

Research Article

Clinical and laboratory profile of TB-HIV co-infected patients with relation to CD4 counts in a tertiary care hospital

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ABSTRACT

Background: Tuberculosis is the commonest opportunistic infection in HIV infected individuals. Global TB report by WHO estimates 0.4 million deaths by TB in 2014 in HIV infected individuals. The clinical profile of TB in HIV infected individuals are variable from region to region based upon the prevalence of HIV in the region. The aim of the present study was to determine the clinical profile of tuberculosis and the distribution of pulmonary and extra pulmonary tuberculosis in HIV infected individuals with relation to their CD4 counts.

Methods: A prospective cross sectional study was done for a period of two years from January 2013 to December 2014 at a tertiary care hospital in south India. Sputum samples were screened for Mycobacterium tuberculosis from 150 HIV seropositive individuals in the study. AFB positive smears were graded as per RNTCP guidelines. Clinical profiles of the cases in the study were noted and the Chest X ray, ultrasonogram and other relevant investigations were performed in smear negative individuals to diagnose pulmonary and extra pulmonary tuberculosis.

Results: In our study 26-35 years was the major age group (37.33%) with male preponderance. Heterosexual mode of acquisition was common (88.67%) and in 6% the mode was unknown. Fever was the most common symptom (100%) followed by cough with expectoration in 84% of HIV-TB co-infected cases. 44% of cases were smear positive for AFB bacilli and 57.58% were graded 3+, 65.33% of cases had pulmonary infiltrates on chest X-ray followed by 16% with effusion. Lymphadenopathy was the most common extra pulmonary involvement seen in 28.67% of cases followed by 14.67% with meningeal involvement. Overall in the study isolated pulmonary tuberculosis was seen in 43 (28.67%) patients, isolated EPTB was seen in 13 (8.67%) patients and both were seen in 84 (56%) patients. In all cases of EPTB CD4 cell counts were <200cells/μl.

Conclusions: To conclude HIV more commonly affects the economically productive age group with more males than females. Sputum positivity depends upon the stage of HIV infection. Lymphadenopathy is more common form of EPTB and diagnosis can be made by FNAC and Histopathological examination.

Keywords: HIV, CD4 counts, Extra pulmonary tuberculosis, Pulmonary tuberculosis

INTRODUCTION

Tuberculosis is an ancient disease known to mankind mentioned even in Vedas and Ayurvedic samhithas. Caries spine was identified even in Egyptian mummies in 3500 B.C. *Mycobacterium tuberculosis* the causative

agent was identified by Robert Koch. Globally Tuberculosis killed many than any other disease throughout the world, making it as the captain of death. No country globally has been declared free of Tuberculosis by World health organization [WHO]. WHO declares annual global report of TB every year

since 1997. Tuberculosis accounts for 5% of global deaths world wide and 9.6% of adult deaths in 15 -59 years economically productive age group.¹ Latest Global report of TB by WHO estimates 9.6 million new TB cases in year 2014, more among men than women.

With the introduction of Human immune deficiency virus [HIV] in 1981, the prevalence of TB has increased further making it difficult to treat and eliminate. Tuberculosis is the most common opportunistic infection [OI] in HIV infected individuals making TB as the common cause of death in HIV individuals. TB WHO report estimated 0.4 million deaths in HIV infected individuals in 2014 because of TB.²

The proportion of TB cases co infected with HIV were highest in countries of Asian and African continent .In India Tuberculosis became a public health problem with HIV making difficult to treat because of organism becoming drug resistant.

60 -70% Of HIV infected individuals will develop TB during their life time. ³ In India HIV seropositivity ranges from 0.4% to 20.1%.⁴ HIV infection favours the progression of latent TB to active form by making significant alterations in the immune system of HIV individuals. The clinical presentations of TB in HIV individuals are typical in early HIV and atypical with many forms including extra pulmonary and disseminated forms in late stages of HIV making diagnosis and management difficult.

Effective implementation of National health programmes integrating HIV and TB are essential in reducing the mortality and morbidity of TB in HIV infected individuals. The present study aims to identify the clinical and laboratory profile of Tuberculosis in HIV seropositive individuals. Estimating the profile makes an impact in early diagnosis and interventions required in modifying the treatment and outcomes in TB and extra pulmonary tuberculosis [EPTB].

METHODS

This was a prospective cross sectional Hospital based study done at Santhiram Medical College and General Hospital, Nandyal a tertiary care Hospital in Andhra Pradesh, India.

The present study was carried over a period of 24 months from January 2013 to December 2015. A total of 150 HIV seropositive patients who were screened and confirmed with Pulmonary and EPTB were included in the study. The study was approved by the institutional research and ethical committee of the college.

Inclusion criteria

All the patients attending the Department of Pulmonology who were suspected with HIV and

Tuberculosis, Known HIV patients attending the Anti-retroviral treatment center [ART] for follow up were included in the study.

Informed consent was obtained from all the participants in the study. The inclusion criteria was all the adult patients between 18 to 65 years were included assuming that children less than 18 years and adults above 65 years were sexually inactive.

Exclusion criteria

Participants less than 18 years and above 65 years of age, known tuberculosis cases and on ATT were excluded from the study.

Methodology

The socio demographic data of the participants which included age, sex, marital status, occupation, complaints, history of exposure, present and past history of disease etc were interviewed by a counsellor and entered in to a predesigned questionnaire sheet. Pre-test counselling was done.

Diagnosis of HIV

The sera samples obtained from the patients were tested for HIV status by three antigenically different kits [ELISA- MICROLISA Kit: J.Mithra and Co Pvt Limited, NewDelhi, rapid and simple kits: J.Mithra and Co Pvt Ltd, NewDelhi] as per the National HIV testing Policy by NACO.⁵

Diagnosis of tuberculosis

All the confirmed cases of HIV were examined clinically and further confirmed by

- Sputum smears microscopy by Zeil-Neelson staining for Acid fast bacilli.
- Chest radiograph.
- Fine needle aspiration Cytology [FNAC] examination of Lymph node aspiration with Granulomatous reaction in case of extra pulmonary tuberculosis [EPTB].
- Fluid analysis in case of effusion.
- Clinical features and response towards Anti tubercular therapy [ATT].

Estimation of CD4 cell counts was performed in all cases by flow cytometry analysis using FACS count machine with Facscount™ reagents [Becton Dickinson, USA]. ART was started after estimation of CD4 cell counts for eligible patients as per National ART guidelines.⁶

Other necessary investigations like CT scan, MRI and ultra-sonogram were performed based on the necessity of clinical examination.

Statistical analysis

All the collected data was entered in a Microsoft excel sheet by trained paramedical personnel and analyzed by a statistician. P value <0.001 was considered significant.

RESULTS

HIV is considered as the primary risk factor in acquisition of tuberculosis. A total of 150 known HIV seropositive cases, with 103 males (68.67%) and 47 females (31.33%) were included in the study. Males outnumbered the females in our study. The most common age group affected in our study was 26-45 years (37.33%) followed in order by 18-25 years (28.67%), 36-45 years (18.67%) and >45 years (15.33%).

Table 1: Socio-demographic profile of cases in study.

Age	No	%
18-25 years	43	28.67
26 - 35 years	56	37.33
36-45 years	28	18.67
>45 Years	23	15.33
Gender		
Male	103	68.67
Female	47	31.33
Marital status		
Married	75	50.00
Unmarried	25	16.67
widow	24	16.00
widower	13	8.67
divorced	12	8.00
Occupation		
Labourer	79	52.67
Salaried	30	20.00
No job	41	27.33
Mode of acquisition		
Heterosexual	133	88.67
Drug abuse	4	2.67
Transfusion	4	2.67
Unknown	9	6.00

The mean age group in the study was 39.4 years. 79 (52.67%) were labourers, 41 (27.33%) were jobless and 30 (20%) were salaried. 50% were married, 25% were unmarried, 16% were widows, 8.67% widower and 8% divorced. 133 (88.67%) members acquired HIV by unprotected heterosexual contact which was the major mode of HIV transmission followed by drug abuse and blood transfusion each 4 (2.67%) and in 9 cases (6%) the mode was unknown. out of 133 members who acquired by heterosexual route 104 (78.2%) had history of visits to commercial sex workers, 18 (13.53%) had extra marital affairs and 11 (8.27%) had both (Table 1).

Out of 150 HIV-TB co infected cases , fever was the most common symptom (100%) followed by cough with

expectoration(84%), loss of weight (82.67%), loss of appetite (68%), hemoptysis (64%) and others like chest pain, dyspnoea, (54.67%). The mean duration of fever was 8 weeks while cough and weight loss was around 10 and 14 weeks respectively. Oral candidiasis was observed in 98 (65.33%) cases making it as commonest opportunistic fungal infection (Table 2).

Table 2: Clinical profile of cases.

Clinical features	No	%
Fever	150	100
Cough with Expectoration	126	84
Hemoptysis	96	64
Loss of weight	124	82.67
Loss of appetite	102	68
Others	82	54.67
Oral candidiasis	98	65.33

Sputum was collected from all the 150 cases and performed Zn staining and AFB positive smears were graded as per RNTCP guidelines.⁷ 84 (56%) were negative by staining and 66 (44%) were microscopy positive. Out of 66 smear positive, 38 (57.58%) were 3+ followed by 16 (24.24%), 12 (18.18%) graded 2+ and 1+. In the present study pulmonary tuberculosis by staining of sputum was seen in 66 (44%) patients, and in rest of 84 cases diagnosis of TB was confirmed by other clinical, radiological and pathological findings. Only extra pulmonary tuberculosis was observed in 13 cases with lymphadenopathy in 8, effusion in 4 and 1 meningeal involvement.

Chest X ray was done in all the cases and pulmonary infiltrates was the commonest (65.33%) followed by effusion (16%), cavity (8.67%), fibrosis (5.33%) and miliary lesions (4.67%). Extra pulmonary involvement was found in 97 cases with lymphadenopathy being the commonest (28.67%) followed in order by meningeal involvement in 22 (14.67%), effusion in 18 (12%) and disseminated involvement in 14 (9.33%) of cases. CT scan of head was performed in all meningeal cases and confirmed (Table 3).

In 14 Disseminated cases, Splenomegaly was identified in 8 cases by ultra-sonogram abdomen; spine involvement was seen in 4 cases by Magnetic resonance imaging [MRI] of spine and tuberculomas in rest of 2 cases by CT scan of head. In 18 cases of tubercular effusion, pleural was commonest with 14 cases followed by ascites in 3 and 1 pericardial effusion.

In the total study out of 150 patients, isolated pulmonary tuberculosis was seen in 43 (28.67%) patients, isolated EPTB was seen in 13 (8.67%) patients and both were seen in 84 (56%) patients (Table 3).

CD4 counts were done in all the patients. 87 (58%) of them had CD4 counts <100cells/ μ l, 39 (26%) had cell

counts between >101-200cells/ μ l and 24 (16%) had cell counts >200 cells/ μ l. The mean CD4 cell count was 134cells/ μ l (males: 112cells/ μ l, females: 128cells/ μ l). Patients with EPTB had CD4 cell counts <200/ μ l and CD4 counts <100cells/ μ l were found in disseminated tuberculosis and cases with meningeal involvement (Table 3).

Table 3: Laboratory profile of HIV-TB co-infected cases.

Microscopy	No	%
Smear Negative for AFB by Zn staining	84	56
Smear Positive for AFB by Zn staining	66	44
3+	38	57.58
2+	16	24.24
1+	12	18.18
Chest X-ray		
Pulmonary infiltrates	98	65.33
Effusion	24	16.00
Cavity	13	8.67
Fibrosis	8	5.33
Miliary lesions	7	4.67
Extra - pulmonary tuberculosis		
Lymphadenopathy	43	28.67
Axillary	14	32.56
Cervical	12	27.91
Abdominal	10	23.26
Generalized	7	16.28
Effusion	18	12.00
Pleural	14	77.78
Ascites	3	16.67
Pericardial	1	5.56
Disseminated	14	9.33
Splenomegaly	8	57.14
Potts spine	4	28.57
Tuberculoma	2	14.29
Meningeal	22	14.67
CD4 counts		
\leq 100 cells/ μ l	87	58
>101 -200 cells/ml	39	26
\geq 200cells/ml	24	16

Peripheral lymphadenopathy was present in 23 cases in our study and abdominal lymphadenopathy in 10 cases. Axillary lymphadenopathy was the commonest lymph node involvement seen in 14 patients followed by cervical lymphadenopathy in 12 patients. 7 patients had generalized lymphadenopathy. Tubercular lymphadenopathy was diagnosed by FNAC and lymph node biopsy. AFB staining was positive in 22 cases and rest on the basis of Granulomatous reaction and response to anti tubercular therapy. Patients with tubercular lymphadenopathy and AFB staining positive had CD4 counts <200/ μ l.

DISCUSSION

Pandemic of HIV in India has caused a resurgence of tuberculosis which showed a decline due to implementation of control programmes. TB is the most common opportunistic infection in HIV infected individuals. TB and HIV co-infection has become global problem of public health concern.⁸ Clinical, radiological and laboratory profile of TB-HIV co-infected patients differs from region to region based on the prevalence and distribution of both.

In present study, 26-35 years (37.33%) was the most common age group which is sexually active and productive age group in the entire life. As mentioned in the Global TB report 2015, male predominance was noted (68.67%) which coincides with the findings in studies of Deivanayagam et al and Bhagyabathi DS et al and many other studies globally.^{9,10}

Most of them acquired the infection by unprotected heterosexual contact, which is the most common mode of acquisition globally. Heterosexual promiscuity and casual sex were found to be the common risk factors in acquisition of HIV by most of the authors internationally.^{11,12}

50% of cases were married and 52.67% were labourer's indicating more prevalence of HIV in daily workers like truck drivers and in females most of them were house wives. However findings of Mohanthy et al reported 36.8% as manual labourers, while Rajasekharan et al reported 55.6% as farmers. The percentages of professions identified are variable in different studies because of variation in the study group selected.^{13,14}

The most common clinical symptom was fever observed in 100% of patients while 84% had cough with expectoration. Mohanthy et al in his study mentioned fever as the most common symptom (98%) and Rajasekharan et al reported Cough as the most common (94%) followed by chest pain (92%).

The clinical presentation of TB depend on the stage of HIV and associated hosts immune status. Oral Candidiasis was observed in 65.33% of cases indicating that Candidiasis is the most common opportunistic fungal infection which is in par with the findings of many studies.

In our study 66(44%) of cases were sputum positive by Zn staining and 38 were graded 3+ followed by 16 ,12 with 2+ and 1+.These findings are in contrast with the findings of Patel et al, Mohanthy et al and Devinayagam et al who reported 22.58%, 31.59% and 15% in their studies.¹⁵

This is explained by the reason that most of the participants in our study were in HIV stage I. The finding indicates that Zn staining is not a sensitive diagnostic tool

in diagnosing PTB in HIV individuals, because smear positivity is better in early HIV infection only. EPTB is more common in HIV/TB patients especially with advanced immunosuppression than in non HIV/TB patients.¹⁶

Pulmonary infiltrates was the commonest finding in chest X-ray (65.33%) followed by pleural effusion (16%), Cavity (8.67%), fibrosis (5.33%) and miliary lesions (4.67%). Findings of our study are in par with findings of Zuber Ahmed et al.¹⁷ Isolated PTB was seen in 28.67% and EPTB in 13 (8.67%) patients and both were seen in 84(56%) patients. Other studies also reported the high prevalence of EPTB of 53-63% of total tuberculosis cases in HIV infected patients, and was seen more frequently in severely immunocompromised patients in later stages of HIV.¹⁸

Lymphadenopathy was the commonest extra pulmonary form (28.67%) followed by Meningeal (14.67%), effusion (12%) and disseminated form (9.33%). Findings of our study correlates with the findings of Brig S K Sharma et al where lymphadenopathy was commonest followed by meningeal involvement.¹⁹ However study findings by SK Sharma et al found disseminated tuberculosis in 25.20% of patients. This can be explained because in our study more of patients were hospitalized and later found to be immunocompromised.²⁰ Jayral et al reported CNS tuberculosis as the most common form of EPTB in his study (33.84%).²¹

In our study we found CD4 counts <200cells/ μ l in all disseminated and EPTB cases which coincides with the findings of many studies. CD4 counts <100cells/ μ l were found in all cases with meningeal involvement. CD4 level is one of the parameter to determine the stage of HIV infection that represents the degree of host immunity.

All the cases of lymphadenopathy (Cervical & Axillary) were diagnosed by FNAC and staining for AFB in smears. Histopathological examination for Granulomatous reaction was observed in cases which are negative for AFB bacilli by staining. In all cases with lymph node involvement the CD4 counts were <200/ μ l. In the overall study only 24 cases (16%) had CD4 counts >200cells/ μ l.

CD4 counts provides a significant laboratory tool in identification of patients progressing from latent form to active or end stages of HIV infection. The diagnostic role of FNAC and AFB smear examination has also been reported by Artenstein et al and fine needle aspiration is more reliable in patients with HIV infection because of the higher Mycobacterial burden, and should be the initial diagnostic procedure in these patients.²²

CONCLUSION

To conclude HIV more commonly affects the economically productive age group with more males than

females. Heterosexual mode of acquisition is commonest and more in labourers like truck drivers etc. Pulmonary tuberculosis is more common than extra pulmonary tuberculosis. Sputum smear microscopy is not a sensitive tool in diagnosing TB in HIV infected individuals. Sputum positivity depends upon the stage of HIV infection. Lymphadenopathy is more common form of EPTB and diagnosis can be made by FNAC and Histopathological examination.

CD4 counts are <200/ μ l in all forms of EPTB making estimation of CD4 counts a good tool in prompt and early diagnosis of EPTB. Hence regular screening of HIV infected individuals by sputum microscopy along with chest X ray and CD4 counts estimation provides a good strategy in early diagnosis of TB and EPTB thus significantly reducing the morbidity and mortality in HIV infected individuals due to TB. FNAC provides a good investigation in diagnosis of TB lymphadenopathy.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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