A STUDY OF CLINICAL, BACTERIOLOGICAL AND RADIOLOGICAL PATTERN OF PULMONARY TUBERCULOSIS AMONG HIV SEROPOSITIVE INDIVIDUALS IN A TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

BACKGROUND

Tuberculosis is the number one infectious disease killer worldwide. TB and HIV combination forms the deadly synergy in India. HIV increases the risk of progression of latent TB infection to active TB disease. The study of the clinical, radiological and bacteriological manifestations of pulmonary tuberculosis in HIV infected patients helps in early detection and treatment of tuberculosis, so that we can prevent the spread of tuberculosis.

MATERIALS AND METHODS

This is a cross-sectional study conducted during January 2015 to August 2015. Study sample being 64 patients among 150 patients who attended ART OP and were admitted in General Medicine Ward, KMCH with Tuberculosis and HIV during the study period investigations that include Complete blood count, Liver function test, Renal function test, Sputum Microscopic Examination for Acid Fast Bacilli, Chest x-ray PA view, Mantoux test (Intradermal tuberculin skin test), CD4+ cell count. CBC, RFT and LFT are done using the conventional laboratory methods.

RESULTS

There was significant correlation between Mantoux vs CD4 count, sputum AFB vs CD4 count, sputum AFB vs Mantoux and military mottling vs CD4 count and DM and lower lobe lesions, cough and CD4 count.

CONCLUSION

Thus, a high level of clinical suspicion is required in diagnosis of TB in HIV infected, especially when they are in the later stages of disease which is indicated by CD4 counts < 350 cells/ μ L. Hence, the diagnosis of tuberculosis must be suspected in HIV positive persons irrespective of the type, site and extent of radiological lesions.

KEYWORDS

HIV, TB, Radiological, Bacterial, Clinical.

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BACKGROUND

Tuberculosis is caused by bacteria, mycobacterium tuberculosis. TB and HIV combination forms the deadly synergy in India. HIV increases the risk of progression of latent TB infection to active TB disease, thus increasing risk of death if not timely treated for both HIV and TB. TB is the most common opportunistic infection and cause of mortality among PLHA patients. Pulmonary infections have diverse presentations in the HIV patients, creating difficulty in diagnosis and treatment. "The chest x-ray appearance of patients presenting with pulmonary symptoms are frequently nonspecific."

"50% of adult Indian population is infected with Mycobacterium tuberculosis." Those patients, early in the course of HIV infection would be expected to present

similarly, to non-HIV individuals with normal cellular immunity, while those late in the course of HIV may have a different presentation.

"India ranks second in the globe that contribute to 10% - 15% of HIV-associated TB."

Indian Scenario

Number of people living with HIV: 2.5 million.

India ranks 3rd in total number of HIV patients in the world, prevalence rate in adult male is 0.43%.

Prevalence rate in adult female is 0.29%. Prevalence in general population is 0.36%.

Percentage of coverage of ART for prevention of mother to child transmission is < 25%.

Scenario in Tamilnadu in 2014

No. of PLHA: 135000

No. of CLHA - 6700

No. of New Infections - 2900

No. of AIDS related Deaths - 8700

HIV Prevalence in different Population is as follows

Antenatal clinic attendees - 0.25%.

STD clinic attendees - 8%.

Female sex workers - 4.62%.

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Men having sex with men - 5.60%.

Intravenous drug abusers - 24.2%.

This study aims to evaluate the clinical, bacteriological and radiological pattern of pulmonary tuberculosis among HIV seropositive patients in Kilpauk Medical College.

MATERIALS AND METHODS

Study Group - HIV Seropositive with Tuberculosis patients attending ART Clinic and those patients admitted in the medical ward Govt. Kilpauk Medical College Hospital.

Study Design - Descriptive study {Cross-sectional study}.

Place of Study - Govt. Kilpauk Medical College.

Duration of Study - 8 months.

Conflict of Interest - Nil.

Collaborating Depts. - Microbiology, Bio-Chemistry, Radiology, Chest Medicine.

Sample Size N - $Z^2 \{P*Q\}/l^2$

Z; With 95% confidence interval Z value is taken as 1.96.

P; Prevalence of tuberculosis in HIV patients is 20%.

Q; 100-p.

L; Relative precision taken is 50%.

So applying these variables in the formula, sample size is 64.

Inclusion Criteria

Patients with symptoms like fever, cough with expectoration lasting for more than two weeks, loss of appetite and loss of weight who are found to have HIV seropositive with tuberculosis.

Patients with Tuberculous Pleural Effusion were included in the study.

Exclusion Criteria

Patients who are suffering from Extra-Pulmonary Tuberculosis like TB pericarditis, TB meningitis, TB abdomen, isolated TB lymphadenopathy, Pott's Spine and other seriously ill patients.

No consensus among all the three independent observers regarding the x-ray features of tuberculosis infection.

Methodology

HIV seropositive patients attending ART Clinic and Medical Wards of Kilpauk Medical College were screened for tuberculosis infection. Among 150 HIV seropositive patients screened for tuberculosis, 64 of them were found to have infection.

A brief history of illness was taken from the seropositive individuals and these patients were subjected to the following further investigations that include Complete blood count, Liver function test, Renal function test, Sputum Microscopic Examination for Acid Fast Bacilli, Chest X-Ray PA view, Mantoux test (Intradermal tuberculin skin test), CD4+ cell count. CBC, RFT and LFT are done using the conventional laboratory methods.

Patients were considered to be suffering from Tuberculosis if,

1. Sputum is positive for AFB.
2. The Mantoux test reading shows induration above 5 mm.
3. X-ray features were suggestive of Tuberculosis. Since there is a high reporting of both inter-observer and intra-observer variations, opinions were obtained from

three persons separately - a general physician, a thoracic physician and a radiologist and their Tuberculosis status confirmed.

Diagnosis of Tuberculosis

Sputum AFB.

Chest X-Ray.

Sputum Culture (Solids and liquids).

Mantoux Test.

Molecular Methods ("GENE XPERT - RIF").

Interferon Gamma Release Assay.

Serological Methods.

Mean Time to Diagnose TB Cases

GENE Xpert - 90 minutes.

Sputum Microscopy - 24 hrs.

Liquid Culture - 18 days.

Solid Culture Medium - > 32 days.

Figure 1. Algorithm used in Diagnosis of TB in HIV Patients

"A definitive diagnosis of tuberculosis can only be made by culturing Mycobacterium tuberculosis organisms from a specimen taken from the patient."⁽¹⁾ Sputum smears and cultures should be done for acid-fast bacilli if the patient is producing sputum. "The preferred method for this is fluorescence microscopy (Auramine-Rhodamine staining), which is more sensitive than conventional Ziehl-Neelsen staining." But in our study, we used Ziehl-Neelsen method for demonstrating the organism.

If no sputum is being produced, specimens were obtained by inducing sputum, a laryngeal swab, bronchoscopy with bronchoalveolar lavage or fine needle aspiration of a collection.⁽¹⁾

If molecular methods were used to diagnose TB we can get the results within 100 mts., sensitivity increased upto 92% if 3 samples were tested."⁽²⁾ They are more useful for diagnosing HIV with TB cases and to detect MDR TB cases. "IGRA, used to diagnose LTBI is particularly useful in profoundly ill patients and those with severe malnutrition." "There are two in vitro tests to detect latent tuberculosis Quantiferon TB Gold and T spot - TB test. The problem with IGRA is more expensive, skill needed and not suitable for serial testing. The advantage is high specificity and single patient visit enough. WHO banned use of serology to diagnose TB.

Statistics

The collected data was analysed with SPSS 16.0 version. To describe about the data, descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean and S.D were used for continuous variables. To find the significant difference between the bivariate samples in independent groups, the unpaired sample t-test was used. To find the significance in categorical data Chi-square test was used. In both the above statistical tools, the probability value of .05 is considered as significant level. Using this computer software multiple variables like mean range percentages, standard deviation, chi square and p value etc., are used to test for the statistical significance of the study. A p value of less than 0.05 denotes significant relationship.

RESULTS

The age of subjects ranged from 21 - 46. The mean age was 35.48. Minimum age is 21 for female and 31 for male, maximum age of patient in this study for both male and female is 46. Out of the 64 patients, 76.6% (49 patients) were males, 23.4% (15 patients) were females.

Occupation	Total No. of Patients	Percentage (%)
Agriculture	9	14.1
Business	8	12.5
Driver	31	48.4
Housewife	13	20.3
SL	3	4.7
Total	64	100.0

Table 1. Distribution of Patients according to Occupation

Out of 64 patients, driver was the most common occupation 48.4%, in which CD4 count < 350 is 23 members.

Among the symptoms cough was the most common symptom, out of 64 patients 52 patients had cough. Next one is loss of weight and appetite.

Mantoux Test	Total No. of Patients	(%)
< 5	46	71.9
> 5	18	28.1
Total	64	100.0

Table 2. Mantoux Test Result Distribution

The proportion of sputum positivity was found to be higher in those patients with CD4 count > 350, 10 patients. In patients with CD4 count < 350, sputum positivity was present only in 3 patients.

Figure 2. Distribution of Sputum AFB Results among Study Population

CD4 Count	Total No. of Patients	Percentage (%)
> 350	20	31.3
< 350	44	68.8
Total	64	100.0

Table 3. CD4 Count Result Distribution

44 patients had CD4 count < 350 (Male 36, Female 8 patients), 20 patients had CD4 count > 350 (Male 13, Female 7 patients).

In chest x-ray, upper lobe lesion was seen in 26 patients (5 cavity and 21 infiltration), in which CD4 count < 350 was 16 patients. Lower lobe lesion in 26 patients (4 cavity and 22 infiltrations). Pleural effusions present in 15 patients (23.4% of 64 patients).

Miliary mottling was seen in 7 patients among 64 study group, pleural effusion was seen in 15 patients.

Figure 3. Comparison of Age with CD4 Count among Study Population; P value - 0.064 (Not Significant)

Figure 4. Comparison of Gender with CD4 Count among Study P value - 0.141 (Not Significant)

Figure 5. Comparison of Mantoux with CD4 Count among Study Population; P value - 0.000 (Highly Significant)

Figure 6. Comparison of Sputum AFB with CD4 Count among Study Population; P value - 0.000 (Highly Significant)

	Upper Lobe		Lower Lobe	
X-Ray Findings	> 350	< 350	> 350	< 350
Cavity	3 (15%)	2 (4.5%)	3 (15%)	1 (2.3%)
Infiltration	5 (25%)	16 (36.4%)	6 (30%)	16 (36.4%)
None	12 (60%)	26 (59.1%)	11 (55%)	27 (61.4%)
	P = 0.291		P = 0.148	

Table 4. Comparison of X-Ray Findings with CD4 Count

In CD4 count < 350 patients' cavity was comparatively less in both upper lobes and lower lobes.

X-Ray Findings	Pleural Effusion		Miliary Mottling	
	> 350	< 350	> 350	< 350
No	15 (75%)	34 (77.3%)	20 (100%)	37 (84.1%)
Yes	5 (25%)	10 (22.7%)	0 (0%)	7 (15.9%)
	P = 0.842		P = 0.059	

Table 5. Comparison of X-Ray Findings with CD4 Count

Figure 7. Comparison of Mantoux Test with Sputum AFB among Study Population; P value - 0.021 (Significant)

Figure 8. Comparison of Symptoms with CD4 Count among Study Population; P value - 0.141 (Not Significant)

Figure 9. Comparison of Upper Lobe Findings with Symptoms among Study Population; P value - 0.539 (Not Significant)

Figure 10. Comparison of Lower Lobe Findings with Symptoms among Study Population; P value - 0.356 (Not Significant)

Figure 11. Comparison of Pleural Effusion with Symptoms Result among Study Population; P value - 0.792 (Not Significant)

Figure 12. Comparison of Results of Miliary Mottling with Symptoms among Study Population; P value - 0.556 (Not Significant)

Figure 13. Comparison of Results of Upper Lobe Findings with Sputum AFB among Study Population; P value - 0.431 (Not Significant)

Figure 14. Comparison of Results of Lower Lobe Findings with Sputum AFB among Study Population; P value - 0.938 (Not Significant)

Figure 15. Comparison of Results of Pleural Effusion with Sputum AFB among Study Population; P value - 0.443 (Not Significant)

Among 15, two pleural effusion cases had sputum positivity.

Figure 16. Comparison of Results of Miliary Mottling with Sputum AFB among Study Population; P value - 0.157 (Not Significant)

No miliary mottling was there in sputum positive patients.

Summary

- Majority of patients were in the age group 30 - 40 years (42%).
- Out of 64 people, 76.6% were males and 23.4% females.
- Most common presenting symptoms were cough (81.3), loss of weight and appetite (75%).
- Among x-ray findings unilateral upper zone infiltrative lesions were more common than lower zone infiltrations in sputum positive patients.
- Sputum positivity was seen in 20.3% of patients.
- Mean CD4 count in this study was 295.19; 313.53 in females, 289.57 in males.
- Most of the patients (68%) had CD4 counts < 350 cells/ μ L.
- 100% of miliary TB had sputum negativity, all had CD4 count < 350.
- 27 patients are Diabetic, out of that 4 patients had miliary TB, 8 patients had pleural effusion; 20 patients had CD4 count < 350. Lower lobe lesions seen in 10 patients.

- Mantoux > 5 mm were seen in 18 patients, out of which 12 patients had CD4 count > 350.
- In this study, there was highly significant correlation between Mantoux vs CD4 count and sputum AFB vs CD4 count present.
- In this study, there was significant correlation between sputum AFB vs Mantoux and miliary mottling vs CD4 count present.
- On comparing diabetes with lower lobe lesions, there was significant correlation present, p - value was 0.022.
- Among the symptoms cough had significant correlation with CD4 count, p value was 0.025.

DISCUSSION

The majority of the TB-HIV co-infection patients were in the age group 31 - 40 years (42%), which is similar to the other Indian studies, Purushotham et al (34.3%) and Padyana et al (55%).⁽³⁾ Males outnumber females in our study (76.6% vs 23.4%), whereas in the study by Padyana et al it is 55% vs 63%.⁽³⁾ occupation of the most of the patients in our study was driving, whereas it is unskilled manual labourers^(3,4) in Padyana et al and Purushotham et al. Cough was the most common symptom in our study (81.3%), whereas Dev et al and Padyana showed loss of weight and appetite as the most common, 100% and 82% respectively.⁽³⁾ The intradermal test was positive in 28% in our study, whereas Dey et al showed 52.2%.⁽⁵⁾ The chest x-ray findings in CD4 < 350 according to our study was infiltration (36.4%), Pleural effusion (22.7%), Miliary mottling (15.9%), Cavity (4.5%). In CD4 > 350, it was Infiltration (30%), Pleural effusion (25%), Cavity (15%) and Miliary mottling (0%). According to Padyana it was in CD4 < 200, infiltration (39%), consolidation (30%), cardiomegaly and cavity (11%), pleural effusion (9%) and miliary mottling (7%). In CD4 > 200, it was infiltration (37.5%), miliary mottling (25%) and cavity (25%).⁽³⁾

CONCLUSION

"Thus, a high level of clinical suspicion is required in diagnosis of TB in HIV infected, especially when they are in the later stages of disease which is indicated by CD4 counts < 350 cells/ μ L." Tuberculosis is said to be the commonest opportunistic infection in patients with HIV/AIDS. The most common symptom in these patients was cough and expectoration followed by fever and weight loss.

Hence, the diagnosis of tuberculosis must be suspected in HIV positive persons irrespective of the type, site and extent of radiological lesions.

Further, since tuberculosis could be present even in persons with a normal chest x-ray, the presence of symptoms warrants detailed investigations.

Limitations of the Study

Sample size was achieved with 10% absolute precision; hence the results of the study will have wide variability. Due to limited resources and practical constraints, this study is being carried out with a small sample size. Thus, the appropriate representation of the population and better outcomes could be attained by increasing the sample size.

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