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HIV-TB co-infection among ICTC attendees in a tertiary care teaching hospital Hyderabad

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Abstract
Background: The emergence of Human immunodeficiency virus (HIV) and Tuberculosis (TB) co-infection created a serious threat worldwide. In recent scenario multidrug resistant TB have become more prevalent. Therefore HIV and TB co-infection is major health problem globally, mostly in developing countries like India. Materials and Methods: This cross-sectional study was conducted in ICTC centre of Malla Reddy Hospital, Hyderabad. A total of 2,500 individuals attended ICTC were included in this study. HIV status was confirmed as per NACO guidelines and TB diagnosis as per RNTCP guidelines. Results: Over all TB was reported 45% of HIV infected patients as compared to 33% in seronegative patients, which was statistically significant. The prevalence rate of pulmonary TB was higher in HIV reactive individuals. Conclusion- An optimum strategy be devised to monitor and act on the issue of HIV-TB co-infection so as to facilitate early diagnosis, treatment and prevention of this co-infection. Such a strategy will not only allow for a reduction of the total tuberculosis load in the community, but will also positively impact the lives of PLHA (People Living with HIV/AIDS) both qualitatively and quantitatively.

Keywords: Human immunodeficiency virus (HIV), Mycobacterium tuberculosis, HIV and TB co-infection.

Introduction
Tuberculosis has ravaged the human population since time immemorial. While the prevalence of the condition peaked between the 1600s and 1800s, a steady decrease in rates was observed from thereon kindling hope that one day; tuberculosis would be a chronic manageable condition. The advent of anti-tubercular therapy after the 1950s reinforced this belief in public health authorities. However the emergence of HIV as the causative agent of AIDS (Acquired Immunodeficiency Syndrome) in 1983 resulted in new challenges as the condition renders individuals susceptible to almost any kind of infection with tuberculosis being no exception. Tuberculosis is caused by the bacterium, *Mycobacterium tuberculosis* which has a predilection for the upper lobes of the lungs though any part of the lung may be affected. While estimates vary, it is estimated that around 20% of all cases of tuberculosis globally are extra pulmonary. The problem is intensified in HIV infected individuals as the classic signs and symptoms of tuberculosis may not always show resulting in the diagnosis being easily missed. According to WHO reports, tuberculosis is estimated to be the leading cause of HIV/AIDS related deaths globally, with 1.1 million cases of HIV-associated tuberculosis and 360,000 deaths in 2013 [1]. As far as India is concerned, 2.5 million people are currently infected with HIV, of whom 40% are also co-infected with tuberculosis [2, 3]. The problem is further exemplified by the fact that the risk of developing tuberculosis in HIV infected patients in India is 6.9/100 person years as compared to 10% lifetime risk of developing tuberculosis in HIV negative persons [4]. Associated with this risk, comes the suppressed response of the immune system to the tubercular bacilli rendering routine diagnostic procedures susceptible to variable results. The easy susceptibility of individuals coupled with the highly progressive nature of the condition allows for easy dissemination of the bacilli resulting in involvement of several systems and not just the lungs. Due to this alarming situation the World Health Organisation (WHO) declared tuberculosis a global emergency in 1993 and the Government of India has launched a Revised National Tuberculosis Control Programme (RNTCP) with directly observed therapy, short course (DOTS) as a solution for its control [5]. In India, the RNTCP has been the flagship program for control of tuberculosis by means of early detection, diagnosis and initiation of anti-tubercular therapy through designated DOTS centres throughout the country.

Despite the availability of effective anti-tubercular and anti-retroviral drugs, the HIV-TB co-infection poses a myriad of new problems ranging from variable efficacy of treatment to rapidly evolving drug resistance patterns. This is made more complex by the unavailability of high quality antiretroviral drugs in several parts of India and several systemic side effects which leads to improper adherence to the drug regimen by the patient. This leads to treatment failure and routine switchovers to different anti-retroviral regimens essentially paving the way for multiple drug resistant strains of HIV. The presence of concomitant MDR-TB (Multi Drug Resistant Tuberculosis) or XDR-TB (Extensively Drug Resistant Tuberculosis) further compounds this dilemma. While the early recognition and treatment of tuberculosis is of direct consequence with regards to the overall prognosis, the benefits of timely initiation of anti-tubercular prophylaxis also must not be overlooked. Such a formulated action plan is of immense relevance in certain areas with a high prevalence of tuberculosis wherein the availability of anti-retroviral drugs is limited.

Materials and methods

This cross-sectional study was conducted in the ICTC (Integrated Counselling and Testing Centre) of the department of microbiology of a tertiary care facility in Hyderabad, Telangana from February 2018 to February 2019. All manner of patients who attended the ICTC during this time frame were included in this study which amounted to 2,500 patients (N= 2,500). The institute's ethical committee provided the ethical approval after a review by its board members. With respect to the study, free and informed consent was obtained from all the patients and the confidentiality of information was upheld in accordance with the principles embodied in the declaration of Helsinki and the international guidelines for ethical review of epidemiological studies. A structured questionnaire was given to the patients as part of the study. The intention of this questionnaire was to obtain a thorough history of each and every case with regards to the socio-demographic variables, history of the present illness, any history of past illness and any relevant family history if present. After a complete history taking, each candidate was subjected to a head to toe physical examination for signs of any underlying infections with special emphasis on lymphadenopathy. This was followed by testing of serum specimens for the presence of HIV infection by means of CLIA (Chemiluminescence Immunoassay). Irrespective of the serological status, both seropositive and seronegative patients were referred to the DOTS centre within the same institute for the screening of tuberculosis as per the RNTCP guidelines. Sputum smear negative patients were further examined by means of a chest X-ray PA view. Suspected cases of extrapulmonary tuberculosis were analysed by Fine Needle Aspiration Cytology (FNAC) of enlarged lymph nodes, pleural fluid analysis, ascitic fluid analysis and abdominal ultrasonography in addition to microbiological screening modalities to localise the involved area in extrapulmonary tuberculosis. Data analysis: The data was compiled and subjected to analysis by the SPSS software version 20.0.

Results

Out of a total of 2,500 study subjects, 278 participants (11.12%) were seropositive whereas the remaining 2,222 participants (88.88%) were seronegative. Among the 278 seropositive cases, 156 of them were males (56.11%) and 122 were females (43.88%). The age distribution of the seropositive cases was highest in the age group between 31 to 40 years of age with 202 cases (72.66%). Most of the subjects had an educational qualification of primary education with 127 falling under this category (45.68%). The vast majority of seropositive individuals were married, 242 (87.05%). Occupation wise the majority of seropositive subjects were housewives, 96 (34.53%), closely followed by drivers, 85 (30.57%) (Table 1). Cough > 3 weeks was the most common presenting symptom of pulmonary tuberculosis in both seropositive, 124 (44.60%) and seronegative 789 (35.50%) subjects. Fever > 3 weeks was the next most common presenting symptom with 108 (38.84%) seropositive patients and 663 (29.83%) seronegative patients. Weight loss > 10 % of body weight was observed more frequently in the seropositive clients, 14 (5.03%) than the seronegative clients, 7 (0.31%). Haemoptysis as a presenting symptom was observed in 20 (7.19%) seropositive clients but only in 13 (0.58%) of the seronegative clients. Sputum smear examination yielded positive results in only (11.51%) of the seropositive cases and 254 (11.43%) of the seronegative cases. Chest radiographs revealed pulmonary changes such as infiltrates, hilar lymphadenopathy and pleural thickening in 61 (21.94%) of the seropositive cases and in 302 (13.59%) of the seronegative cases. The most common presenting symptom of extra-pulmonary tuberculosis was painless lymphadenopathy accounting for 46 (16.54%) cases among the seropositive group and 113 (5.08%) in the seronegative group. These enlarged lymph nodes were subjected to further analysis by FNAC and staining of the aspirate by haemotoxylin and eosin staining and Ziehl-Neelsen staining for detection of tubercle bacilli. Meningeal involvement was the next most common with 6 (2.15%) seropositive cases and 21 (0.94%) seronegative cases. Pleural fluid analysis revealed 5 (1.79%) seropositive and 24 (1.08%) seronegative cases to possess pleural involvement. Ascitic fluid analysis and ultrasonography of the abdomen and pelvis revealed lesions suggestive of abdominal tuberculosis in 3 (1.07%) seropositive cases and in 19 (0.85%) seronegative cases. Among these, abdominal lymphadenopathy was the most common finding in patients presenting with abdominal pain, fever and occasional diarrhoea (Table 2). The number of seropositives with pulmonary tuberculosis was higher, 66 (23.74%) than the number of seronegatives with pulmonary tuberculosis, 402 (18.09%). Similarly the number of seropositives with extra pulmonary tuberculosis was higher, 59 (21.22%) than the number of seronegatives with extra pulmonary tuberculosis, 336 (15.12%) (Table 3).

Table 1: Socio-demographic profile of the study population

Characteristics	HIV positive (n=278) with P value	HIV negative (n=2,222) with P value
Male	156(56.11%) (0.001)	1,198(53.91%) (0.002)
Female	122(43.88%) (0.004)	1,024(46.08%) (0.005)
Age: 15-20 years	4(1.43%) (1.2)	280(12.60%) (0.065)
Age: 21-30 years	64(23.02%) (1.14)	986(44.37%) (0.005)
Age: 31-40 years	202(72.66%) (0.001)	517(23.26%) (0.09)

Age: 41-50 years	8(2.87%) (1.03)	439(19.75%) (0.9)
Literacy level		
Illiterate	55(19.78%) (1.3)	414(18.63%) (1.243)
Primary	127(45.68%) (0.005)	647(29.11%) (1.132)
Matriculation	74(26.61%) (0.075)	499(22.45%) (1.254)
Secondary	18(6.47%) (0.9)	408(18.3%) (1.143)
Graduate and above	9(3.23%) (1.5)	254(11.43%) (1.67)
Marital status		
Married	242(87.05%) (0.003)	1,857(83.57%) (0.002)
Unmarried	34(12.23%) (1.4)	359(16.15%) (1.21)
Divorced	2(0.71%) (1.8)	6(0.27%) (1.954)
Occupation		
Professional	15(5.39%) (1.265)	159(7.15%) (1.87)
Driver	85(30.57%) (0.97)	476(21.4%) (1.325)
Housewife	96(34.53%) (0.65)	648(29.16%) (0.974)
Student	4(1.43%) (1.6)	227(10.21%) (1.346)
Other (labourer etc.)	78(28.05%) (0.8)	712(32.04%) (0.875)

Table 2: Frequency of symptoms and signs of pulmonary and extra pulmonary tuberculosis in seropositive and seronegative patients.

Pulmonary tuberculosis	HIV +ve with P value	HIV –ve with P value
Fever>3 weeks	108 (38.84%) (0.002)	663 (29.83%) (0.06)
Cough>3 weeks	124 (44.60%) (0.001)	789 (35.50%) (0.004)
Weight loss> 10%	14 (5.03%) (0.056)	7 (0.31%) (1.034)
Haemoptysis	20 (7.19%) (0.1)	13 (0.58%) (1.324)
Sputum smear positive	32 (11.51%) (0.09)	254 (11.43%) (1.437)
Sputum smear negative	246 (88.48%) (0.002)	1968 (88.56%) (0.003)
Chest X-ray findings	61 (21.94%) (0.06)	302 (13.59%) (1.354)
Extra-pulmonary tuberculosis		
Lymphadenopathy	46 (16.54%) (0.64)	113 (5.08%) (1.463)
Pleural tuberculosis	5 (1.79%) (1.00)	24 (1.08%) (1.4)
Abdominal tuberculosis	3 (1.07%) (0.9)	19 (0.85%) (1.6)
Meningeal tuberculosis	6 (2.15%) (0.8)	21 (0.94%) (1.8)

Table 3: Breakdown of pulmonary and extra pulmonary tuberculosis among the patients.

Nature of tuberculosis	HIV +ve with P value	HIV –ve with P value
Pulmonary	66 (23.74%) (0.003)	402 (18.09%) (0.08)
Extra-pulmonary	59 (21.22%) (0.004)	336 (15.12%) (0.09)

Discussion

In our study 278 participants out of 2,500 were seropositive for HIV. Among these, 156 of them were males (56.11%) and 122 were females (43.88%). This is lesser than the prevalence reported by Anshu *et al.* where they reported a prevalence of 63.20% in males and 36.4% in females [6]. The highest prevalence of HIV was noted in the age group between 31-40 years with 202 cases (72.66%) followed by those between 21-30 years, 64 (23.02%). These findings are higher than those of Shukla *et al.* where they reported a prevalence of 81.45% in patients between 20-45 years old [7]. Most of the seropositive subjects had a primary qualification, 127 (45.68%). These findings are higher than those reported by Singh *et al.* where 36.0% of the study subjects had a primary qualification [8]. Among the seropositive patients, the majority of those found infected were housewives (34.53%) followed by drivers (30.57%) and daily wage labourers (28.05%). This data correlates strongly with the findings drawn by Chauhan *et al.* [9]. The high association between HIV infection and housewives has also been reported by Padyana *et al.* who also noted the high prevalence among labourers and drivers as well [10]. The prevalence of seropositive cases with pulmonary tuberculosis, 66 (23.74%) predominated over that of the seronegative cases with pulmonary tuberculosis, 402 (18.09%). These findings are much lower than those reported by Kamath *et al.* where they reported a prevalence as high as 58.8% in the seropositive populace [11]. Shilpa *et al.* also reported a high number of seropositive cases co-infected with pulmonary tuberculosis (54%) [12]. the rate of extrapulmonary tuberculosis was much higher (21.22%) in the seropositive population than the seronegative one (15.12%). This finding is similar to what was reported by Devi *et al.* where they reported a 21.82% of seropositive cases having extra pulmonary tuberculosis [13]. Other studies reported higher findings with as many as 38.46% and 45.6% seropositive cases presenting with extra pulmonary involvement [14, 15]. Of the various presentations, the most commonly observed extrapulmonary presentation in our study among the seropositive cases was lymphadenopathy with 16.54%. Other studies have also reported similar findings with rates of 17.69% and 11.9% respectively [14, 15]. However Shilpa *et al.* reported TB spleen to be the most commonly observed extra pulmonary manifestation with 41% of seropositive individuals presenting with it followed by lymph node enlargement (39%), pleural effusion (12%) and meningitis (8%) [12]. Pleural involvement was reported only in 1.79% of all seropositive cases. This finding is much less than that reported by Mariam *et al.* where they reported a 50% involvement of pleura in patients co-infected with HIV. While 27% of the subjects were reported to have lymphadenitis, this was still higher than the number reported by us [16]. Other studies have also reported higher number of cases with pleural involvement with 13.85% and 9.5% respectively [14, 15]. Tuberculous meningitis was noted in 2.15% of seropositive cases. This is much lesser than the number reported by Ajay *et al.* who reported 33.84% of seropositive cases to be suffering from tuberculous meningitis [17]. Similarly they also

reported a much higher prevalence of abdominal tuberculosis (26.15%) in seropositive subjects [17]. Abdominal tuberculosis was observed only in 1.07% of seropositive subjects in our study. In the present study, the most commonly reported findings were cough lasting more than 3 weeks and fever lasting more than 3 weeks in both the seronegative and seropositive cases. These findings were consistent with the reports of Nunn *et al.* and Putong *et al.* where they reported fever and cough to be the most common presenting features in both seropositive and seronegative individuals co-infected with tuberculosis [18, 19]. However weight loss was not a very common finding in our study whereas it was regularly observed in the findings reported by Nunn *et al.* and Putong *et al.* [18, 19]. In our study, the most common presentation of pulmonary tuberculosis in both seropositive and seronegative individuals was cough more than 3 weeks (44.60% and 35.50%) though the prevalence was higher in the seropositive individuals. This was followed by fever more than 3 weeks (38.84%) as the next most common presentation among the seropositive cases. These findings were much lesser as compared to those reported by Zuber *et al.* where cough was present in 83.07% of the seropositive cases and 89.23% of them presented with fever as the most common symptom [14]. A different author has reported weight loss to be the most common presenting feature, being present in 93.5% of all seropositive cases followed by fever (87.1%), cough (74.2%) and anorexia (54.8%) [20]. This is not consistent with our finding of weight loss being reported in only 5.03% of all seropositive cases. Cough was reported to be the most common presenting symptom, present in 94% of all seropositive cases, followed by fever (86%) and weight loss (78%) by Anand *et al.* [21]. These findings correlated with our findings of cough and fever being the two most common presenting features in HIV-TB co-infection but they were much higher than our observed values. Another study by Soumya *et al.* also reported cough as the most common presenting feature with 97% of all seropositive cases presenting with it. However they also reported weight loss (94%) being more common of a presenting symptom than fever (79%) [22]. Our reported findings were much lesser than these but they still correlate well with the fact that cough was the most common presenting clinical feature in HIV-TB co-infected subjects. Sputum smear positivity was only 11.51% in seropositive subjects which is much lesser than the smear positivity rate reported by another author wherein it was as high as 25.6% [21]. The conclusion that must be drawn from the above study is that the presence of HIV-TB co-infection is a major public health challenge in the state of Telangana. This is rendered worse by the two pronged nature of the condition wherein one pathogen amplifies the effects of the other perpetrating a vicious cycle of prolonged deterioration. While the situation is far from completely under control, the increased availability of various anti-tubercular and anti-retroviral medications, dedicated health programs, exclusive diagnosing and counselling centres have allowed a greater proportion of the affected populace to reach out and seek these services to better their chances at survival. Collaboration between the ICTC, DOTS and associated microbiologists and physicians is essential to form a tight knit network of outreach, early suspicion, detection, diagnosis and initiation of treatment for this condition.

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