks of treatment, CXR showed regression in 82% and 90%, stable finding in 13.1% and 5.8%, progression in 1.6% and 1.2% in HIV positives and negatives patients respectively (Table 3). We found out a higher proportion of stable CXR findings in HIV positive TBC cases but this difference was not statistically significant.

4. DISCUSSION

The prevalence of HIV and TBC co-infection in our study population was 38.2%, which is comparable to the average estimate for the African region (43%) and to an earlier report by Noronha et al. [1,7]. It was comparatively lower than the average estimate for sub-Saharan Africa 50-70% and an earlier report from the same DOTS clinic 52.2% [1,8-12] which could be due to the fact that our study involved only SSP individuals who are more likely to be immune competent than sputum smear negative patients. On the contrary, our finding is higher than the WHO estimate for Ethiopia (10%), global average across all regions (20%), 21% among 41 high burden countries and an earlier report from southern Ethiopia (17.5%) [1,13]. The possible reason for a higher prevalence in our study population compared to the national estimate could be due to the fact that our study patients subjects are from a referral hospital where there are more seriously sick and more HIV prevalence in the source population.

Radiographic patterns of Pulmonary TBC in adult patients has been shown to be post primary pattern in immune competent patients and primary pattern in immunocompromised patients. Miliary, atypical patterns, or normal CXRs are frequently observed in patients with far advanced immune suppression, at a CD4 count of <50cells/ml [5,14-16].

In this study we have demonstrated that the presence of cavities ($p<0.001$), upper lobe disease ($p=0.001$) and increased mean number of lung lobes involved ($p<0.05$) were significantly higher in HIV negative TBC patients compared to HIV positive. Whereas, the presence of enlarged mediastinal and/or hilar lymph nodes was significantly higher in HIV co-infected patients (0.028). The presence of pleural effusion was more common in HIV co-infected patients, though it was not statistically significant. But, when pleural effusion occurs together with LAP it became significantly associated with HIV co- infection. ($p=0.01$, 95% CI (0.16–0.78)) and in this respect our finding is in accordance many studies [2,5,15,16].

Considering the overall pattern, we found a typical CXR pattern of pulmonary TBC in 91.3% despite the fact that 38.2% of the patients were HIV positive which implies that the impact of immune suppression was moderate which was also favored by the selection of SSP patients. A published data from the same DOTS clinic, with smear positive TBC patients, showed a mean CD4 count of 219 in HIV co infected SSP TBC patients which reflected that our study population could have such comparable level of moderate immune suppression [17].

A Fibronodular lesion was the most common radiographic pattern both in HIV negative (85.2%) and co infected patients (79.9%), but we have not observed any significant difference between the two. Lobar pneumonic consolidation was more common in HIV co-infected patients (58.2% vs 44.5%, $p=0.056$) with marginal level of significance.

The higher frequency of cavities and other post primary patterns in HIV co-infected patients may be due to the high incidence and prevalence of TBC in the region where the disease presenting in the early stages of HIV infection when the immune system is relatively preserved. More over the selection of SSP patients also might have favoured selection of patients with high bacterial loads which tend to have more intact immunity with cavities. A culture facility was not available in our setting to allow inclusion of culture verified sputum smear negative pulmonary TBC patients which could have been common among HIV patients with advanced immune suppression [14].

Though Cavitary lesion was significantly higher among HIV negative patients (71.1%), P=0.001, it was one of the most common radiographic presentations in HIV co-infected (43%) patients. Many other studies similarly reported a higher occurrence of cavities in immune competent patients [15,18-22]. Unlike ours and most others reports, Rizzi et al. [23] reported an equal distribution of cavities between CD4 count <200cells/ml and above >200cells/ml and suggested that HIV related pulmonary TBC is typical in its radiological features because the appearance was consistent with those seen in the general population.

There are conflicting reports regarding pleural effusion; while some studies showed an association of pleural effusion with HIV co-infection [20,24,25], many others agree with our finding of no significant association [5,14,21,26-28]. In favour of our finding, Jones et al reported that the occurrence of pleural effusion in HIV co-infected TBC patients were more common in patients with CD4 count >200cells/ml which reflect a strong immune reaction in the pleura. We also found that all patients with pleural effusions except one, had an associated parenchymal lesion. Even an apparently normal CXR cannot confirm the absence of a parenchymal lesion unless CT scan of the chest is performed [2,29].

The presence of LAP in HIV co-infected patients ranges from 9%-60% in different studies and a higher rate of occurrence of LAP observed in CD4 count <200cells/ml [15,18,21,30,31]. Our study revealed a significantly higher occurrence of LAP in HIV co infected patients (19% vs 8.6%, p=0.028) compared with HIV negative patients, which is in agreement with many studies from Africa, US, South America and India [5,15,16,18-28,30-32].

The typical miliary CXR pattern of TBC, though reported to occur more frequently in HIV co-infected patients and in those with severe immune suppression [2,12], such associations were not observed in our study (HIV positives and HIV negatives 2.5% vs 2.3% respectively**)** which is in accordance with Olufemi et al. [27].

Normal CXR pattern has been reported at a frequency between 1-14% in pulmonary TBC and this figure increased to 10-40% when associated with HIV co-infection and more advanced immune suppression [26,30,31,33,34]. On the contrary, other authors reported no significant association of normal chest radiograph with HIV [5,18,19,21,22,27]. We detected only 1 case with a normal CXR which is even lower than a previous report from Ethiopia [5], this could be due to the fact that we have studied only SSP TB.

The radiological response, sputum smear conversion and regression of clinical symptoms, after 8 weeks of anti TBC treatment, were similar regardless of HIV status. This finding is in line with Murray J et al. [32] which showed comparable cure rates between HIV positive and HIV negative patients with TBC after excluding patients who died. But, one of findings was that pleural lesions resolved faster in HIV negative patients than in HIV co-infected patients with TBC ($p<0.01$).

5. CONCLUSION

Though the prevalence of HIV in our study population was 38.2%, 91.3% presented with typical CXR patterns of TBC. Post primary pulmonary TBC was the most common pattern of presentation in both HIV positive and HIV negative patients. The presence of LAP was significantly associated with HIV co-infection. HIV negative patients had an increased rate of Far advanced extent of CXR involvement compared with HIV positive patients. Despite the difference in CXR presentation at the time of diagnosis, we have observed no significant difference in radiographic and clinical response after 8 weeks of anti TBC treatment between HIV negatives and HIV positive patients. This may indicate a need for revision of the current radiological classification.

Therefore, clinicians and radiologist should be aware that the majority of immunocompromised patients present with typical CXR patterns of TBC and few immune competent patients may have atypical presentation.

Further studies are warranted in representative population including both smear negative and smear positive, utilizing culture and GenXpert in smear negative cases and assessing the level of immune suppression using CD4 count.

6. LIMITATIONS OF THE STUDY

We studied only SSP TB patients as it was difficult to make a definitive diagnosis TBC in sputum smear negative cases since there was no TB culture facility in our institution during the study period. Another important limitation was lack of CD4 count for HIV positive patients since the test was not available during the study period.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

ACKNOWLEDGMENT

We acknowledge Gondar University Hospital, staffs of DOTS clinic and department of Radiology and clinical laboratory staffs.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=616&id=12&aid=5569