

Radiological manifestations of Pulmonary Tuberculosis in HIV Sero-Positive adult patients.

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ABSTRACT

Background: Tuberculosis is the most common co-infection among HIV Sero-Positive individuals. Radiological diagnosis of Pulmonary Tuberculosis is not a primary tool but having some importance in resource poor country like India, where there is lack of universal accessibility of molecular diagnosis. Radiographic presentation of tuberculosis differs in patients with HIV or without HIV infection. Objective: To compare radiological presentation in patients of pulmonary tuberculosis among HIV Sero-Positive and HIV Sero-Negative individuals. **Methods:** In this cross-sectional observational study we analysed the radiological manifestation of pulmonary tuberculosis among HIV Sero-Positive & HIV Sero-Negative patients at V.S.S. Medical College, Burla, Odisha, India from September 2013 to August 2015. **Results:** Unilateral infiltrative lesions are commonest form of radiological manifestation in both HIV Sero-Positive & HIV Sero-Negative groups. The prevalence of Cavitory lesion was statistically less ($p < 0.001$) in the HIV sero-positive groups than HIV Sero-Negative group. Hilar lymphadenopathy was observed only in the HIV Sero-positive group. Involvement of multiple chest radiological zone was statistically less ($p = 0.01$) seen in HIV Sero-Positive groups than to HIV Sero-Negative groups. Minimal lesions were statistically more ($p = 0.001$) seen in HIV Sero-Positive individuals & moderately advance lesion were statistically more ($p < 0.0001$) in HIV Sero-Negative patients. **Conclusion:** In HIV Sero-Positive individuals, radiological manifestation of pulmonary tuberculosis is not similar to HIV Sero-Negative patients. Physicians should consider Pulmonary Tuberculosis when atypical radiological manifestation seen in HIV Sero-Positive cases for early diagnosis & treatment.

Keywords: HIV, Pulmonary tuberculosis, Radiological manifestation.

INTRODUCTION

One fourth of the global incident TB cases occur in India annually. As per WHO Global TB Report 2015, 28 lakh TB cases were estimated to have occurred in India out of estimated global incidence of 104 laks TB cases.^[1] Likewise 1.1 lakh TB HIV cases were estimated occurred in India out of estimated global incidence of 11.7 lakh TB HIV cases.^[1] India bears second highest number of estimated HIV associated TB in the world. In 2015 under Revised National Tuberculosis Control Programme, 91,32,306 TB suspects were examined by sputum smear microscopy and 14,23,181 cases were registered for treatment.^[2] Out of which 79% of all registered TB cases knew their HIV status.^[2] Tuberculosis is the most common opportunistic infection amongst HIV-infected individuals in India.^[2] Patients with HIV infection are more likely to have active TB by a factor of 100 when compared with an HIV-negative population.^[3] This sets the stage for a deadly synergy between the two infections.

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Pulmonary tuberculosis is the most common clinical presentation of TB worldwide. In country like India, diagnosis of pulmonary tuberculosis depends on clinical manifestation, chest radiography, sputum smear examination for acid-fast bacilli and a positive tuberculin skin test.^[4] Sputum smear microscopy is the primary tool for diagnosing PTB as it is more specific and has less inter and intra-reader variability than chest X-ray.^[2] However, chest X-ray plays an important role in the diagnosis of tuberculosis among people living with HIV especially sputum smear negative TB.^[5] Because the radiographic presentation of tuberculosis depends on the severity of immune system reactions and the bacillary load in the lung. Such characteristics differ in patients of PTB with or without HIV.^[6] Therefore, HIV sero-positive patients may have radiographically atypical presentations. HIV epidemic will lead to increased

number of TB cases including smear-positive cases, reactivation of TB and susceptibility to new TB infection. The risk of death in HIV infected persons with clinically symptomatic TB is about three to seven-fold than in HIV infected persons without TB.^[7,8] While in patients with AIDS, the development of TB increases the overall mortality by one-third.^[9] HIV fuels the spread of drug-resistant TB. HIV stigma may lead to inadequate supervision of anti-TB chemotherapy and delay in seeking care by TB suspects. HIV infection leads to high default rates because of adverse reactions. There is insufficient data on the radiographic presentation of tuberculosis in HIV-infected patients from India. This study aimed to determine whether there are differences in the radiological presentation of pulmonary TB between HIV sero-positive and HIV sero-negative patients. Objective of this study to observe, compare and contrast the radiographic features of pulmonary tuberculosis in HIV-Sero-Positive and HIV Sero-Negative adult patients.

MATERIALS AND METHODS

Study was carried out at Department of Pulmonary Medicine, V.S.S. Medical College, Burla, Odisha, India from September 2013 to August 2015. It was an observational cross sectional study. PTB was diagnosed based on clinical history, physical examination & Sputum smear examination for Acid Fast Bacilli using Ziehl-Neelsen technique as per Revised National Tuberculosis Control Programme guideline and presence active tubercular lesion in chest X-ray. Chest X-ray was analysed & consensus by at least two experts, out of which one was radiologist. Radiographic findings were noted based on the types of lesion (consolidation, cavitation, pleural effusion, miliary disease, hilar and mediastinal lymphadenopathy), radiological zone (Upper zone, middle one, lower zone, multiple zone) involved, radiological extent of lesion (minimal, moderately advance, far advance) & unilateral / bilateral involvement. In all study subjects HIV serological status was assessed using three recombinant enzyme-linked immunoassay (ELISA) methods as per NACO guidelines.^[10] Testing positive by all three methods was considered as diagnostic of HIV-infection. CD4+ T-lymphocyte counts in HIV Sero-Positive patients were assessed using CYFLOW counter based on flow cytometry technique. Routine investigation & other special investigation were done as per the need. Patients with previous pulmonary disease, on long-term immunosuppressant therapy or having co-existing immunosuppressed conditions e.g. Diabetes mellitus, Chronic Kidney Disease were excluded from our study. 162 New Pulmonary Tuberculosis Patients were taken into the study.

Statistics

The statistical analysis was performed with help of MedCalc- version 17.2. Continuous variables as mean (\pm SD) & categorical variables as proportion were expressed. Different variables were tested for normality besides, by chi square test in case of comparison of proportion and by t test in case of comparison of means. P-value of 0.05 or less was considered statistically significant.

Ethics

Verbal & informed consent were taken from all participants of this study. The research was approved by the institutional ethics committee.

RESULTS

162 Pulmonary Tuberculosis patients were included in this study. Out of which 60 numbers of patients are HIV Sero-Positive & 102 Patients are HIV Sero-Negative. In both groups, predominant are male, 80% in HIV Sero Positive & 51% in HIV Sero-Negative group. In both the groups, majority of male patient belonged to the age group 31-40 years. Likewise in both group majority of female patient belong to 21-30 years. Mean (\pm SD) age in HIV sero-Positive & HIV sero-negative group was 34.7 \pm 8.9 and 36.80 \pm 13.64 year respectively. Mean (\pm SD) age in Male patient of HIV sero-positive & HIV sero-negative was 36.3 \pm 9.11 and 37.5 \pm 12.32 years respectively. Likewise mean (\pm SD) age in Female patient of HIV sero-positive & HIV sero-negative was 28 \pm 3.95 and 36.12 \pm 14.98 years respectively.

Commonest occupation in HIV sero-positive group was driving. In both group commonest constitutional symptoms were anorexia whereas commonest respiratory symptoms was cough with/without expectoration.

Mean (\pm SD) BMI in Male patient of HIV sero-positive & HIV sero-negative was 18.92 \pm 1.57 and 19.16 \pm 1.33 respectively which is statistically not significant ($p=0.41$) on comparison between two means. Likewise mean (\pm SD) BMI in Female patient of HIV sero-positive & HIV sero-negative was 17.35 \pm 1.60 and 17.77 \pm 1.07 respectively which is also statistically not significant ($p=0.27$) on comparison between two means. In both the groups, there were 20% cases having presence of peripheral Lymphadenopathy.

Infiltrative lesions are more frequently seen in both HIV Sero-Positive & HIV Sero-Negative patients. Unilateral lesions are more common than bilateral in both groups. The occurrence of cavitations was less in the HIV sero-positive group compared to the HIV Sero-Negative group and which was found to be statistically significant ($p < 0.001$). Hilar lymphadenopathy was observed only in the HIV Sero-positive group and in none of the cases in the HIV Sero-Negative group and which was statistically significant ($p < 0.0001$). [Table 1]

In the HIV Sero-Positive radiological zone most commonly involved was the upper zone. HIV Sero-Negative group the most commonly involved radiological zone was involvement of multiple zones which was statistically significant ($p < 0.05$) in compare to HIV Sero-Positive.[Table 1]

As per the radiological classification of pulmonary tuberculosis by the National Tuberculosis Association of USA,^[18] minimal lesions were seen more in HIV Sero-Positive group & moderately advance lesion were more in HIV Sero-Negative group which was statistically significant ($p < 0.05$) in comparison to other group.

The CD4+ cell count was available for 36 patients in this study. The median CD4 count was

173.33(Range: 5 to 665) cells/mm³. Infiltrative lesions were the most common radiological findings in the HIV Sero-Positive study group in both patients with CD4 cell count < 200 as well as in those with CD4 count ≥ 200 . Consolidation as radiographic finding is only seen in CD4 count ≥ 200 group which is statistically significant ($p < 0.05$). Multiple zones were most commonly involved in cases with CD4 count < 200 while middle/lower zones were most commonly involved in cases with CD4 count ≥ 200 . Mid/lower zone involvement was more seen in those with CD4 count ≥ 200 compared to those with CD4 count < 200 and this finding was statistically significant ($p < 0.05$).

Table 1: Radiological patterns & distribution of lesion in PTB with HIV Sero Positive & HIV Sero -Negative Patients.

Radiological pattern	HIV Sero-Positive PTB (n=60)			HIV Sero-Negative PTB (n=102)			P value
	Unilateral	Bilateral	Total (%)	Unilateral	Bilateral	Total (%)	
Infiltrates	24	8	32 (53.3)	28	22	50 (49.0)	0.59
Exudates	4	2	6 (10.0)	6	12	18 (17.7)	0.22
Cavitations	2	2	4 (6.7)	26	6	32 (31.4)	0.0003
Consolidation	6	0	6 (10.0)	18	2	20 (19.6)	0.10
Fibrosis	0	0	0 (0.0)	6	0	6 (5.9)	0.055
Hilar lymphadenopathy	12	6	18 (30.0)	0	0	0 (0.0)	< 0.0001
Pleural effusion	10	0	10 (16.7)	16	0	16 (15.7)	0.86
Reticulonodular opacities	0	0	0 (0.0)	0	2	2 (1.9)	0.28
Others	4	0	4 (6.7)	4	4	8 (7.8)	0.79
Radiological Zone							
Upper zones	18	0	18 (30)	26	2	28 (27.5)	0.73
Middle zones	8	0	8 (13.3)	10	2	12 (11.8)	0.78
Lower zones	10	0	10 (16.7)	8	0	8 (7.8)	0.08
Multiple zones	2	14	16 (26.7)	6	42	48 (47.1)	0.010

Sputum positive status of HIV Sero-Positive Pulmonary TB patients was 30% whereas in HIV Sero-Negative group was 80% which is statistically significant ($p < 0.0001$). It has been seen that in all grades of sputum positivity (3+, 2+, 1+, Scanty), more percentage of patients seen in HIV Sero-negative groups in compare to other group which was also statistically significant. On analysing the different type of lesion among smear positive patients, it has been found that more proportion of HIV sero positive patients had infiltrative lesion in compare to HIV Sero Negative patients ($P=0.014$) in contrast more proportion of HIV sero Negative patients had Cavitory lesion than to HIV Sero Positive patients ($P=0.0038$).

DISCUSSION

The Gold standard for the diagnosis of Tuberculosis is by microbiological conformation of mycobacterium tuberculosis. Sputum smear examination for demonstration of Acid Fast Bacillus one of the quickest & easiest method for diagnosis of PTB. But sensitivity of direct sputum smear examination is reduced in HIV Sero-positive patients in compared to HIV sero- negative patients with PTB. In resource poor country like India, due to non-availability or universal un-accessibility of molecular technique for the diagnosis of PTB the

radiographic identification of active lesion is one of the important tools for diagnosis of PTB which is widely available. Diagnosis of PTB in HIV-infected patients is often difficult due to atypical radiographic findings and radiological lesion resemblance to other opportunistic pulmonary infections.

The most common radiological pattern seen in this study was infiltrates in both HIV Sero-Positive as well as HIV Sero-Negative groups which is similar to other study.^[11-15] Cavitory patterns were observed more in HIV Sero-Negative group than to HIV Sero-Positive individuals (which was irrespective of sputum for AFB status) and also statistically significant like other study.^[12,14] For the formation of cavity on lung parenchyma requires good delayed type of hypersensitivity response and as well as good cell mediated immunity which is lacking in HIV Sero-positive individuals. However this is in contrast to studies by Nwonwu et al in Nigeria in which the frequency of Cavitory lesions was more common in the HIV sero-positive group.^[16] Hilar lymphadenopathy was seen only in HIV Sero-Positive patients as similar to finding seen in other study.^[12,14] Fibrosis was not seen in any of cases in the HIV Sero-Positive study group due to poor cellular inflammatory response. Unilateral Pleural effusion was observed in both groups without statistically significance which is similar to Nwonwu

et al but dissimilar to studies where the incidence of pleural effusion was significantly more common in the HIV Sero-Positive group.^[11,12,16]

Overall the multiple radiographic zones involved were lesser in the Sero-Positive group compared to the Sero-Negative group. This difference was statistically significant. It is comparable to the study by Swaminathan S et al which reported similar findings.^[17] The fewer radiographic zones involved indicate the poor cellular inflammatory response mounted by HIV positive persons.

In the present study, for determining the extent of radiological lesions in chest X-ray, the classification criteria from National Tuberculosis Association of USA were used.^[18] As per this classification, minimal lesions on chest roentgenogram were observed more in HIV Sero-Positive group than Sero-Negative group. Moderately advanced & far advanced lesions were less common in the HIV Sero-Positive study group than HIV Sero-Negative patients. This indicates that in HIV co-infected patients with PTB there are fewer demonstrable parenchymal radiological lesions compared to HIV Sero-negative PTB patients probably related to poor inflammatory response as a result of immunosuppression associated with HIV co infection.

Unlike in other series and reports,^[11,19] in this study the middle and lower lung zones were more commonly involved in patients with CD4 counts ≥ 200 cells/mm³ compared to patients with lower CD4 counts which could be due to the less number of patients in this study but it also indicates that atypical radiological patterns can also be seen in patients with higher CD4 counts and not just in those with CD4 counts < 200 . The vice-versa may also be true.

Sputum smear positivity was more common in HIV Sero-Negative group which is similar to finding in Desalu et al but in contrast to that of Swaminathan S et al sputum smear positivity was reported in 60% of HIV Sero-positive patients.^[11,20]

Among the sputum positive cases in the HIV Sero-Positive study group, upper zone involvement was more common while in the HIV Sero-Negative group multiple zones were more commonly involved. This is in consistent with the association of sputum positivity with post primary pattern of PTB which commonly involves upper zones.

It is evident from the present study that the radiological patterns of presentation of PTB in HIV Sero-Positive patients may be mixed and varied. The radiological presentations of PTB in HIV depend upon the degree of immunosuppression in the individual. Chest X-ray abnormalities are even more non-specific in HIV infected patients than in HIV negative patients, which may result in under diagnosis of PTB. Thus although the HIV Sero-Positive patients in this study had significantly higher incidence of atypical patterns like hilar

lymphadenopathy and significantly lower incidence of typical patterns like cavitations compared to the Sero-Negative group, there was no significant statistical difference in the radiological patterns with respect to CD4 counts or sputum status. This could be due to the less number of patients in my study as well as the less number of CD4 counts available in my study.

The limitations of this study was small size of sample population, CD4 cell counts not available for all cases of sample population, response to therapy following diagnosis and follow up of patients were not taken into account in all cases.

CONCLUSION

Infection with HIV has now emerged as the strongest risk factor for the development of active tuberculosis. With the increasing prevalence of HIV infection in India, physicians need to be aware of the different manifestations of tuberculosis in HIV positive patients.

This study highlights the fact that radiographic features of tuberculosis are significantly different in HIV infected patients compared to those who are negative. In HIV-infected individuals the radiographic manifestations of pulmonary tuberculosis can be atypical or different and the diagnosis requires a high index of suspicion. In this study also a higher prevalence of atypical radiological presentation of pulmonary tuberculosis was found in HIV patients in the form of hilar lymphadenopathy and lesser number of cavitations.

In other words no radiological pattern is absolutely typical of PTB, especially with underlying HIV infection. The presence of atypical and unusual lesions poses a clinical challenge. The diagnosis of TB in HIV positive persons, therefore, requires a high index of suspicion and a combination of clinical, radiographic and bacteriologic investigations. While there could be a variety of infectious and non-infectious causes for an abnormal chest radiograph, a normal radiograph does not rule out tuberculosis.

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