

ORIGINAL ARTICLE

A COMPARATIVE STUDY ON SYMPTOMS AND MICROBIOLOGICAL STATUS OF TUBERCULOSIS IN HIV POSITIVE PERSONS

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ABSTRACT

Background: In HIV positive and HIV negative individual clinical symptoms of Tuberculosis (TB) varied widely. Chances of Smear negative tuberculosis are high in HIV positive cases and it is the leading cause of death of HIV patients.

Objective: To study the relationship between bacteriological status of TB cases and TB symptoms in HIV patients.

Methods: A cross-sectional analytical study was conducted during 2011 in a representative sample of 100 HIV infected persons visiting a tertiary care hospital located in western India. Laboratory investigation of Tuberculosis was done by AFB staining and culture in Ogawa medium. Data collected in structured questionnaire and laboratory profile of the patients were entered into Microsoft excel and analyzed using Epi-info.

Results: Twenty three percent prevalence of TB is observed in HIV patients. Eighty one percent of the total TB cases were smear negative cases. Significant relationship was observed between the TB symptoms and Smear positive TB cases ($p < 0.05$) but no significant relationship could be established between TB symptoms and smear negative cases ($p > 0.05$). Prevalence of *Mycobacterium avium* complex was higher than *M. tuberculosis*.

Conclusion: In HIV patients, the utility of direct microscopy of AFB stained smear is limited because most of these patients were smear negative and are asymptomatic. So, direct microscopy in combination with Culture is recommended for higher case finding of TB in HIV patients.

Key words: HIV, TB, smear negative, smear positive, culture

INTRODUCTION

Among different HIV related opportunistic infections, tuberculosis is the most common one as suggested by the fact that more than a quarter of the 42 million people infected with HIV worldwide are also co-infected with TB.¹

HIV associated TB has a marked increased mortality rate: up to 25% of patients with Sputum smear positive results and 40-50 % of those with AFB smear negative results die of TB.² As the types of TB in HIV positive patients differs from those occurring in HIV negative individual, particular features must be taken into account in the case detection, diagnosis and treatment of TB in HIV positive patients. Of importance, the bacteriological status is the key issue concerned with the management of HIV related TB. "Smear negative" and "Smear positive" are the most important bacteriological classification of pulmonary TB cases. Smear positive TB cases means those TB patients with at least two sputum specimen positive for AFB by microscopy or at least one sputum specimen positive for AFB by microscopy,

and abnormal chest radiography/Culture positive for *Mycobacterium tuberculosis*. Smear negative TB cases means those TB patients with at least 2 sputum specimen negative for AFB by microscopy and culture positive for *M.tuberculosis*.³

Directly observed treatment Short-course (DOTS) is the worldwide accepted TB control strategy which still relies on passive case finding methods. This basic approach in TB control is supposed to be insufficient to control TB in high HIV prevalence region.⁴

Cough is the most common symptom of TB and present in 95% of the smear positive cases. However, it is not a specific sign of TB since it is present in many conditions affecting the lower respiratory tract i.e. most patients with cough do not suffer from TB. Similarly, cough and smear positive TB is less common in HIV patients. Often a PTB suspected patients (i.e. PTB suspects) has one or more of the following symptoms as well as cough:

Respiratory symptoms: Shortness of breath, chest pain, haemoptysis.

Constitutional symptoms: Weight loss, loss of appetite, fever, night sweat and tiredness.³

Although microscopic examination of appropriately stained sputum specimen for tubercle bacilli is the quick and easier method it is less reliable in certain cases because it requires between 5,000–10,000 tubercle bacilli per milliliter sputum for detection of AFB. So, examination by bacteriological culture provides the definitive diagnosis of tuberculosis because as few as ten viable bacilli per milliliter sputum can be detected. Culture increases the number of TB cases often by 30-50 times and it is essential to distinguish different mycobacterial species.⁵ Atypical mycobacterial lung disease, mainly due to *Mycobacterium avium* complex, is most prevalent in HIV patients.⁶

Until now in developing countries diagnosis of smear negative Tuberculosis is rarely done due to concerns regarding the feasibility and cost. However several studies have revealed that smear negative tuberculosis constituted the significant proportion in HIV patients.³ So far, the guidelines and policies concerning the case detection of TB in HIV patients are same as that of normal population. The RNTCP program primarily relied on DOTS and quality assured microscopy.

With this back ground, this study was planned to examine the relationship between bacteriological status of TB cases and TB symptoms in HIV patients.

METHODOLOGY

This research was approved by Institutional ethical committee and carried out in a department of TB & Chest in a tertiary care centre in western India during 2011. The cross sectional study was conducted in a representative sample of 100 HIV infected persons registered to Anti Retroviral Treatment (ART) centre of the same hospital. Sampling was done by random sampling method. In this process, the name of all the HIV patients registered in the ART centre were written in sepa-

rate papers and 100 of them were selected by simple random technique without replacement. After taking informed consent, pre structured questionnaires were filled on the basis of which the patients were identified as symptomatic or asymptomatic. Those patients who self reported cough for about 2 weeks along with chest pain and other constitutional/respiratory symptoms are considered as symptomatic; otherwise asymptomatic. Every attempt was made to reduce bias during filling up of questionnaire. Two sputum specimens were collected as per WHO guidelines. As asymptomatic patients could not produce the sputum readily, they were instructed to inhale 3-5% saline mist for 15 minutes to obtain induced sputum. Diagnosis of tuberculosis by conventional methods such as direct microscopy of AFB stained smear, AFB culture and identification tests in Mycobacteriology Laboratory. In direct microscopy three sputum specimens i.e. 1st spot specimen, early morning specimen and 2nd spot specimen were collected, stained by ziehl-Neelsen staining technique and then reporting was done according to WHO positively grading system.⁷ In culture technique, early morning specimen was subjected to modified petroff's method for decontamination and then inoculated into 3% Oga-wa medium followed by incubation at 37°C for 8 weeks. In identification tests, the observation of growth rate and pigmentation, Niacin Test, Nitrate Reductase Test and Catalase Test were performed according to WHO manual, 1998.⁵ The data obtained from questionnaire and laboratory results were entered into Microsoft excel and χ^2 tests and other relevant statistical tools were applied using Epi-info software.

RESULTS

Of the 100 HIV infected persons, 66 (66%) were males and 34 (34%) were females. Majority of them were in the age group 21-30 (60%) followed by 31-40 (31%). The overall prevalence of tuberculosis (including atypical mycobacterial lung disease) was 23%. More males were co-infected than females (male:female = 17:6), and the age group of 21-30 were predominantly co-infected as shown in table 1.

Table 1 Distribution of HIV patients by TB status, age group and gender

Age group	TB positive		TB negative		Total	
	Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
11-20	0 (0.0)	0 (0.0)	1 (2.0)	1 (3.6)	1 (1.5)	1 (3.0)
21-30	12 (70.6)	3 (50.0)	25 (51.1)	20 (71.4)	37 (56.1)	23 (67.7)
31-40	3 (17.6)	3 (50.0)	20 (40.8)	5 (17.8)	23 (34.8)	8 (23.5)
41-50	1 (5.9)	0 (0.0)	2 (4.1)	2 (7.2)	3 (4.5)	2 (5.8)
51-60	1 (5.9)	0 (0.0)	1 (2.0)	0 (0.0)	2 (3.1)	0 (0.0)
Total	17 (100)	6 (100)	49 (100)	28 (100)	66 (100)	34 (100)

Among 5 smear positive cases, 4 cases (80%) presented TB symptoms (Both respiratory and constitutional) showing significant relationship between TB symptoms and smear positive tuberculosis ($\chi^2 = 4.01$, $p < 0.05$) as shown in table 2.

In contrast to this, only 38.8% (7 out of 18) smear negative TB cases presented both types of TB symptoms

and no significant relationship could be established between TB symptoms and smear negative TB ($\chi^2 = 0.82$, $p > 0.05$) as shown in table 3. Analysis of individual symptoms presented by Smear positive, smear negative and Non TB cases reveals that as high as 80% of Smear positive TB cases presented all symptoms of TB where as 38.8% to 55.5% smear negative TB cases presented

different TB symptoms. Cough, the major symptom presented by both the TB cases, is less common (only 28.5%) in Non TB cases (Table 4).

Table 2 Relationship between TB symptoms and Smear Positive TB in HIV cases

Smear positive TB	TB symptoms		
	Yes	No	Total
Yes	4	1	5
No	26	69	95
Total	30	70	100

X², P value -4.01, (p<0.05)

Table 3 Relationship between TB symptoms and Smear negative TB in HIV cases

Smear Negativity	TB symptoms		
	Yes	No	Total
Yes	7	11	18
No	23	59	82
Total	30	70	100

X², P value - 0.82, (p>0.05)

Note: Although 10 smear negative TB cases reported cough, only 7 of them reported chest pain along with cough. So, smear negative TB cases with TB symptoms (including chest pain) would be 7.

Table 4 Relationship between clinical symptoms of TB and bacteriological status of TB in HIV Positive patients

Symptoms	Smear +ve TB cases (n=5) (%)	Smear -ve TB cases (n=18) (%)	TB negative cases (n=77) (%)	Total (n=100) (%)
Fever	4 (80.0)	7 (38.8)	29 (37.6)	40 (40.0)
Cough	4 (80.0)	10 (55.5)	22 (28.5)	36 (36.0)
Chest pain/ shortness of breath	4 (80)	8 (44.4)	31 (40.2)	43 (43)
Night sweat	4 (80.0)	7 (38.8)	22 (28.5)	33 (33.0)
Weight loss	4 (80.0)	10 (55.5)	39 (50.6)	53 (53.0)

Note- Actually 7 cases are chest pain and one case is shortness of breath (but not chest pain). So if consider only those persons exhibiting cough for 2 weeks along with chest pain also, as the TB symptomatic, we should consider only seven cases as TB symptomatic. This is because we are considering those patients complaining merely shortness of breath (but not chest pain) as TB asymptomatic, whether or not they complain cough.

Although culture detected higher number of TB cases in comparison to direct microscopy of AFB stained smear, one case was detected only by direct microscopy (Table 5). Although one case was culture negative, there was no doubt in smear positive result because the morphology (shape and size) of the mycobacteria is exactly same as that of positive control AFB slide; and positivity grading result of the case was 2+.

Table 5: Comparative evaluation of direct microscopy with cultural technique for TB diagnosis in HIV Positive patients

AFB culture	AFB staining		
	AFB found	AFB not found	Total
Culture positive	4	18	22
Culture negative	1	77	78
Total	5	95	100

Inference: Direct microscopy in combination with culture is appropriate technique for TB case finding in HIV patients.

Table 6 Distribution of Mycobacterium species in HIV Positive patients

Mycobacterium Species	isolates	%
<i>M. avium</i> complex (MAC)	9	40.9
<i>M. tuberculosis</i>	6	27.3
<i>M. kansasii</i>	4	18.2
<i>M. fortuitum</i>	2	9.1
<i>M. chelonae</i>	1	4.5
Total	22*	100

*One species could not be identified because it was culture negative

Furthermore it was known that the patients were under DOTS treatment and hence dead bacilli might have been seen in direct microscopy but not in culture (which require live bacilli to produce colony). Among 22 culture positive isolates, the predominant species was *M. avium* complex (40.9%) followed by *M. tuberculosis* (27.3 %) as shown in table 6.

DISCUSSION

In this study the prevalence of tuberculosis (including atypical mycobacterial lung infection) is found to be 23% in HIV positive patients which is in concordance with WHO/UNAIDS report stating one third of HIV/AIDS patients co-infected with tuberculosis.⁸

In context to India, it was observed that during 1991-2000, 66% of AIDS cases were co-infected with TB.⁹ Comparatively Lesser prevalence in our study may be due to inclusion of both HIV as well as AIDS cases. Studies done in United Mission Hospital, Tansen showed that TB prevalence in HIV cases increased from 10.8% in 2002 to 39.5% in 2004.^{10,11} These studies shows that high variation of TB prevalence in HIV patients depending on the nature of surveillance. If sampling is done in patients visiting HIV/STI clinics/ hospital bed, the prevalence will be obviously high.

One of the important findings of this study is that HIV patients mostly suffers from smear negative tuberculosis (as high as 81.8 % of the total TB cases) and are usually asymptomatic. Other studies have also shown that the usual symptoms of TB are less common in this group of immune-compromised persons.³ So, they require bacte-

riological investigation of through culture which is found to be more than 4 times effective than direct microscopy. It has been observed that in general, culture increases the case finding rate by 30–40%.⁵ Furthermore, several comparative evaluation of different diagnostic technique for tuberculosis have concluded that case detection rate of direct microscopy is very low although it is simplest and cost effective.¹³ This study suggests that unlike the case finding strategy for general population, the TB case finding strategy for HIV patients needs to adopt different approach / policies because higher number of asymptomatic cases were found to be positive for tuberculosis.

Another important finding of this study is the documentation of alarmingly higher rate of atypical mycobacterial lung disease (mainly due to *Mycobacterium avium* complex). It was documented that as high as 50 % of HIV/AIDS patients of western countries were co-infected with *Mycobacterium avium* complex.¹² This can be justified that the HIV patients being highly immunocompromised, even these less virulent mycobacteria (which are abundantly found in environment) can cause serious lung disease. Diagnosis of smear negative tuberculosis is a difficult task. In developing countries, the majority basis of clinical and chest radiographic findings. Without a standardized clinical work up, the misdiagnosis rates have been estimated as high as 35% to 52%.¹⁴ So, it is recommended to adopt policies concerning the sputum culture, wherever possible.

CONCLUSION

This study has demonstrated that significantly higher number of asymptomatic HIV patients suffer from smear negative TB. The disease is mainly due to atypical mycobacteria which are rarely detected in direct microscopy. Hence, culture is recommended to detect higher number of TB cases in HIV patients.

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