Original Research Article

A Comparative Study on HIV-TB Coinfection and TB in Gandhi Hospital

Sirisha Peddi[1], K. N. Sree Sai Gayathri[2], Venkannagari Vikas Reddy[3], Swetha[4*]

[1]Assistant Professor, Department of Medicine, Gandhi Medical College/ Hospital, Secunderabad, India
[2]Assistant Professor, Department of Medicine, Gandhi Medical College/ Hospital, Secunderabad, India
[3]Post Graduate, Department of Medicine, Gandhi Medical College/ Hospital, Secunderabad, India
[4]Assistant Professor, Department of Medicine, Gandhi Medical College/ Hospital, Secunderabad, India

Received: 13-10-2021 / Revised: 05-12-2021 / Accepted: 21-12-2021

Abstract

Background: Tuberculosis (TB) and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) constitute the main burden of infectious disease in resource-limited countries. In the individual host, the two pathogens, *Mycobacterium tuberculosis* and HIV, potentiate one another, accelerating the deterioration of immunological functions. **Aims:** To compare the clinical presentation of HIV-TB coinfection and TB infection and to study the correlation of CD4 count with the clinical, bacteriological and radiological findings of tuberculosis among HIV positive patients **Materials and methods:** This hospital based non randomised cross sectional observational study was conducted in 50 eligible patients admitted with tuberculosis and HIV coinfection and 50 patients with tuberculosis only in the medical wards. Study has been done to find relationship between CD4 count and the status of sputum smear. **Results:** In our study,26 cases(52%) had pulmonary tuberculosis at the initial diagnosis of HIV infection. Among the 26 cases, CD4 count less than 200 was present in 19(73.1%) . In our study , significant number of TB cases(6 cases 12%) were diagnosed in the first year after HIV infection. Bilateral findings are 25% in both HIV-TB coinfection and TB infection whereas unilateral findings are 75% in both HIV-TB coinfection and TB infection. In HIV-TB coinfection lower zone findings are 17% whereas only 7% of TB infection has lower zones and there was a statistically significant. **Conclusions:** We concluded that sputum smear positivity decreases as the CD4 count decreases and sputum smear microscopy remains a gold standard method for diagnosing pulmonary tuberculosis.

Keywords: Tuberculosis, Human immunodeficiency virus, Sputum smear.

Introduction

Tuberculosis and HIV (**human immunodeficiency virus**)have been associated with each other ever since the emergence of Acquired immunodeficiency syndrome (AIDS). Because of the HIV pandemic, a resurgence in TB epidemic has been observed in India for the last few decades. Tuberculosis remains the most common opportunistic infection in HIV seropositive individuals of which the most common manifestation is pulmonary tuberculosis , irrespective of the degree of immunosuppression . In India, both HIV and TB infection are prevalent maximally in the reproductive age group of 15-49 years ,thus the interface between HIV and TB is increased. The dual infection has been termed "cursed duet"[1] HIV TB co-infection thus presents an urgent and serious public health and an alarming danger to the socioeconomy of our country. Shortening the time for pulmonary TB(PTB) diagnosis and treatment initiation is an important step in decreasing TB-associated mortality and transmission. One of the major challenges in diagnosing PTB[2] is alteration of the presentation of PTB due to HIV infection. TB and HIV infections have an added negative influence on the host immunity. An important marker in assessing the degree of immunosuppression and identifying HIV disease progression is the CD 4 lymphocyte count The presentation of TB in individuals with HIV co infection with normal CD4 count is similar to that of HIV-negative patients[2].However, patients with depressed immunity (low CD4 count) have a pattern that is deviated from the normal, both in clinical features and investigation findings, thus making diagnosis difficult. In countries with high prevalence of TB ,the most cost effective method of detecting PTB among suspects is sputum smear microscopy. WHO states that sputum positivity decreases as CD4 count decreases. But this finding has not been proven in a few studies done in the past. Hence this study has been done in our institution to better understand the relationship between CD4 count and the status of sputum smear.

**Correspondence*
Dr. Swetha
Assistant Professor, Department of Medicine, Gandhi medical College/ Hospital, Secunderabad, India.
E-mail: drsweth5555@gmail.com

Materials and Methods

This hospital based non randomised cross sectional observational study was conducted in Gandhi Medical College Hospital, a tertiary care referral centre located in the Telanagana. After giving written informed consent , 50 eligible patients admitted with tuberculosis and HIV coinfection and 50 patients with tuberculosis only in the medical wards of our hospital from Nov 2018 to May 2020 participated in the study. The research protocol was approved by the Institutional Ethical Committee of Gandhi Medical College.

Inclusion criteria: Patients who have been diagnosed as HIV positive either by Rapid Test or ELISA and who have clinical and investigatory evidence of pulmonary TB or Extra pulmonary TB are enrolled in the study. These patients are picked up from ART Clinic. Those patients who sought medical attention for any form of Tuberculosis at chest clinic OP, who are HIV negative, are chosen as controls. Patients between the age group of 15 to 55 are enrolled in the study.

Exclusion criteria: HIV positive individuals who did not have clinical or investigatory evidence of any form of TB, Patients who had other causes of immunosuppression such as Diabetes, Lymphoma, Leukaemia, visceral malignancy, malnutrition, on immunosuppressive drugs.

Investigations required

Sputum smear for AFB and CBNAAT, PPD reactivity by mantaoux test, HIV test by ELISA ,CD4 count and Chest x-ray PA view, Special investigations were done in patients with extra pulmonary TB like FNAC of lymph node, biopsy and CSF analysis.

Patients were enquired about symptoms such as cough, fever , hemoptysis, weight loss , loss of appetite, etc. and underwent a thorough clinical examination.

Patients were instructed to produce two expectorated sputum samples, of which atleast one is an early morning sample. In the laboratory of RNTCP Designated Microscopy Centre (DMC) of our hospital, sputum samples were tested for AFB by Ziehl Neelson method. 100 microscopic fields were visualised in each smear. Smears were categorised as positive or negative. One specimen positive out of the two is enough to declare a patient as smear positive TB.

Sputum density was further graded as 3+ (>10 AFB/oil field) (20 fields to be examined),

2+ (1 to 10 AFB/oil field) (50 fields to be examined), 1+ (10 to 99 AFB/100 oil fields),

Scanty (1 to 9 AFB/100 oil fields).

Chest X ray posteroanterior view was taken for all the patients. In all the smear negative cases, CT chest was taken and expert opinion given by radiologists of our hospital. In addition to the baseline investigations like Complete Blood Count, blood sugar, urea, creatinine, LFT that were done in biochemistry lab, CD4 count was done in ART plus centre of our hospital by flow cytometry.

Data Analysis

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD)for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Comparison of mean of quantitative variables were analyzed using unpaired t test. Bar charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

Results

50 patients with tuberculosis and **HIV-TB** coinfection who fulfilled the inclusion criteria are compared with 50 patients who have tuberculosis only The observations made were as follows:

Table 1: Age distribution of HIV-TB coinfection and TB

Age Group	HIV-TB Coinfection No.	% Of Cases	TB	% Of Cases
15 - 20 years	3	6	11	22
21 - 25 years	2	4	6	12
26 - 30 years	6	12	3	6
31 - 35 years	9	18	4	8
36 - 40 years	11	22	5	10
41 – 45 years	9	18	7	14
46 – 50 years	6	12	6	12
51 – 55 years	4	8	8	16
Mean (SD)	38.02 (9.25)		35.50 (13.13)	
Total	50	100	50	100
Mean (SD)	36.76 (11.39)			
Gender				
Male	36	72	27	54
Female	14	28	23	46
Others	0	0	0	0
Chi-square test, P Value = 0.062, Not Significant				
Symptoms				
Fever (P Value = 0.538)	45	90	43	86
Cough (P Value = 0.015*)	23	46	35	70
Loss Of Weight (P Value = 0.548)	28	56	26	52
Hemoptysis (P Value = 1.000)	3	6	3	6
Diarrhoea (P Value = 0.161)	10	20	5	10
Weakness (P Value = 0.294)	20	40	15	30
Loss Of Appetite (P Value = 0.074)	10	20	18	36
Other Extra Pulmonary (P Value = 0.673)	16	32	15	30

Unpaired t Test, P value = 0.270, Not significant

Among the HIV-TB COINFECTION group, the minimum age was 1 6 years and maximum age was 55years. Among the TB group, the minimum agewas1 6 years and maximum age was 55 years . Of the 50 HIV-TB COINFECTION patients, 36 were male and 14 were female. B. Of the 50 TB patients, 27 were male and 23 were female.

Table 2: Chest X -ray distribution of HIV-TB coinfection and TB

Radiological findings	HIV-TB Coinfection		TB	
	No.	%	No.	%
Bilateral	7	25	8	25
Unilateral	21	75	24	75
P Value = 1.000				
Radiological findings				
Upper zone	13	46	11	34
Mid zone	2	7	11	34
Lower zone	5	17	2	7
Others (Miliary& diffuse)	8	28	8	25
P value = 0.025*				

Radiological findings				
Typical findings	15	53	22	68
Atypical findings	13	47	10	32
P value = 0.227				
Sputum				
Positive	27	54	31	62
Negative	23	46	19	38

In both **HIV-TB** coinfection and **TB** infection bilateral X-ray findings are 25% and unilateral are 75%. In HIV-TB coinfection , UZ-- 46% MZ--- 7% LZ--- 17% others--- 28% In TB infection UZ ---34% MZ ---34% LZ ---7% others ---25% . In HIV-TB coinfection typical --- 53% atypical --- 47% In TB infection typical --- 68% atypical --- 32 . In HIV-TB coinfection sputum positive – 54% negative --- 46% In TB infection sputum positive -- 62% negative --- 38%.

Table 3: CD4 count and age distribution in HIV-TB coinfection

CD4 Count	16-20 years	21-30 years	31-40 years	41-50 years	51-55 years
0-100	1	2	7	4	1
101-200	0	2	6	3	0
201-300	0	2	4	2	2
301-400	2	1	3	2	1
>400	0	1	1	3	0
		P value =0.706			

Table 4: CD4 count and sex distribution in HIV-TB coinfection

CD4+ count(Cells / µl)	Male		Female	
	No.	%	No.	%
0 – 100	8	16	8	16
101-200	9	18	2	4
201-300	8	16	0	0
301-400	9	18	1	2
>400	2	4	3	6
TOTAL	36	72	14	28
P value = 0.020*				

Chest X-ray findings observed in relation to the CD4 + cell counts is as follows,

Table 5: CD4 count and chest X-ray distribution in HIV-TB coinfection

CD4+ Count	UPP .Z	MID. Z	LO.Z	DIFF	MIL	PL.EFF	CAV
0-100	0	0	1	4	1	0	0
101-200	1	0	0	1	1	1	1
201-300	2	0	2	0	0	1	2
301-400	2	1	0	0	0	3	2
>400	3	0	0	0	0	2	0
P value	0.301			0.160	0.75	0.075	0.255

UPP.Z: Upper Zone MID.Z: Middle Zone LO.Z: Lower Zone DIFF: Diffuse infiltrates MIL: Miliary Mottling PL.EFF: Pleural Effusion CAV: Cavity The Sputum AFB status in relation to the CD4+ cell counts is as follows,

Table 6: CD4 count and sputum distribution in HIV-TB coinfection

CD 4 + Count	Sputum Positives		Sputum Negatives	
	No.	%	No.	%
0 – 100	1	2	16	32
101- 200	7	14	3	6
201- 300	7	14	2	4
301-400	6	12	2	4
>400	6	12	0	0
TOTAL	27	54	23	46
P value <0.001*				

Table 7: Mantoux distribution in HIV-TB coinfection and TB

Tuberculin induration (mm)	No. of patients	Percentage
0-2	16	2
2-5	14	5
6-10	10	10
11-14	7	13
>15	3	20
CD4 count		
0-100	5	38
101-200	3	23
201-300	2	15
301-400	2	15
>400	1	7

Discussion

While many HIV-related opportunistic infections manifest at lower CD4 counts, tuberculosis is one infection which occurs irrespective of CD4 counts, although its incidence increases with increasing immunosuppression. Several studies done in HIV-TB coinfection showed that they have severe immunosuppression at presentation, possessing CD4 counts of less than 200. In our study , a larger proportion of cases were found to be in the CD4 count range of less than 200. This confirms the fact that tuberculosis is the most common opportunistic infection in HIV patients with CD4 count less than 250.

In our study, 26 cases(52%) had pulmonary tuberculosis at the initial diagnosis of HIV infection. This undoubtedly proves the necessity of intensive case finding measures to screen for pulmonary tuberculosis in all HIV patients. The reason for this higher incidence of tuberculosis at the time of initial presentation may be explained by larger number of patients having a CD4 count of less than 200. Among the 26 cases, CD4 count less than 200 was present in 19(73.1%) . In our study , significant number of TB cases (6 cases 12%) were diagnosed in the first year after HIV infection. This finding confirms the fact that the incidence of tuberculosis is higher in the first year of HIV seroconversion.

Our study also showed a declining trend in the occurrence of TB in the third, fourth and fifth year after diagnosing HIV infection. This may be substantiated by the fact the mean CD4 count in these cases was on a higher range, 240, 304 and 241 respectively. In a country like India with resource limited settings, sputum smear microscopy and chest X ray remains the cornerstone methods for diagnosing pulmonary tuberculosis. With respect to comparison of sputum between 50 HIV-TB coinfection and 50 TB, In our study, in HIV-TB Coinfected patients we found that sputum test is positive for 27 members and negative in 23 members. Whereas in TB infection sputum test is positive in 31 members and negative in 19 members indicating that persons who are infected with both HIV and TB have less chance of having sputum positivity.

Studies by Pitchenick et al[3] showed that HIV_TB coinfected individuals are less likely to have sputum smear positivity compared to HIV seronegative individuals. Smith et al observed that acid fast smears occur with equal frequency among HIV infected and non_HIV infected patients[4].

Klein et al[5] showed a decreased sensitivity of sputum smears in pulmonary tuberculosis among HIV patients(45% versus 81%). Long et al[6] found 66% sputum smear positivity among HIV infected individuals compared to 78% among non_HIV infected individuals. Studies by Praveen kumar et al showed a sputum smear positivity of 21.4% among HIV_TB coinfected individuals. Rajasekaran et al[7] reported 15.3% patients as smear positive. Thus there have been wider variations in the occurrence of sputum smear positivity in HIV-TB coinfection. Hence we tried to analyse the relationship between the sputum smear status and the severity of immunosuppression expressed in terms of CD4 count. Applying chi square test there was a statistically significant correlation between sputum smear status and CD4 count. Thus we concluded that sputum smear positivity decreases as the CD4 count decreases. This endorses the fact by WHO that sputum negativity increases with increase in the degree of immunosuppression. In our study symptom presentation of HIV-TB coinfection and TB infection are compared like fever, cough, weight loss, hemoptysis, diarrhea, weakness, loss of appetite and other extrapulmonary symptoms. The findings of our study were indifferent from those done by Sameer singhal et al[8] who showed that acid fast smear positivity to negativity was 1:1 when the CD4 count is between 0 to 200 whereas it was 3:1 in cases with CD4 count above 200. finding corroborated with the findings of previous study done by Muqusi F et al[9]. Hence a high degree of clinical suspicion is needed to diagnose pulmonary tuberculosis among HIV infected individuals especially when CD4 count is less than 200. In our study we also tried to analyse the radiological findings among HIV TB coinfected individuals.

Tuberculosis usually involves the upper lobes unilaterally manifesting as infiltration, cavity, consolidation, fibrosis and volume loss. Mahesha Padyana et al[10] showed in their study that among patients with HIV-TB coinfection, bilateral lung involvement was common. 27.7% bilateral consolidation, 17% miliary pattern occurred in TB /HIV versus 12% pulmonary bilateral consolidation, 4.7% miliary pattern in of HIV negative tuberculosis patients.

Studies by Pearlman *et al* showed infiltrates among 67%, cavity in 20%, pulmonary nodule in 20%, interstitial disease in 17%, pleural effusion in 10% and lymphadenopathy in 7%. 3% of patients had a normal X ray. Observations made by Maniar et al[11] in patients with HIV TB coinfection, showed unilateral involvement in 71.8% patients and bilateral involvement in 28.2% cases .There was involvement of upper zone in 3.7%, middle zone in 62.5% and lower zone in 33.8% of patients. In our study, we found that that bilateral findings are 25% in both HIV-TB coinfection and TB infection whereas unilateral findings are 75% in both HIV-TB coinfection and TB infection. In HIV-TB coinfection lower zone findings are 17% whereas only 7% of TB infection has lower zones are involved. Applying chi square test there was a statistically significant.

Observations of our study correlated with the findings of previous studies done by Praveen kumar et al[3] which showed atypical findings in HIV-TB coinfection and TB infection (47% vs 32%). Therefore our study explains the fact that in early HIV clinical profile of pulmonary tuberculosis mimics post primary tuberculosis whereas the presentation in advanced HIV mimics primary tuberculosis.

Conclusion

HIV TB coinfection is often associated with reduced CD4 counts. Pulmonary tuberculosis in HIV infected individuals has lower sputum AFB positives when compared to TB patients. The most common radiological findings in HIV TB coinfection are infiltration, consolidation and cavity. Atypical findings such as diffuse involvement, mid zone and lower zone involvement and bilateral findings are common in HIV TB coinfection. Our study endorsed WHO"s fact that sputum smear negativity increases as the CD4 count falls below 200. Though sputum smear microscopy remains a gold standard method for diagnosing pulmonary tuberculosis in immunocompromised host with CD4 count more than 200,there is an urgent need for better diagnostic tools in patients with CD4 count below 200.

References

1. Murray J.F. Cursed Duet: HIV Infection and Tuberculosis. Respiration; 57:210- 220.
2. Herzog. H,S. Karger, A.G. Basel. Annie Luetkemeyer, University of California San Francisco (January 20 13) chapter 'Tuberculosis and HIV available at a site 'HIV In Site Knowledge Base' URL http://hivinsite.ucsf.edu/ InSite?page=kb-05-01-06 accessed on 2013
3. Praveen Kumar, Niraj Sharma, N.C. Sharma and Sudhakar Patnaik. Clinical Profile of Tuberculosis in Patients with HIV Infection/AIDS Indian J Chest Dis Allied Sci. 2002; 44:159-163.
4. Smith RL, Yew K, Berkowitz. KA and Aranda CP. Factors affecting the yield of acid fast sputum smears in patients with HIV and Tuberculosis.Chest. 1994; 106:684-6.
5. NC Klein, FP Duncanson, TH Lenox, A Pitta, SC Cohen and GP Wormser. Use of mycobacterial smears in the diagnosis of pulmonary tuberculosis in AIDS/ARCpatients. Chest. 1989; 95:1190-2.
6. Long R, Scalcini M, Manfreda L, Baptiste MJ, Hershfield E. The impact of HIV on the usefulness of sputum smears for the

diagnosis of Tuberculosis. Am J Public health. 1991; 81:1326-8.
7. Rajasekaran S, Uma A, Kamakshi S *et al.* Trend of HIV infection in patients with tuberculosis in rural South India. Indian J Tub. 2000; 47:223-26.
8. Sameer Singhal S, Mahajan SN, Diwan SK, Gaidhane A, Quazi ZS. Correlation of sputum smear status with CD4 count in cases of pulmonary tuberculosis and HIV co-infected patients--a hospital based study in a rural area of Central India. indian J Tuberc. 2011; 58(3):108-12.
9. Mugusi F, Villamor E, Urassa W, Saathoff E, Bosch RJ, Fawzi WW. HIV TB co-infection, CD4 cell counts and clinical correlates of bacillary density in pulmonary tuberculosis. Int J Tuberc Lung Dis. 2006; 10(6):663-9.
10. Harrison‟s principles of internal medicine 18 th edition chapter 165:1340.
11. Maniar JK, Kamath RR, Mandalia S, Shah K, Maniar A. HIV and tuberculosis: Partners in crime. Indian J Dermatol Venereol Leprol, 2006, 72.

Conflict of Interest: Nil
Source of support:Nil