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A Study on HIV/TB Co-infection in and around Khammam, Telangana, India

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A B S T R A C T

A Study on HIV/TB Co-infection in and Around Khammam, Telangana Tuberculosis is the most common opportunistic infection and the major cause of death in HIV positive patients. In India, the incidence of TB is about 40% in general population and about 25-30% extra cases are due to HIV infection. To study the demographical and clinical factors associated among HIV/TB co-infected patients in and around Khammam. A cross-sectional study was conducted among 107 HIV/TB co-infected patients attending ICTC centre in the district hospital Khammam from July-November 2016. HIV/TB positive with CBNAAT, all age groups, both genders were included in the study. 107 HIV patients were found to be positive for TB by CBNAAT. Rifampicin resistance was detected in 10 patients (9.34%). 54(50.4%) were under pre-antiretroviral therapy and 46(42.9%) were under antiretroviral therapy and others were 7(6.5%). 45(42.05%) patients with HIV/TB co-infection showed CD4 count <200 cells/mm3, 32(29.9%) showed 200-349 cells/mm3, and 6(5.6%) showed 350-500 cells/mm3 and remaining showed >500 cells/mm3. Demographical characters were also considered. P value <0.05 was considered to be significant. The major determinants of HIV/TB co-infection were identified to be low CD4 counts, ART and WHO clinical stages.

Introduction

Tuberculosis is the most common opportunistic infection and the major cause of death in HIV positive patients all over the world accounting for 40% of all infections seen in individuals with HIV infection (Pape, 2004) It accounts for about 13% of deaths among HIV positive patients worldwide (Sharma *et al.*, 2004, 2005; Arora *et al.*, 1999; Gothi *et al.*, 2004; Corbett *et al.*, 2003).

In HIV/TB co-infected individual, TB and HIV potentiate one another, resulting in the accelerated deterioration of immunological functions and premature death of the individual if untreated (Getahun *et al.*, 2010). People living with HIV (PLHIV) are more prone to tuberculosis infection as the virus weakens the immune system (Dar es Salaam, Tanzania, 2006) in many ways such as disease progression to active TB, increasing the risk of reactivation of latent TB. Chances of TB infection also increase once exposed to tubercle bacilli in PLHA (Sharma *et al.*, 2005; Badri *et al.*, 2001).

Early and prompt diagnosis of infection and management of tuberculosis leads to the reduction of tuberculosis burden. However, in HIV infected individuals, diagnosis may be difficult as there is scanty sputum production,

lack of caseous necrosis resulting in less no. of bacilli in sputum, and high incidence of non-tubercular mycobacterial infection (Dewan *et al.,* 2015). As a result, there is an increase in smear negative tuberculosis and unremarkable chest radiographs leading to difficulties in reducing the tuberculosis burden (Lucas *et al.,* 1994; Jones *et al.,* 1993). Hence the sensitivity and specificity of sputum microscopy are decreased in HIV infected individuals (Dewan *et al.,* 2015). To overcome these difficulties, sputum culture and sensitivity can be used but it takes 4-8 weeks to get results and not suitable for screening. This results in the delayed initiation of treatment, increasing the risk of transmission of tuberculosis in community and also increases the spread to extra pulmonary sites in the patient (Swaminathan *et al.,* 2000).

CBNAAT, a polymerase chain reaction (PCR) based method which targets rpoB gene of mycobacterium, has been introduced recently for detection of TB and also rifampicin resistance. It is a specific, automated, cartridge-based nucleic acid amplification assay uses real-time PCR and provides results within 100minutes. It targets rpoB gene, a gene associated with rifampicin resistance, by using 3 specific primers and 5 unique molecular probes. Hence it is highly specific test for detection of TB and rifampicin resistance (Swaminathan *et al.,* 2000).

Studies showed an estimate about 9% of all TB cases in adults were prone to HIV infection worldwide and 12% of the total deaths from TB in the year 2000 was directly associated with HIV/TB co-infection (Corbett *et al.*,2003). The situation has become very serious due to increased incidence of TB by >6% per year (Corbett *et al.,* 2003).

In HIV prevalent countries, about 14-54% of HIV infected people were undiagnosed with TB prior to death whose autopsy studies have shown disseminated TB (Haileyeus Getahun *et al.,* 2007). In high burden TB countries, studies showed that several demographic and clinical factors are significantly associated with HIV/TB co-infection (do Prado *et al.,* 2014; Kibert *et al.,* 2013; Liu *et al.,* 2015).

An estimate showed that 3.1 million deaths occur annually due to HIV/TB co-infection in South-east Asia (Joint United Nations Programme on HIV/AIDS and WHO 2002. AIDS Epidemic updates 2004. UNAIDS/04.45E. Geneva: UNAIDS; 2004).

In India, the incidence of TB in general population is estimated to be around 40%; however, studies shown around 25-30% of increased incidence of TB due to HIV infection (Raviglione *et al.,* 1995, 2003).

As there is increased burden worldwide and all over India, this study is taken up to know the burden in and around Khammam. To know the socio-demographic profile along with CD4 count, Rifampicin resistance and ART status in patients with HIV/TB co-infection in our area.

Materials and Methods

A cross-sectional study was conducted among 107 HIV/TB co-infected patients attending ICTC & ART centers in the Government District General Hospital, Khammam from July-November 2016 after obtaining institutional ethical committee clearance. HIV/TB co-infected patients of both genders and all age groups and followed up in ART clinic at district hospital, Khammam were included in the study.

The socio-demographic and clinical variables were collected by reviewing participants' documents using a checklist. HIV positive with TB negative individuals, HIV negative individuals, and HIV negative with TB

positive individuals were excluded in the study.

Operational definitions used

As per the national guidelines, all HIV seropositive individuals were screened for TB routinely.

The diagnostic method used in these patients is CBNAAT which detects the tubercle bacilli along with resistance to rifampicin.

Results and Discussion

Our study comprised a total no. of 107 HIV seropositive and TB positive patients. Out of 107 individuals, 72(67.2%) were males and 35(32.7%) were females (Table 1). In one study by Dewan *et al.*, showed that 76% were males, 24% were females (Dewan *et al.*, *JIACM* 2015).

In other studies, it is observed that HIV/TB co-infection in males was 75.3% (Kamath *et al.*, 2013) and 82% (Patel *et al.*, 2011) respectively which are correlating with our study.

Our study included the individuals of age group 10-60yrs with mean age of 35years. Majority of HIV-TB coinfection is seen in 31-40years with 37(34.5%) followed by 34(31.7%) in the age group of 21-30years (Table 1). Similar observations are seen in a study which showed 76% belongs to age group of 21-40 years (Patel *et al.*, 2011) which shows that this is the age of high sexuality and reproductive age.

In other study by Sandhya *et al.*, observed that the most common age group affected was 21-40years (47.5%) than other age groups (Sawant *et al.*, 2011).

The present study showed that HIV/TB coinfection was high in married individuals (87.8%) which indicates that heterosexual transmission is common (Table 1). In one study, Bernard J Ngwoki *et al.*, (2008) observed that HIV/TB co-infection is more in married individuals (50%). Other study by Ramanchandran Kamat *et al.*, showed 56.1% of HIV/TB coinfection in married individuals (Kamath *et al.*, *Lung India* 2013).

Our study showed that HIV/TB co-infection was more among individuals who are illiterates (51.4%) followed by inidividuals with primary education (30%) and it is less in individuals with above secondary education (3.7%) (Table 1).

This high prevalence among illiterates and primarily educated individuals may be due to lack of awareness regarding modes of transmission of HIV and preventive measures. In studies, (Mohanty *et al.*, 1993 and Rajsekaran *et al.*, 2000) observed that 36.8% were manual laborers and 57.6% were farmers respectively.

Bhattacharya *et al.*, 2011 reported 22.8% were illiterates and 60.9 % were educated up to primary school.

Our study reported that Majority of HIV/TB co-infected individuals (42.1%) were having CD4 count <200cells/mm^3 and 30% of individuals were having CD4 count of 200-349 cells/mm^3 (Table 2).

Tuberculosis occurs at any stage of CD4 cell count but majority of co-infection occurs with depletion of cell count. In HIV infected individuals, there is severe immunosuppression due to low CD4 cell count and the person is susceptible to TB infection or reactivation of latent infection leading to rapid progression of disease.

Table.1 Socio-demographic profile among HIV/TB co-infected individuals

Socio-demographic characteristics	Number of patients	Percentage (%)
SEX		
Male	72	67.2
Female	35	32.7
P value	**<0.05**	
AGE IN YEARS	**NUMBER**	**PERCENTAGE (%)**
10-20	4	3.7
21-30	34	31.7
31-40	37	34.5
41-50	21	19.6
51-60	8	7.5
>60	3	2.8
MARITAL STATUS	**NUMBER**	**PERCENTAGE (%)**
Married	94	87.8
Unmarried/single	9	8.4
Widow/divorced	4	3.7
EDUCATION LEVELS	**NUMBER**	**PERCENTAGE (%)**
Illiterate	55	51.4
Primary school	32	30.0
Secondary school	16	14.9
Inter & above	4	3.7

Table.2 Distribution of CD4 count among HIV/TB co-infected individuals

CD4 COUNT (CELLS/MM$^{3)}$	NUMBER	PERCENTAGE
<200	45	42.1
200-349	32	30.0
350-500	6	5.6
>500	24	22.4

Table.3 Rifampicin susceptibility among HIV/TB co-infected indviduals

RIF SENSITIVITY	NUMBER	PERCENTAGE
Rif resistance	10	9.3
Rif sensitivity	97	90.6
P VALUE	**<0.05**	

Table.4 ART status among HIV/TB co-infected individuals

PRE-ART/ART	NUMBER	PERCENTAGE
Pre-ART	54	50.4
ART	46	42.9
Others*	7	6.5
P VALUE	**<0.05**	

***not taking treatment, transferred to native districts and does not come for follow-up.

TB in turn increases 6-7times of viral load in HIV seropositive individuals (Nissapatorn *et al.,* 2003) our data correlates with other studies which showed 65% of HIV/TB co-infected patients had CD4 cell count <349cells/mm^3 (Bernard J Ngwoki *et al.,* 2008). Some other studies observed that HIV/TB coinfections are more common in individuals with CD4 count <200cells/mm^3 than compared to HIV infection alone which shows that TB coinfection will enhance the morbidity and progression of HIV infection(Iredia *et al.,* 2011 and Vajpayee M *et al.,* AIDS Patient Care STDS 2004). In one study (Seada Mohammed *et al., Int J of Pharma Sciences and Research* 2015), observed that 82% of HIV positive patients had CD4 cell count 200-500cells/mm^3 and most of the TB infection occurred in individuals(57.8%) with CD4 cell count <200cells/mm^3. This clearly shows that TB coinfection increases in HIV positive individuals with decrease in CD4 cell count. Similar observations were done by some studies where CD4 cell counts were <200cells/mm^3 and severe immuno-suppression in HIV/TB co-infected individuals when compared to HIV infection alone (Kamath *et al.,* 2013; Belay *et al.,* 2013; Taha M Deribew *et al.,* 2011; Giri *et al.,* 2013; Maruza *et al.,* 2011). It is also important to detect MDR-TB in India where TB is endemic with a prevalence of 3% in new cases and 12-18% in old tested cases (Chauhan, 2008) the sensitivity of sputum microscopy will be less in HIV/TB co-infection but can be detected better by CBNAAT. Sensitivity and specificity of CBNAAT were reported to be 95%. In our study, we have identified Rifampicin susceptibility to detect MDR-TB by CBNAAT. Out of 107 HIV/TB co-infected patients, only 10(9.3%) were resistant to Rifampicin and remaining 97(90.6%) were sensitive to Rifampicin (Table 3). In one study, it is observed that out of 40 patients who were tested by CBNAAT 10 (25%) were resistant to Rifampicin and 9/10 were MDR-TB (R Dewan *et al.,* 2015). In one study in northern Tanzania, it is observed that there is resistance to at least one drug among 10.8% of HIV/TB co-infections (Kibiki *et al.,* 2007) which is correlating with our study. Studies (Sudha Mishra *et al.,* 2015) reported that there is 14.71% of patients were resistant to rifampicin tested by conventional methods. Thus early screening of MDR-TB is important in HIV/TB co-infected patients.

In our study, out of 107 HIV/TB co-infected individuals, 54(50.9%) were on Pre-Antiretroviral Therapy (Pre-ART) and 46(42.9%) were on Antiretroviral Therapy (ART) and the treatment status was not known in few individuals (Table 4). Among 10 individuals who were resistant to rifampicin, 8(80%) were on Pre-ART and 2(20%) were on ART which shows that with ART there is a decrease in MDR-TB. A study from Combodia shows that there is decrease in the resistance to anti-tubercular drugs from 48% in 1999 to 7.9% in 2004 with the introduction of antiretroviral therapy (Sungkanuparph *et al.,* 2007).

TB is the most common opportunistic infection in HIV infected individuals with CD4 cell count <350cells/mm^3 however it can occur at any stage of CD4 cell count. HIV/TB coinfections are more common in the age group of 21-40years affecting mainly males. Due to heterosexual transmission, married individuals are highly infected. Coinfections are commonly seen in illiterates due to lack of awareness regarding modes of transmission and prevention. In endemic areas like India, it is important to screen MDR-TB cases especially in the immunosuppressed individuals to identify early resistance and also to prevent the spread of MDR-TB.

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