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Research Article

RESULTS OF TUBERCULOSIS TREATMENT IN HIV INFECTED PATIENTS

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A B S T R A C T

Tuberculosis (TB) and HIV co-infections place an immense burden on health care systems and pose particular diagnostic and therapeutic challenges. Infection with HIV is the most powerful known risk factor predisposing for Mycobacterium tuberculosis infection and progression to active disease, which increases the risk of latent TB reactivation 20-fold. TB is also the most common cause of AIDS-related death. Thus, M. tuberculosis and HIV act in synergy, accelerating the decline of immunological functions and leading to subsequent death if untreated. The mechanisms behind the breakdown of the immune defense of the co-infected individual are not well known. This is study aimed to assess the outcome of TB treatment and its predictors among HIV infected patients. Medical records of 130 TB/HIV co-infected patients who attended the TB clinic were taken and data was analyzed. by Statistical Package for Social Sciences version 21. Multivariable binary logistic regression analysis was carried out to identify predictors of treatment outcome. Statistical significance was considered at p-value <0.05. The treatment outcomes of TB patients included in this study were 13(10.0%) cured, 14 (10.64%) defaulted, 18 (12.47%) died and 29 (22.04%) completed the treatment. Initial World Health Organization (WHO) clinical stage III and stage IV were associated with unfavorable outcome. Both WHO stages (III, IV) at the time of HIV diagnosis were independent predictors of poor treatment outcome. However, smear positive TB was an independent predictor of a favorable treatment outcome. This study revealed that treatment outcome of TB patients was unsatisfactory, which signals a need for improved care. Advanced WHO clinical stages were predictors of poor outcome, while smear positive TB favors good outcome.

INTRODUCTION

Tuberculosis (TB) is the only opportunistic infection, which is transmissible to the healthy immunocompetent host. HIV is the most important known risk factor that promotes progression to active TB in people with Mycobacterium tuberculosis infection. The lifetime risk of tuberculosis in immunocompetent persons is 5% to 10%, but in HIV positive patients, there is a 5% to 15% annual risk of developing active TB disease. During the past two decades, TB has become the major opportunistic infection complicating the HIV epidemic worldwide, especially in Asia and Africa. India has one of the world's highest burdens of both TB (~2.1 million cases annually) and HIV infection (2.3 million prevalent cases). While TB occurs in all socioeconomic strata and ethnic groups, prevalence rates have been clearly linked to poverty. It has been estimated that undernutrition, HIV, smoking and diabetes are all strong risk factors for TB. Maternal TB in an HIV-infected woman is a risk factor for transmission of HIV to the infant and is associated with premature delivery or low-birth weight and with higher maternal and infant mortality.

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TB treatment outcome is poor among HIV positive TB patients compared with HIV negative TB patients. There is a continuing need to routinely assess the likely reasons for poor treatment outcome among TB/HIV co-infected patients. This is particularly important in developing countries, where economic instability, low literacy level and inadequate access to health care facilities might lead to the increased incidence of poor outcome. Treatment outcome is viewed as an important indicator of TB control programs, as suggested by WHO. Previous studies, conducted in different settings, reported variable results with respect to factors associated with unfavorable outcome of TB in HIV infected patients. The previous study conducted in India revealed that CD4 count <200 cells/μL and retreated TB patients, as compared with new cases, were significantly associated with unfavorable outcome, while other sociodemographic and clinical characteristics were insignificant. Similarly, the study conducted in Northern Ethiopia showed that a CD4 count <200 cells/μL was associated with unfavorable outcome. Besides, WHO clinical stage IV and age >45 years were predictors of unfavorable outcome. The study conducted in Northwest Ethiopia reported that being bedridden and experiencing anti-TB medication side effects were associated with treatment failure. Nevertheless, the issue of outcome of TB treatment and its predictors has not

been well addressed in the study area. Thus, the purpose of this study was to evaluate the treatment outcome of TB and associated factors among TB/HIV co-infected patients.

MATERIALS AND METHODS

Study design : This is a prospective cross-sectional study.
Approval : This study received approval from college ethical committee.
Setting : Govt General & Chest Hospital, Hyderabad.
Participants : patients admitted in the Hospital.
Study period : January 2018 - June 2018

OBSERVATIONS AND RESULTS

Sociodemographic Characteristics of Patients

A total of 2190 TB adult patients' medical records at Government Chest Hospital, Hyderabad from January 2018 to June 2018 were reviewed, of which 130 were TB/HIV co-infected. The prevalence of HIV among TB patients was 10.80%. The HIV status of all TB patients was recorded. All TB/HIV co-infected patients fulfilled the inclusion criteria, hence, they were included in the final analysis. The mean age of participants was 31.36±7.8 years. The baseline sociodemographic characteristics of study participants are summarized in Table 1.

Table 1 Demographic characteristics of TB patients co-infected with HIV

Variables	Category	Frequency
	Sex	
	Male	71(55%)
	Female	59(45%)
	Age Group	
	15-29	62(48%)
	30-44	66(50.7%)
	45-59	1(1%)
	≥60	1(1%)
	Marital Status	
	Single	48(37%)
	Married	43(33%)
	Divorced	21(16%)
	Widowed	18(14%)
	Educational Status	
	Illiterate	39(30%)
	Primary	41(32%)
	Secondary	46(35%)
	College	4(3%)

Clinical Characteristics of Participants

Of the participants, 60(46%) patients were new HIV cases diagnosed with provider initiated counseling and testing at the time of anti-TB treatment initiation. The remainder was previously diagnosed HIV patients, all of whom were on ART during TB diagnosis. All nevirapine-based regimens were changed to efavirenz at the commencement of TB treatment due to drug interaction. The majority of patients had <1 year duration of HIV during TB diagnosis; with a mean duration of 1.36±1.97 years. One hundred and sixteen (89%) patients were new TB cases, while one(0.8%) case was due to the failure of previous treatment (Table 2).

Table 2 Clinical characteristics of HIV infected TB patients

Variables	N(%)
TB Case	
New	117(90%)
Relapse	10(6.5%)
Default	3(2.5%)
Smear Status	
Negative	103(79%)
Positive	27(21%)
TB Type	
SNPTB	78(60%)
SPPTB	34(26%)
EPTB	18(14%)
CD4 Counts At TB Dx	
≤350	112(86%)
350-500	15(12%)
>500	3(2%)
WHO Stage At TB Dx	
III	93(71.9%)
IV	37(28.1%)
ART Regimen During TB Treatment	
TDF/3TC/EFV	108(83%)
AZT/3TC/EFV	22(17%)
ART Regimen At TB Dx	
TDF/3TC/EFV	26(20%)
AZT/3TC/NVP	52(40%)
AZT/3TC/EFV	47(36%)
TDF/3TC/NVP	5(4%)
ART Regimen Change Due To TB Treatment	
Yes	30(23%)
No	100(77%)
Anti TB Regimen	
RHZE	116(89%)
RHZES	14(11%)
History of TB	
Yes	22(16.5%)
No	108(83.5%)
Duration Of RVI In Years	
<1	82(63%)
1-5	38(29%)
>5	10(8%)

Of HIV-infected TB patients, 18(14%) had EPTB. The type of EPTB reported were TB lymphadenitis (8 cases), TB meningitis (5 cases), and TB spondylitis (1 cases). Among 188 TB/HIV co-infected patients, 37(28.1%) were WHO stage IV and 112(86%) patients had CD4 count <350 cells/mm^3 during TB diagnosis (Table 2). The median CD4 count during TB diagnosis was 193cells/mm^3 (interquartile range of 200). One hundred and sixteen (89%) patients received a combination of the standard four anti-TB drugs (rifampicin, isoniazid, ethambutol, pyrazinamide) on intensive phase, while 14 patients received five drugs (standard four drugs plus streptomycin).

Treatment Outcome and Associated Factors

The overall treatment outcome of TB was 13(10.0%) cured, 14 (10.64%) defaulted, 18 (12.47%) died and 29 (22.04%) completed the treatment. A high proportion of patients were transferred to other health facilities. The patients who were transferred were more likely to be WHO stage III at the time of HIV diagnosis (p=0.041) than those patients with other outcome variables. In terms of other sociodemographic and clinical characteristics, there was no statistically significant difference between transferred patients and patients with other outcome types. Treatment failure was not reported among the study participants during the review period (Table 3).

Table 3 Treatment outcomes of HIV infected TB patients

Variables	TB Treatment Outcome				Total N(%)
	Cured	Defaulted	Treatment Completed	Died	
			Sex		
Male	8(6.2%)	9(7%)	13(10%)	8(6%)	38(29.2%)
Female	5(4%)	9(7%)	16(12%)	11(8%)	41(31%)
			Age Group		
15-29	4(3%)	7(5%)	10(8%)	8(6%)	29(22%)
30-44	8(6%)	8(6%)	13(10%)	4(3%)	33(25%)
45-59	0(0%)	0(0%)	3(2%)	1(1%)	4(3%)

≥60	0(0%)	0(0%)	0(0%)	1(1%)	1(1%)
Marital Status					
Single	4(3%)	3(2%)	10(8%)	8(6%)	26(19%)
Married	5(4%)	8(6%)	10(8%)	7(5%)	30(23%)
Divorced	4(3%)	4(3%)	3(2%)	3(2%)	13(10%)
Widowed	4(3%)	4(3%)	8(6%)	1(1%)	17(13%)
Educational Status					
Illiterate	7(5%)	4(3%)	8(6%)	7(5%)	26(19%)
Primary	4(3%)	7(5%)	9(7%)	4(3%)	25(18%)
Secondary	4(3%)	7(5%)	10(8%)	4(3%)	26(19%)
College	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
TB Type					
SNPTB	0(0%)	10(8%)	23(18%)	13(10%)	46(36%)
SPPTB	10(8%)	4(3%)	0(0%)	4(3%)	18(14%)
EPTB	0(0%)	0(0%)	8(6%)	4(3%)	12(6%)
TB Case					
New	13(10%)	10(8%)	23(18%)	16(12%)	62(48%)
Relapse	1(1%)	1(1%)	4(3%)	1(1%)	8(6%)
Default	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Hx Of TB Treatment					
Yes	13(10%)	13(10%)	23(18%)	16(12%)	65(50%)
No	1(1%)	4(3%)	4(3%)	1(1%)	10(8%)
CD4 Counts At TB Dx					
≤350	13(10%)	13(10%)	23(18%)	16(12%)	65(50%)
350-500	1(1%)	1(1%)	4(3%)	0(0%)	6(5%)
>500	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
WHO Stage At TB Dx					
III	10(8%)	13(10%)	23(18%)	8(6%)	54(42%)
IV	4(3%)	4(3%)	4(3%)	10(8%)	22(17%)
Anti TB Regimen					
RHZE	13(10%)	13(10%)	36(20%)	16(12%)	68(52%)
RHZES	1(1%)	4(3%)	4(3%)	4(3%)	13(10%)

DISCUSSION

HIV infection of TB patients is considered a major public health problem, particularly in resource constrained settings like India. Poor treatment outcomes in our study, including "defaulted" and "died", were higher than reported in previous studies. The overall default rate in the current study was almost comparable to 8.1% in Ethiopia and 9% in Nigeria reported among HIV infected TB patients. The difference in default rates in the study area might be due to the valuable effect of DOT, an increase in patients' awareness of infectious diseases and treatment adherence, and expansions of health institutions in the country, which can minimize dropout rate. Worldwide, the segment of TB patients who died during treatment remained more than three times higher among HIV positive TB patients than HIV negative TB patients. Despite this figure being lower in the African Region, HIV positive TB patients were still almost twice as likely to die compared with HIV negative TB patients. According to the result of our study, the mortality rate among the participants was slightly higher than global data. The high rate of mortality in this study might be partly due to improper selection of anti-TB medication in patients who had a prior history of TB treatment where a five-drug combination must be used, while in the study area among patients who were candidates for Rifampicin, Isoniazid, Ethambutol, Pyrazinamide, and streptomycin, five patients received Rifampicin, Isoniazid, Ethambutol, and Pyrazinamide instead. Previously conducted studies showed varying results with regard to mortality of TB/HIV co-infected patients, ranging from 1.8% to 29%. Mortality is different with geographical location and the year at which the studies were conducted. This variability is attributed to difference in TB care in different areas and improvement of care over the years. Patients with advanced immunosuppression, WHO stage III and IV during initial diagnosis of HIV, were linked with increased risk of unfavorable treatment outcome, consistent with the literature. Patients with advanced disease might be faced with multiple opportunistic infections and low CD4 count which directly affect TB treatment outcome. However, smear positive status was an independent predictor of successful treatment outcome which was also reported in Nigeria. Patients with smear positive results might have enough immunity to fight the infection, which enhances favorable TB treatment outcome. The major limitation of this work is the use of retrospective secondary data, which is totally restricted to whatever is documented in the TB registers. Predictor variables which might affect outcome like treatment adherence level, comorbidities, other opportunistic infections as well as behavioral and social factors, were not recorded. In addition, follow-up smear status (2nd month) was not recorded in the chart. Moreover, many patients were transferred to other health facilities where it is difficult to track what happened thereafter. As per WHO definition, those patients transferred were included under unfavorable outcome, but it does not necessarily mean that they died or failed treatment after being transferred.

CONCLUSIONS

This study revealed that treatment outcome of TB in TB/HIV co-infected patients was significantly low. Mortality and default rates were high in the study area, which signals the need to improve counseling regarding medication adherence, and health education to reduce treatment interruption. Advanced clinical WHO stage of HIV is an independent predictor of poor treatment outcome. Hence, early initiation of ART can facilitate immunologic recovery and subsequent improvement of treatment outcome

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