http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v8i5.59

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Clinical and Radiological Profile of Pulmonary Tuberculosis in HIV Seropositive Patients in Relation to CD4 Count

Authors

Dr Mohammed Hidayath Hussain[1], Dr Hina Afreen[2*]

[1]Professor Department of Pulmonary Medicine, Shadan Institute of Medical Sciences, Hyderabad Telangana State

[2]Post Graduate, Department of Pulmonary Medicine, Shadan Institute of Medical Sciences, Hyderabad Telangana State

*Corresponding Author

Dr Hina Afreen

Post Graduate, Department of Pulmonary Medicine, Shadan Institute of Medical Sciences, Hyderabad Telangana State, India

Abstract

Background: *Tuberculosis and HIV make up a synergistic and devastating partnership, each exacerbating & quickening the progression of the other Infection with HIV being the most powerful known risk factor predisposing for Mycobacterium tuberculosis infection and progression to active disease. The risk of tuberculosis in HIV- infected persons continues to increase as HIV disease progresses and CD4 cell count decreases. Thus co infection with HIV and tuberculosis is not only a medical malady, but a social and an economic disaster and is aptly described as the 'cursed duet'. Understanding the clinical and radiological profile of the HIV-Tuberculosis co-infection is of great importance because of increasing prevalence of co-infection, severity of clinical presentation of tuberculosis in HIV- positive patients, rapid progression of HIV disease in tuberculosis patients, and challenges in treatment of co-infected patients given possibly of drug interactions and immune reconstitution syndrome.*

Methods: *Hospital based cohort study was done for a period of two years at a tertiary care hospital. This study was carried on 110 patients with HIV & TB co infection. Diagnosis of tuberculosis apart from clinical manifestations is based on sputum for acid fast bacilli and chest X- ray to know the extent of the disease.AFB positive smears were graded as per RNTCP guidelines.CD4 count was done for the serum samples found positive for HIV.*

Conclusions: *The clinical manifestations of tuberculosis in HIV infected patients are quite varied and generally show different pattern in relation to CD4 cell count. Patients with low CD4 count presented with more number of symptoms. The majority of patients with HIV-related pulmonary tuberculosis in this study had atypical radiological presentation when CD4 count was <200/µl.*

Keywords: *pulmonary tuberculosis, HIV seropositive patients, CD4 counts.*

Introduction

Tuberculosis ranks high in the list of deadly infections, claiming thousands of lives every year and crippling lakhs of population across the world. Though it was detected as far back as 10,000 BC it still remains a major health problem to be conquered.

Tuberculosis is a life-threatening bacterial disease with 8 million new cases, and 3 million deaths reported worldwide each year to the World Health Organization; the vast majority of these cases are in developing countries. Poorly treated patients can develop drug resistance and potentially incurable forms of tuberculosis[1].

There has been a resurgence of tuberculosis in the recent times across the world despite effective chemotherapy, due to its association with HIV/AIDS pandemic, resulting in increased morbidity and mortality. Tuberculosis and HIV make up a synergistic and devastating partnership, each exacerbating & quickening the progression of the other.

The primary impact of HIV on tuberculosis is that the risk of developing tuberculosis becomes higher in patients with HIV. HIV co-infection is the most powerful known risk factor for progression of *M.* tuberculosis infection to active disease, increasing the risk of latent TB reactivation 20-fold[12],[13]. Likewise, TB has been reported to exacerbate HIV infection[14],[15]. Various lines of evidence indicate that inborn errors of immunity, as well as genetic polymorphisms, have an impact on susceptibility to TB and HIV[16]

Throughout the course of HIV infection, there is an increasing risk of tuberculosis, which is detectable as early as HIV seroconversion, and the risk of tuberculosis almost doubles during the first year after HIV seroconversion. The risk of tuberculosis in HIV- infected persons continues to increase as HIV disease progresses and CD4 cell count decreases. The higher risk of HIV infected individuals to develop tuberculosis disease includes rapid progression of recently acquired tuberculosis as well as reactivation of latent infection, making it the most common opportunistic infection in HIV infected individuals Just as HIV infection can contribute to the severity of tuberculosis, there is increasing evidence that tuberculosis can affect HIV disease progression. Patients with active tuberculosis were found to have higher plasma viral loads than asymptomatic patients with HIV and those with opportunistic infections other than tuberculosis[2, 3].

HIV and Tuberculosis are intricately linked to malnutrition, unemployment, alcoholism, drug abuse, poverty and homelessness. Thus co infection with HIV and tuberculosis is not only a medical malady, but a social and an economic disaster and is aptly described as the 'cursed duet'.

Although the immune response to *Mycobacterium tuberculosis* is important in controlling disease, immune activation may also be associated with increased HIV viral load and accelerated progression of HIV infection[5] .

The clinical and radiological presentation of tuberculosis in HIV patients differs according to the degree of immunosuppression. Clinical presentation of tuberculosis in early HIV infection resembles that observed in immunocompetent persons and manifests with the typical features of fever, cough with expectoration and weight loss. As the CD4 count drops the manifestations become atypical as shown in several studies.

Methods

This is a hospital based cohort study, done at a tertiary care centre over a period of 24 months. A total of 110 HIV seropositive patients who were screened and confirmed with Pulmonary and EPTB were included in the study. This study was considered as minimal risk in human research & was approved by the ethics committee.

Inclusion Criteria

All the patients attending the Department of Pulmonology who were suspected with HIV and Tuberculosis between the ages of 15 to 60 years were included in the study. Informed consent was obtained from all the participants in the study.

Exclusion Criteria

Participants less than 18 years and above 65 years of age, patients with past use of ATT or ART were excluded. Also patients with diabetes or intake of other immunosuppressive drugs were excluded.

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. Routine blood and urine examinations were carried out in all patients.

Diagnosis of HIV and CD4 Counts

After pre-test counselling and obtaining written and informed consent, patients were tested for antibodies to HIV by three different kits (Test-I Comb aids, Test-II Tridot, and Test-III EIA Comb) at Integrated Counselling and Testing Centre (ICTC). Three tests were performed in random as recommended by the World Health Organisation and adopted by the National Aids Control Organisation, Government of India. The serum samples found positive by all three tests were considered positive to HIV and for these patients CD4 count was done by FACS Calibre system.

Diagnosis of Tuberculosis

Diagnosis of tuberculosis apart from clinical manifestations is based on sputum for acid fast bacilli and chest X- ray to know the extent of the disease.

Sputum Examination

As recommended by WHO Smears can be graded according to the number of bacilli seen with Ziehl- Neelsen staining.

- Negative == no bacilli seen in 100 oil immersion fields;
- Scanty+ == 1-9 AFB per 100 oil immersion fields;
- (1+) == 10-99 AFB per 100 oil immersion fields;
- (2+) == 1-10 AFB per oil immersion field (examine 50 fields);
- (3+) == >10 AFB per oil immersion field (examine 20 fields)

Radiological Findings

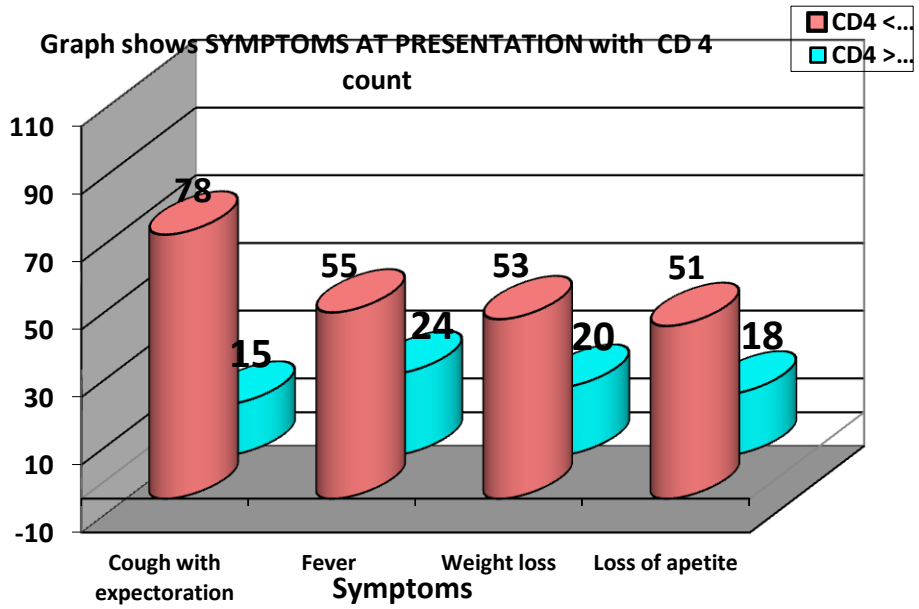
Patients were assigned to one of two groups. Those with findings characteristic of reactivation or post-primary tuberculosis (typical pattern) or those with findings uncharacteristic of reactivation tuberculosis (atypical pattern). The criteria for the typical and atypical pattern were established prior to the interpretation of the radiographs. The atypical pattern included those subjects with lower and middle lobe opacities, anterior segment of upper lobe opacities, mediastinal or hilar lymphadenopathy, pleural effusions, diffuse opacities, interstitial nodules, or a normal chest radiograph. The typical pattern included reactivation or post-primary disease pattern included upper lobe opacities.

Results

HIV is considered as the primary risk factor in acquisition of tuberculosis. A total of 110 known HIV seropositive and tuberculosis cases, with 85 males (77.2%) and 25 females (22.7%) were included in the study. Males outnumbered the females in our study. The most common age group affected in our study was 30-39 years (48.2%) followed in order by 40-49 years (24.5%), 15-29 years (20%) and >50 years (7.3%).

AGE GROUP (in years)	MALES		FEMALES		TOTAL	
	PATIENTS	%	PATIENTS	%	PATIENTS	%
15-29	13	11.8 %	9	8.2 %	22	20 %
30-39	41	37.3 %	12	10.9 %	53	48.2 %
40-49	23	20.9 %	4	3.6 %	27	24.5 %
50-59	8	7.3 %	_	_	8	7.3 %

Out of 110 patients, Cough with Expectoration was seen most commonly in 84.5%,it was more common in patients with CD4 count < 200 (52.7 %). Fever was second most common presenting symptom in 71.8 % of 110 patients mostly in Patients with CD4 count <200 (50 %). Weight loss & loss of appetite seen in 65 % of all Patients.



On examination, out of 110 patients in the study, 50% of the patients had muscle wasting and 32% had a CD4 count <200. respiratort distress was seen in 42 patients that is 38.2% and among them, 28.2% have CD4 count <200. Lymphadenopathy was seen in 30% patients-18.6% have CD4count < 200 and 18.6 % have generalized lymphadenopathy. Oral thrush was seen in 36.4 % and all have CD4 count < 150. 3.64 % that is 4 patients have no clinical findings

SIGN	NUMBER		CD4 < 200		CD4 > 200	
Muscle wasting	55	50 %	35	32 %	20	18 %
Respiratory distress	42	38.2 %	31	28.2 %	11	10 %
Oral thrush	40	36.4 %	32	29 %	8	7.4 %
lymphadenopathy	33	30%	27	24.5 %	6	15.5%
clubbing	18	16.4 %	10	9.1 %	8	7.3 %

The different radiological pattern of pulmonary tuberculosis in HIV positive patients and Bilateral diffuse infiltrates was the most common (50 %) followed by Milliary Tuberculosis -13.6 %, Lower lobe infiltrates -10.9 %, Cavitation - 9.9 %, Normal chest X – ray -10 %, Upper lobe infiltrates -7.2 %, Pneumothorax- 6.3 % and the least common was Hydro Pneumothorax- 2.7 % .

LESION	PATIENTS #		CD4 < 200		CD4 > 200	
Normal X-ray	11	10 %	6	5.4 %	5	4.5 %
Opacities UL	8	7.2 %	3	2.7 %	5	4.5 %
Opacities LL	12	10.9 %	10	9 %	2	1.8 %
Opacities extensive	55	50 %	45	41 %	10	9 %
pneumothorax	7	6.3 %	3	2.7 %	4	3.6 %
cavitation	11	9.9 %	3	2.7 %	8	7.2 %
Hydropneumothorax	3	2.7 %	1	1 %	2	1.8 %
Milliary TB	15	13.6 %	11	10 %	4	3.6 %

Radiological pattern of pulmonary Tb in relation to cd4 count

71 Patients had CD4 count < 200, 65 patients had atypical presentation. 39 Patients had CD4 count > 200, 26 patients had atypical presentation. Out of 55 Patients having bilateral diffuse infiltrates, 45 Patients had CD4 count < 200. Out of 15 Patients with milliary TB, 11 patients had CD4 count < 200. Out of 12 Patients with lower lobe infiltrates, 10 had CD4 count < 200. Out of 11 Patients with cavitation, 8 had CD4 count > 200. Out of 8 Patients with Upper lobe infiltrates, 5 had CD4 count > 200.

Radiological findings	CD4 count < 200	CD4 count > 200
ATYPICAL	65	26
TYPICAL	6	13
TOTAL	71	39

Discussion

Pandemic of HIV in India has caused a resurgence of tuberculosis which showed a decline due to implementation of control programs. TB is the most common opportunistic infection in HIV infected individuals. TB and HIV co-infection has become global problem of public health concern[4]. Clinical, radiological and laboratory profile of TB-HIV co-infected patients differs from region to region based on the prevalence and distribution of both.

Clinical observations show that the response of HIV-infected tuberculosis patients to anti-tuberculous drugs is similar to HIV-uninfected, indicating that the increased morbidity and mortality in co-infected patients is attributable to the worsening of HIV disease[6]. It is suggested that HIV-infected individuals co-infected with tuberculosis have an ineffective immune responses against M.Tuberculosis as shown by total Lymphocyte count and reduced CD4+ T cell count and decreased IFN-γ expression[2]. Although the lung could be a preferential organ for HIV Replication during active tuberculosis, available data indicate that an increase as high as 5- to 160-fold in plasma HIV viraemia may occur during the acute phase of M.tuberculosis disease[3].

Most of our study group patients (48.3%) belonged to the age group of 30-39 yrs. who are sexually active AND also 77.3%of the patients were males. The striking male predominance noted in present study has also been reported by Deivanayagam et al (2001), Rajasekharan et al (2000)[7]

The occupational profile of our patients revealed that a majority of them were labourer followed by drivers. Most of the females were housewives with promiscous male partners. *Rajasekharan et al* (2000)[7] reported that majority of their patients were from the farming profession, while the transporters accounted for a smaller portion. *Purohit et al*[8] and *Thanasekharan et al*[9] reported that majority of their patients were truckers. *Mohanthy et al*[10] reported 36.8% patients working as manual labourers. Whilemajority 80% of the female seropositive were commercial sex workers. The percentage of the profession is thus seem to vary in different studies, largely due to difference in occupational pattern and source from there the patients were selected. Sexual route (Heterosexual) was found to be the major risk factor while one patient got infection through blood/ blood product transfusion. None of the patient had history of IV drug abuse in our study. Majority of females acquired infection through their husbands, who in turn got infection from commercial sex workers. This observation is similar to other study in India by Kumaraswamy et al (1995)[11].

The most common symptom was cough and expectoration in 93 (84.5%) patients, while fever was present in 79 (71.8%) and weight loss in 77 (66.3%) patients. In the series reported by *Thanasekharan et al, Deivanayagem et al* and *Arora et al* cough with expectoration was the most common complaint, our study also showed similar results

Present study shows that symptoms are more common in patients with CD4 count less than 200cells/μ, when compared to the patients

withCD4 count more than 200 cells/µl,this may be probably due to majority of patients (64.5%) are in the group of CD4 count <200cells/µl.

The radiological manifestations were varied. The typical radiological feature of post pulmonary tuberculossiie, upper zone infiltrates and cavitary lesions were seen in 7.2% and 9.9% patients respectively in our study, while atypical features such as lower zone infiltrates, milliary tuberculosis, diffuse shadows and normal chest x-ray seen in 10.9%, 13.6%, 50% and 10% cases respectively. Out of 110 patients 71 (64.5%) had CD4 count < 200 cells/µl and 39 (35.5%) had CD4 count >200 cells/µl. 65 (92%) of 71 patients with CD4 count <200cells/µl and 26 (67%) of 39 patients with CD4 count > 200cells/µl presented with atypical pattern of pulmonary tuberculosis. It shows p value of <0.001 and it is highly significant. Present study is comparable with the study of *Mark D. Keiper et al*. (1995), conducted a study "CD4 T lymphocyte count and radiographic presentation of pulmonary tuberculosis", in that CD4 count <200 cells/µl is more commonly associated with atypical pattern (92%)

Conclusion

In the present study reasonable following conclusions can be drawn relating to clinicoradiological profile of pulmonary tuberculosis in HIV positive patients in relation to CD4 count. Our data suggest that the most common mode of transmission of HIV in young males is heterosexual transmission from commercial sex workers. The clinical manifestations of tuberculosis in HIV infected patients are quite varied and generally show different pattern in relation to CD4 cell count. Patients with low CD4 count presented with more number of symptoms. The majority of patients with HIV-related pulmonary tuberculosis in this study had atypical radiological presentation when CD4 count was <200/µl. Patients with high CD4 count also presented with atypical pattern. This may be a sign of changing trend of tuberculosis presentation in HIV positive patients in relation to CD4 count, and this needs further study.

References

1. TB India 2006, RNTCP status report, DGHS, Ministry Of Health and Family Welfare, New Delhi.
2. Toossi Z, Johnson JL, Kanost RA, Kansot RA, Wu M, Luzze H, et al. Increased replication of HIV-1 at sites of Mycobacterium tuberculosis infection: Potential mechanisms of viral activation. J. Acquir. Immune Defic. Syndr 2001; 28: 1-8.
3. Kassim S, Sassan-Morokro M, Ackah A, Abouya LY, Digbeu H, Yesso G, Coulibaly IM. Two-year follow-up of persons with HIV-1 and HIV-2 associated pulmonary tuberculosis treated with short course chemotherapy in West Africa. AIDS1995; 9(10):1185-91.
4. Arora VK, Gupta R. Trends of extra-pulmonary tuberculosis under revised national tuberculosis control programme: A study from South Delhi. Indian J Tuberc. 2006;53:77.
5. Praveen Kumar, Niraj Sharma et al. Clinical Profile of Tuberculosis in Patients with HIV Infection/AIDS Indian J Chest Dis Allied Sci 2002; 44 : 159-163
6. Deivanayagam CN, Rajasekharan S, Senthilnathan V, et al. Clinicoradiological spectrum of tuberculosis among HIV seropositives: A Tambaram study. Indian J Tuberc2001; 48: 123-27.
7. Deivanayagam CN, Rajasekharan S, Senthilnathan V, et al. Clinicoradiological spectrum of tuberculosis among HIV seropositives: A Tambaram study. Indian JTuberc2001; 48 : 123-27.
8. Purohit SD, Gupta RC, Bhatura VK. Pulmonary tuberculosis and human immunodeficiency virus infection in Ajmer. Lung India 1996; 14: 113-20.

9. Thanasekaran V, Krishna Rajasekhar OR, Madhvi S, et al. Pulmonary disease in HIV infected patients: An analysis of 16 cases. Lung India 1994; 12 : 123-28.
10. Mohanty KC, Sundrani RM, Nair S. HIV infection in patient with respiratory disease.Indian J Tuberc 1993; 40 : 5-12.
11. Kumaraswamy N, Solomon S, Purnima M, Tokhuga Yepthomi, C. Venkatesan, R. Edwin Amalraj, et al. High plasma viral load in persons co-infected with HIV and tuberculosis in south India. 9th international congress on Infectious Diseases; 2000 April, 10-13; Buenos Aires, Argentina.
12. IV infection-associated tuberculosis: the epidemiology and the response. Getahun H, Gunneberg C, Granich R, Nunn P Clin Infect Dis. 2010 May 15; 50 Suppl 3():S201-7.
13. prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. Selwyn PA, Hartel D, Lewis VA, Schoenbaum EE, Vermund SH, Klein RS, Walker AT, Friedland GHN Engl J Med. 1989 Mar 2; 320(9):545-50.
14. Accelerated course of human immunodeficiency virus infection after tuberculosis. Whalen C, Horsburgh CR, Hom D, Lahart C, Simberkoff M, Ellner J Am J Respir Crit Care Med. 1995 Jan; 151(1):129-35.
15. Effect of treating co-infections on HIV-1 viral load: a systematic review. Modjarrad K, Vermund SH Lancet Infect Dis. 2010 Jul; 10(7):455-63
16. Current findings, challenges and novel approaches in human genetic susceptibility to tuberculosis. Möller M, Hoal EG Tuberculosis (Edinb). 2010 Mar; 90(2):71-83.