HIV-TB Co-Infection among Clients Attending an Integrated Counselling & Testing Centre at Agra: Comparison with Studies in other Regions of India

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Abstract: Settings: This prospective cross-sectional hospital based study was carried out in order to determine the prevalence of HIV-TB co-infection among patients attending an ICTC of this Institute at Agra.

Methods: The socio-demographic characteristics and clinical profile of 5391 clients attending the ICTC were analyzed at the time of testing in the context of symptoms. All clients were screened for the presence of the signs and symptoms of TB disease. TB patients were referred to DOTS centre and HIV-positive patients were referred to ART centre, S.N.Medical College, Agra for further care and management.

Results: In this study, HIV prevalence among clients was found to be 24% and HIV-TB co-infection was 12%. Major symptoms among these clients, at the time of testing, were weight loss, fever, cough and chronic diarrhea. Both HIV-positivity and HIV-TB co-infection were found to be higher among males, in the age group of 21-35 years, married, illiterate and working as daily laborers.

Conclusion: Our study emphasizes the need for routine screening of clients for HIV and TB patients which, in turn, would guide the clinicians in deciding the appropriate treatment regimens in the management of HIV- TB co-infected patients.

Keywords: HIV-TB, co-infection, ICTC, Agra, India.

INTRODUCTION

In resource-limited countries, Tuberculosis (TB) and human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) contribute to the burden of infectious diseases.

As per WHO Global TB Report, 2016, an estimated 1.2 million people living with HIV worldwide fell ill with TB in 2015. TB is the leading cause of death among people living with HIV, accounting for some 390,000 people who died from HIV-associated TB in 2015. Globally people living with HIV are 19 times more likely to fall ill with TB than those without HIV. People living with HIV face the threat of drug-resistant TB. If diagnosis is delayed, there is increased risk of mortality from multidrug-resistant and extensively drug-resistant TB [1]. Co-infections of Mycobacterium tuberculosis-HIV put forth challenges of diagnosis and treatment and exert tremendous pressure on health care systems with large populations of co-infected individuals in African and Asian countries [2, 3]. M. tuberculosis and HIV, the two pathogens, accelerate the deterioration of individuals are dually infected worldwide. In developing countries, TB is the predominant cause of death in the setting of AIDS, accounting for about 26% of AIDSrelated deaths [4-7]. HIV co-infection is the risk factor for progression of *M. tuberculosis* infection to active disease and likely to increase the 20-fold risk of latent TB reactivation [8, 9]. This study was carried out to determine the prevalence of HIV-TB co-infections and correlate the socio-demographic and epidemiological factors associated with dual infection among clients attending an Integrated Counselling & Testing Centre (ICTC) at the National JALMA Institute for Leprosy & other Mycobacterial Diseases. The ICTC at this Institute caters to the needs of general and high-risk group clients (voluntary as well as referred cases) of Agra and neighboring districts (Firozabad, Mathura, Fatehpur, Dholpur, etc.) by offering HIV counseling and testing services, free of cost. This is the first report of co-infections of HIV-TB

immunological functions, potentiating one another and leading to premature death, if untreated, in the

individual host. It is estimated that about 14 million

among clients in Agra in the northern region of the country.

MATERIALS AND METHODS

The methodology of this hospital based crosssectional prospective study was based on guidelines by

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the National Framework for Joint HIV/TB Collaborative Activities, 2009 [13].

The Ethics Committee as well as the Scientific Advisory Committee (SAC) of the Institute examined the detailed plan of study and approved the assumptions for human research.

Subjects

A total of 5391 clients attended the ICTC during the study period. The socio-demographic profile were recorded using a questionnaire of the NACO (National AIDS Control Organisation). All clients coming to ICTC were screened for the presence of the signs and symptoms of TB disease. These along with the clinical assessment, radiological and bacteriological findings formed the basis of confirmation for the diagnosis of active TB disease.

Methodology

5 ml venous blood samples, were collected aseptically, after obtaining written informed consent from each of the clients. The sera samples collected after centrifugation at 2500 g were tested by 2 ERS (ELISA, Rapid and Simple assays as is the strategy of NACO (National AIDS Control

Organisation) to assess the HIV status. ELISA was done using Genedia HIV-1/2 EIA kit (Greencross, Korea). Those found positive were confirmed by 2 rapid and simple assays, namely HIV Capillus latex aggregation assay (Trinity Biotech PLC, Ireland) and/or Instachk HIV 1 + 2 (One Step Anti-HIV(1&2).

Screening for Active TB

The TB screening process was performed when the patient visited the ICTC. Screening was done on every patient visit. For the purpose of this study, however, we only describe the results of screening on the first visit. The screening for active TB followed the Revised National TB Control Programme (RNTCP) guidelines, which are based on WHO guidelines on how to identify suspected active TB amongst persons seeking care [13, 14]. For the TB screening, all clients presenting to the ICTC were asked whether they had already been diagnosed with TB and were on TB treatment. If the answer was yes, this was recorded and the patient was not asked again about TB until completion of TB treatment. If the answer was no, the patient was screened for symptoms by trained staff, based on the RNTCP guidelines. Briefly, patients with cough for ≥ 2 weeks or any suspicion of active pulmonary TB (PTB) or extra-pulmonary TB were categorised as having presumptive TB and were further investigated to confirm the disease. Two same-day sputum specimens from presumptive TB patients were collected in the ICTC and given to the DMC (Designated microscopy centre) of the Institute, for sputum smear microscopy by Ziehl-Neelsen staining. Patients with negative sputum smears or extra-pulmonary TB suspects underwent appropriate investigations such as chest radiography to confirm TB. All patient data were recorded on treatment cards and captured in an electronic database [15, 16].

Referral

As a part of routine procedure, TB patients, irrespective of their HIV status were referred to DOTS centre for TB treatment as per RNTCP guidelines.

HIV-positive patients were referred to ART (Anti-Retroviral Treatment) centre in the S.N.Medical College, Agra after post-test counseling, for further care and management.

Statistical Analysis

The demographic and clinical data were analyzed by Pearson's Chi-Squares (χ^2) test at 5% level of significance and were used to measure the association between the variables and infection rates. Normal t-test was applied to test the equality of proportion.

RESULTS

In this study, 5391 clients were screened for HIV-1/2 antibodies during a period of 3 years. Out of 5391 clients, 960 were TB patients referred from other health centres. Table **1** shows that 1331 were found to be HIV-positive, thus, prevalence of HIV infection among clients in Agra is 24.68%. Among the HIV-positive patients, 164 were having TB, thus, co-infection was found to be 12.3%. Table **2** shows the sociodemographic features of the clients, HIV-positive and

Table 1: Depicts the HIV Positivity among the Clients and HIV-TB Co-Infected Patients

| | ts screened 5391) |
|--------------|----------------------|
| HIV-Positive | 1331 (24.68%) |
| ТВ | 960 (17.80%) |
| HIV-TB | 164 (12.32%) |

| Parameters | | No. of patients screened for HIV (n = 5391) | HIV-positive patients [n = 1331(24.68%)] | Statistical analysis, χ² (df), p value | HIV-TB co-infected patients (n = 164) | Statistical analysis, χ² (df), p value | |
|-----------------------------------|---------------------|--|---|--|---|--|--|
| Gender | Male | 3664 | 934 (70.17%) | 3.9562 (1), | 119 (72.56%) | 1.6409 (1), | |
| Gender | Female | 1727 | 397 (29.82%) | p = 0.047 | 45 (27.43%) | p = 0.200 | |
| _ | 21-35 | 3994 | 1069 (80.31%) | 56.3308 (2), P = | 109 (66.46) | 5.1203 (2), p = 0.077 | |
| Age (in years) | 36-50 | 1167 | 246 (18.48%) | 0.000 | 46 (28.04) | | |
| (iii yeais) | 51-65 | 230 | 16 (1.2%) | - | 09 (5.48%) | | |
| | Married | 3202 | 913 (68.59%) | 255.0394 (2), P | 96 (58.53%) | 19.4360 (2), p = 0.000 | |
| Marital Status | Unmarried | 1722 | 214 (16.07%) | = 0.000 | 39 (23.78%) | | |
| olaido | Divorce/Widow | 467 | 204 (15.32) | - | 29(17.68) | | |
| Educational Qualificatio ns | Illiterate | 2156 | 553 (41.54%) | 89.0679 (3), P = | 63 (38.41%) | 4.9828 (3), | |
| | Primary school | 1737 | 395 (29.67%) | 0.000 | 47 (28.65%) | p = 0.173 | |
| | Secondary school | 997 | 327 (24.56%) | - | 41 (25%) | | |
| | College & above | 501 | 56 (4.21%) | - | 13 (7.92%) | | |
| | Daily wages | 1457 | 361 (27.12%) | 41.4526 (3) P = | 56 (34.14%) | 11.3088 (3), p = 0.010 | |
| | Regular Job | 523 | 101 (7.58%) | 0.000 | 24 (14.63%) | | |
| Occupation | Housewife | 1279 | 395 (29.67%) | | 31 (18.9%) | | |
| | Others | 2132 | 474 (35.61) | | 53 (32.31%) | | |

| Table 2: Depicts the Socio-Demographic Profile of HIV-Positive and HIV-TB Co-Infected Patients | Table 2: | Depicts the Socio-Demo | graphic Profile of HIV-Positive | and HIV-TB Co-Infected Patients |
|--|----------|------------------------|---------------------------------|---------------------------------|
|--|----------|------------------------|---------------------------------|---------------------------------|

HIV-TB co-infected patients. The results show that there is gender bias in clients attending the ICTC, i.e., 56% males attended the ICTC while 43.29% females came for HIV testing. Of these, 70% of the males and 29% females were HIV-positives. Among the age groups, which were divided into 21-35, 36-50 and 51-65 years, 80% of HIV positivity was observed in the age group, 21-35 years of age. The sexually active age group was a significant factor in HIV-positivity (p<0.000). 68% of married patients, 16% of unmarried and 15% were divorcee/widow/widower were HIVpositive. The observed difference in HIV-positivity among the married as well as the single patients when compared with unmarried patients is statistically significant (p<0.000). 41% of the HIV-positive patients were illiterate. 27.12% of laborers, i.e., migrant workers were HIV-positive whereas 29% housewives were HIVpositive. Literacy status and occupation had a

statistically significant (p<0.000) impact on HIVpositivity. Major symptoms among these clients, at the time of testing, were weight loss (24.56%), fever (39.81%), cough (16.07%) and chronic diarrhea (12.69%).

HIV-TB co-infection was found to be higher among males (72%), in the age group of 21-35 years (66%), married (58%), illiterate, i.e., having less than primary level of education (38%), working as daily laborers (34%) and those having no specific job. Marital status appeared to be the statistically significant (p<0.000) factor among the HIV-TB co-infected patients.

Table **3** shows the clinical profile of the HIV-TB coinfected patients. Among HIV-TB co-infected patients, 27% were having pulmonary and 72% were having extra-pulmonary TB.

| Table 3: | Shows the Type of TB among the HIV-TB Co-Infected Patients |
|----------|--|
|----------|--|

| No. of TB patients screened | Pulmonary | Extra-pulmonary |
|---|--------------|-----------------|
| (n = 960) | 343 (35.72%) | 617 (64.27%) |
| No. of HIV-TB co-infected patients (n = 164) | 45 (27.43) | 119 (72.56) |

| Author | Place of study | Year of study | No. of HIV-TB cases | No. of HIV- positive cases (%) |
|--------------------------------------|--|--|--|--|
| Agarwal <i>et al.</i> [17] | ART centre at LRS Institute of TB & Respiratory Diseases, New Delhi, | January, 2006 - June, 2007. | 251 HIV infected patients | 73 (29.1%) were diagnosed with concurrent active tuberculosis. |
| Bhattacharya <i>et al.</i> [18] | National Institute of Cholera & Enteric Diseases, Kolkata | February 2004-October 2006 | 109 HIV-seropositive individuals were screened. | 36 (33%) had HIV/TB co-infection |
| Chandrasekaran <i>et al.</i> [19] | ART center at a district hospital in southern India | July 2008 - June 2012 | 684 patients on ART as well as pre-ART | HIV-TB co-infection was diagnosed in 18.9% with higher prevalence among males (75.3%), in the sexually active age group 31-45 years (61.3%), with less than primary education (44.15%), who were married (56.1%), laborers (42.4%), from rural backgrounds (88.2%), and having low income-earning capacity (94.4%). |
| | | | | prevalence of HIV-TB co-infection recorded in this sample was 18.86%. |
| Chauhan <i>et al.</i> [20] | ICTC, Indira Gandhi Medical | 1 st Jan., 2007 - 31 st | 525 | 198 (37.7%) were HIV-seropositive, |
| | College, Shimla Himachal Pradesh | Aug.,2007 | | 17.7% of HIV-positives were suffering from PTB infection |
| Devi <i>et al.</i> [21] | Manipur | | 100 HIV positive patients and 100 HIV negative patients | TB was found in 55% of HIV infected patients compared to 25% in sero-negative patients, Combined pulmonary and extra-pulmonary form of TB were significantly more common in HIV sero-positive patients |
| Ghiya <i>et al</i> . [22] | HIV Referral Clinic at Vadodara, Gujarat | | 500 HIV positive patients | Using convenience sampling method, 246 HIV- positive patients co-infected with tuberculosis were enrolled. 246 (49.2%) were co-infected with tuberculosis. Out of 246 co-infected cases, 35(14.2%) presented with demonstrable and documented tuberculosis whereas in 211(85.8%) cases, tuberculosis was extemporaneously detected by actively screening the patients. |
| Jaiswal <i>et al.</i> [23] | District Tuberculosis Center, Jhansi, TB clinic & Tuberculosis ward of MLB Medical College, Jhansi District | Dec.2007- Dec. 2008. | | TB-HIV co-infection cases - 8.65% |
| Kamath <i>et al.</i> [25] | ART center of the Udupi district hospital in southern India | July 2008 - June 2012 May and August 2012 | 684 HIV-TB co-infected patients | The prevalence of HIV-TB co-infection was 18.86%. From this study, the profile emerged of higher prevalence of co-infection among males in the sexually active age group with little or no education, being married, working as laborers, living in the rural setting and belonging to the lower socioeconomic rung. Coinfection is associated with lower CD4 counts than those with HIV alone, which could translate into increased morbidity and progression of HIV to AIDS. |
| Naha <i>et al.</i> [26] | Kasturba Hospital, Manipal, Karnataka | January,2008 - December, 2010 | patients newly diagnosed with HIV infection & ART-naive HIV positive patients | Of 140 patients satisfying the inclusion criteria, 52 had mild tuberculosis with no other evidence of immune-suppression, 52 had tuberculosis of variable severity with associated evidence of immune-suppression, and 36 had severe tuberculosis with no other evidence of immune- suppression. |

| Table 4: Depicts a Comparison of Studies on HIV-TB Co-Infections in | India |
|---|-------|
|---|-------|

| | | | | (Table 4). Continued |
|---|--|--|--|--|
| Author | Place of study | Year of study | No. of HIV-TB cases | No. of HIV- positive cases (%) |
| Patel <i>et al.</i> [28] | OPD or hospitalized in Guru Gobindsing Hospital and Shree M. P. Shah Medical College, Jamnagar, Gujarat | 50 adult TB - HIV patients | | pulmonary TB (PTB) was seen in 20 (40%) patients, while only EPTB was seen in 5 (10%) patients (three – pleural, one – lymph node, one – CNS) |
| Rajasekaran <i>et al.</i> [29] | Govt. Hospital of Thoracic Medicine, Tambaram Sanatorium, Chennai (GHTM, Tambaram) | 2005 | 28,086 patients with HIV disease | 2,448 (56%) patients with HIV had pulmonary TB, 1,935 (44%) patients detected to have extra- pulmonary TB & disseminated TB |
| Roshana <i>et al.</i> [30] | Puducherry | 2014 | | A total of 340 cases were diagnosed as sputum positive pulmonary tuberculosis among which 7 cases (2.6 %) were sero positive for HIV antibodies. |
| Shastri <i>et al.</i> [40] | Karnataka | 2010 -2011 Apr.1, 2010 - Dec.31, 2010. | 6,480 adult co-infections | 1/3 occurred in women; 78% of patients were initiated on ART. Among the cohort 73% had pulmonary TB, and 46% reported sputum positivity for acid fast bacilli. Treatment success among co-infected patients not on ART (54%) were significantly lower compared to those already on ART (80%); death and default rates were higher in the non-ART group. Treatment success proportions (75%) for the co-infected patients were similar to those for the 51,966 patients registered under the TB program. Death rates among co-infected patients (15%) were twice as high as for TB patients under the program, though default and failure rates were lower. |
| Shrivastava <i>et al.</i> [32] | Urban Health Center located in an urban slum of Malwani, Mumbai. were referred to TB clinic for ruling out TB. | August, 2010 - January, 2011 | HIV-positive & HIV- negative | Out of the 305 patients referred from ICTC to TB clinic, 61 (20%) were diagnosed with TB. Out of 264 TB patients referred from TB clinic to ICTC, 27 (10.2%) were diagnosed as seropositive. TB- HIV co-infection was present in 27(10%) of subjects. Out of the 33 extra-pulmonary TB (EPTB) cases, majority were 25(76%) TB lymph node followed by 4(12%) of bone TB and 4(12%) of central nervous system TB. |
| Singh <i>et al.</i> [33] | ART centre at Khagaria district in Bihar | April' 2014 - March' 2015 | 194 patients of HIV screened for TB | 25 cases (12.9%) were co infected with pulmonary tuberculosis. |
| Vajpayee <i>et al.</i> [34] | New Delhi | 2003 | 421 subjects with HIV infection studied, | 105 (24.9%) were positive for TB (HIV+TB+). A statistically significant difference (p = 0.0001) was found in the median CD4+ counts between the HIV+TB- (297.5 per microliter) and HIV+TB+ (181 per microliter) groups. TB was found to be the indicator disease for HIV infection in 36 (34.2%). |
| Vijay <i>et al.</i> [35] | South India | June, 2007 - March, 2008 | All TB patients | 468 (8.8%) of all registered TB patients were HIV-infected; 177 (37%) were documented to have also |
| Present study, Hussain <i>et al.</i> | Agra | 2008 - 2010 | 5391 clients | received any ART. 1331 (24%) were HIV- positive. Among the HIV- positive patients, 164 (12%) were having TB. |

DISCUSSION

In this study, HIV prevalence among clients attending the ICTC was found to be 24% and HIV-TB co-infection was 12%. Major symptoms among these clients, at the time of testing, were weight loss, fever, cough and chronic diarrhea. Both HIV-positivity and HIV-TB co-infection were found to be higher among males, in the age group of 21-35 years, married, illiterate, working as daily laborers and those having no specific job. A low prevalence of HIV-TB co-infection is associated with active surveillance in the region.

It is imperative that physicians treating HIV-infected patients should aggressively identify those with *M. tuberculosis* in order to reduce the associated comorbidity resulting from dual infections. Table **4** depicts the studies on HIV-TB co-infections reported from other regions of the country by many authors. These periodic studies indicated that the rates of HIV-TB co-infections vary in different regions of India [17- 34] with the rates of prevalence ranging from 0.5% to 20%.

Around the world, attempts are being made to improve collaboration between HIV and TΒ programmes. With the emergence of TB as a lethal counterpart in the epidemiology of HIV, there is an urgent need to understand possible multi-factorial associations to this partnership. This study attempted to determine the underlying correlates of HIV-TB coinfection. In the HIV-infected persons, low CD4 cells suppressed immunity and indicate increased susceptibility to new TB infection, reactivation of latent infection and rapid deterioration of condition. TB contributed to a six-fold to seven-fold increase of viral load in HIV positive population [35, 36]. TB is unique in that it can occur over a wide range of CD4 counts, although it is more frequent at CD4 counts < 300 cryptococcal cells/µl unlike meningitis or toxoplasmosis, which occur at very low CD4 counts [37, 38]. Therefore, all HIV-infected individuals need to be tested for TB before the initiation of ART in TB endemic countries like India. Other tests like sputum cultures and chest X-ray, if done, for all will lead to early detection. treatment and reduction of transmission of disease.

are Anti-tuberculosis and anti-retroviral drugs required to be administered concurrently in the treatment of HIV-TB co-infected patients. There are drug many challenges namely. interactions. toxic effects, overlapping pill burden, patient compliance and immune reconstitution inflammatory syndrome (IRIS) [39, 40].

CONCLUSION

HIV-TB co-infections are a public health concern. Our study emphasizes the need for routine screening of clients for HIV and TB patients which, in turn, would be helpful to the Clinicians for opting the appropriate treatment regimens in the management of co-infected patients.

Good co-ordination and communication between the two programmes, RNTCP and NACP, is the mainstay for bi-directional screening of HIV-infected persons for TB and TB patients for HIV infection. Linkage to ART (anti-retroviral treatment) centre is urgently needed to prevent mortality of co-infected patients. Physicians should be trained about the peculiarities in management of these patients effectively. The Three I's for HIV/TB (Intensified case finding for TB, Isoniazid preventive therapy (IPT), and Infection control) will reduce the burden of TB among people living with HIV and therefore, needs to be implemented by all health facilities offering HIV care services. HIV prevention programs and cost-effective treatment regimens are urgently required for HIVpositive TB patients in all regions of the country in order to reduce morbidities and mortalities.

LIMITATIONS

The findings of hospital-based analysis of the HIV-TB co-infected patients in this study might not be generalizable.

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This research did not receive any specific grant from funding agencies in the public, commercial, or notfor-profit sectors.

CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

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