SHORT REPORT

Diabetes mellitus and HIV as co-morbidities in tuberculosis patients of rural south India

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KEYWORDS
Tuberculosis; HIV; Diabetes mellitus; Occupation

Summary
Objectives: Incidence of tuberculosis (TB) is greatest among patients with impaired immunity. India is experiencing a double epidemic of HIV and diabetes mellitus (DM), both of which are strongly associated with immuno-suppression. This study aimed to discover the prevalence of HIV and DM in both the pulmonary and extra-pulmonary TB patients of rural south India, retrospectively.

Methods: Medical records of 192 microbiologically diagnosed pulmonary TB and 37 extra-pulmonary TB patients were thoroughly studied and data were extracted. The frequency distribution of HIV and DM was evaluated along with other demographic details such as age, sex and occupation in both groups.

Results: The mean age of the pulmonary TB patients was 41.11 ± 15.7 years, with significantly higher (p < 0.0001) preponderance of DM (31.8%) over HIV (8.9%). 72.13% of the diabetic patients belonged to the age group of 41—60 years. Extra-pulmonary TB patients had a mean age of 34.62 ± 12.9 years with a significantly higher (p < 0.006) HIV prevalence of 32.43% over DM (5.4%). 75% of the HIV patients belonged to the age group of 41—60 years. Occupationally, the majority of the pulmonary TB patients were agricultural labourers (25.2%) while the majority of the extra-pulmonary TB patients were housewives or self employed (18.92%).

Conclusion: Though more importance is being given to HIV-TB coinfection, we cannot overlook DM, which showed a significantly higher prevalence in pulmonary TB patients compared to HIV. The rising prevalence of DM in high TB burden countries may adversely affect TB control.

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Introduction

In India, despite control strategies, tuberculosis (TB) still remains a major public health problem. One third of the world population is currently infected with TB and 1.8 million new cases of TB arise annually in India alone [1,2]. India, home for around 2.5 million HIV/AIDS patients [3] is among the 15 countries with the highest rate of HIV/TB co-infection [4]. It is believed that the HIV epidemic has paved the way for a resurgence of TB. Though HIV is considered to be the most powerful risk factor for the development of TB, we cannot ignore diabetes mellitus (DM), which has recently been linked with TB. DM has reached epidemic proportions globally as well as in India and is projected to rise in the future [5]. As with HIV, there is an immuno-suppression in diabetes also due to impaired phagocytosis and cellular immunity [6]. Several retrospective and prospective studies have associated DM with an increased risk for active TB [7–12]. While DM has been mostly associated with pulmonary TB, extra-pulmonary TB has been mostly indicated in HIV infection [4,7,13–15].

This study aimed to discover the prevalence of HIV and DM in both pulmonary and extra-pulmonary TB patients of south India, retrospectively.

Study population and methods

In a span of 2 years (2005–2006), 192 microbiologically diagnosed pulmonary TB patients and 37 extra-pulmonary TB patients attending Kasurba Hospital, Manipal, a tertiary care hospital in coastal Karnataka, south India were identified. Pulmonary TB patients were identified based on sputum smear microscopy and/or culture, while extra-pulmonary TB patients were identified based on smear microscopy and/or culture or polymerase chain reaction. The medical records of these patients were thoroughly studied and a study of relevant data were extracted. In both pulmonary TB and extra-pulmonary TB patients the frequency distribution of HIV and DM along with other demographic details like age, sex and occupation were evaluated. The patients were categorized into six age groups including <20 years, 21–30 years, 31–40 years, 41–50 years, 51–60 years and >60 years and occupationally into agricultural labourers, non-agricultural labourers, skilled professionals, housewives, students, self-employed, non-workers and semi-skilled workers. Statistical analysis was carried out using Chi-square test and Fisher’s exact test using GraphPad statistical software (http://www.graphpad.com/quickcalcs/contingency2.cfm).

Results

In the pulmonary TB group (n=192), there was a male predominance with a male to female (M:F) ratio of 3.6:1. The mean age of the pulmonary TB patients was 41.11 ± 15.7 years, with the highest prevalence of 25% in the age group of 21–30 years (n=48), significantly more compared to <20 years (n=15) (χ² = 19.4; p < 0.0001), >60 years (n=22) (χ² = 10.9; p = 0.001) and 31–40 years (n=31) (χ² = 4.08; p = 0.04). Preponderance of DM (n = 61; 31.8%) was observed over HIV (n = 17; 8.9%) (p < 0.0001), while 59.4% (n=114) presented with no DM or HIV. 72.13% of the DM patients were in the age range of 41–60 years which was significantly higher compared to other age groups. All of the HIV patients were in the age range of 21–60 years, without any significant difference among the age groups. Refer to Table 1.

In the extra-pulmonary TB group (n=37), the mean age of the patients was 34.62 ± 12.92 with 59.5% (n=22) of the patients belonging to the age group of 21–40 years, and a male predominance of (M:F) 3:1:1. In the extra-pulmonary cases HIV (n = 12; 32.43%) was more prevalent than DM (n = 2; 5.4%) (p < 0.006). 66.7% (n = 8) of the HIV patients were in the age group of 31–40 years and 25% (n = 3) were in the age group of 41–50 years. There were two diabetic patients belonging to the age group of 41–50 years and 51–60 years each, among which one of the patients had both DM and HIV as co-morbidity. 64.86% (n = 24) did not suffer from DM or HIV. Depicted in Table 1.

Disseminated TB (n = 11; 29.7%) was observed to be the most common form of extra-pulmonary TN, followed by spinal (n = 6; 16.2%), lymph node (n = 5; 13.5%), meningitis (n = 2; 5.4%), genito-urinary (n = 2; 5.4%), miliiary (n = 2; 5.4%) and others (n = 6; 16.2%) comprising of cold abscess, arthritis, shoulder joint, endometrial, empyema and pericarditis. Among the HIV patients, disseminated TB (n = 6; 54.5%) was found to be the most common form.

Among the pulmonary TB patients, the majority belonged to the occupational group of agricultural labourers (25.2%), followed by skilled professionals (14.1%), housewives (12.5%), non-agricultural labourers (11.9%), students (11.5%), semi-skilled workers (9.9%), non-workers (8.33%) and the self-employed (6.25%). The prevalence of extra-
Table 1  
Frequency distribution of HIV and diabetes mellitus in tuberculosis patients along with age, sex and occupational distribution.

<table>
<thead>
<tr>
<th>Age groups</th>
<th>PTB</th>
<th></th>
<th></th>
<th>EPTB</th>
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<tr>
<td></td>
<td>DM</td>
<td>HIV</td>
<td>M:F</td>
<td>Total</td>
<td>DM</td>
<td>HIV</td>
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<tr>
<td>&lt;20 years</td>
<td>1</td>
<td>0</td>
<td>9/6</td>
<td>15</td>
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<td>0</td>
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<tr>
<td>21—30 years</td>
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<td>4</td>
<td>34/14</td>
<td>48</td>
<td>0</td>
<td>1</td>
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<tr>
<td>31—40 years</td>
<td>6</td>
<td>5</td>
<td>24/7</td>
<td>31</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>41—50 years</td>
<td>22</td>
<td>6</td>
<td>34/8</td>
<td>42</td>
<td>1</td>
<td>3a</td>
</tr>
<tr>
<td>51—60 years</td>
<td>22</td>
<td>2</td>
<td>32/2</td>
<td>34</td>
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<td>0</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>10</td>
<td>0</td>
<td>17/5</td>
<td>22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>17</td>
<td>150/42</td>
<td>192</td>
<td>2</td>
<td>12</td>
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</table>

<table>
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<tr>
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<th></th>
<th></th>
<th>EPTB</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DM</td>
<td>HIV</td>
<td>M:F</td>
<td>Total</td>
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<td>HIV</td>
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<tr>
<td>Agricultural labourers</td>
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<td>49/0</td>
<td>49</td>
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<td>1</td>
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<tr>
<td>Non-agricultural labourers</td>
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<td>23/0</td>
<td>23</td>
<td>1a</td>
<td>3a</td>
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<tr>
<td>Skilled professionals</td>
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<td>3</td>
<td>23/4</td>
<td>27</td>
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<td>0</td>
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<tr>
<td>Housewives</td>
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<td>1</td>
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<tr>
<td>Students</td>
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<td>0</td>
<td>12/10</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Self-employed</td>
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<td>2</td>
<td>0/12</td>
<td>12</td>
<td>1</td>
<td>3</td>
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<tr>
<td>Non-workers</td>
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<td>2</td>
<td>14/2</td>
<td>16</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Semi-skilled workers</td>
<td>7</td>
<td>4</td>
<td>17/2</td>
<td>19</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>17</td>
<td>192</td>
<td>2</td>
<td>12</td>
<td>28/9</td>
</tr>
</tbody>
</table>

* One of the non-agricultural labourers in the age group of 41—50 years having extra-pulmonary TB had both DM and HIV as comorbidity.
pulmonary TB was observed more frequently among housewives and the self employed (18.9%) followed by skilled professionals (16.2%), non-workers (13.5%), non-agricultural labourers (10.8%), semi-skilled workers (8.1%) and the least in agricultural labourers (5.4%) are shown in Table 1.

DM was observed more than HIV in all the occupational groups of pulmonary TB, while the reverse was observed in the cases of extra-pulmonary TB.

Discussions

Incidence of TB is greatest among patients with impaired immunity. India is experiencing a double epidemic of DM and HIV, both of which are strongly associated with immuno-suppression. Though HIV/TB co-infection is a known problem and HIV is considered to be the most important risk factor in the progression of TB infection to disease, DM cannot be ignored as various earlier studies have associated DM with development of TB disease [5,7–12]. This study has retrospectively looked into the role of HIV and DM as risk factors in the TB patients (pulmonary and extra-pulmonary) of rural south India. There is very little data on the association between DM and HIV with both forms of TB from this region of India. In this study it was observed that 31.8% of the pulmonary TB patients had DM as a co-morbid factor, which was significantly higher than HIV (8.85%). Conversely, in the case of extra-pulmonary TB the situation was reversed, with 52.43% HIV and 5.4% DM. Extra-pulmonary TB is more prominent among patients with HIV-co-infection [4,13,14], as there is an unchecked proliferation of Mycobacteria due to HIV induced immuno-suppression.

In India, studies have been conducted on HIV/TB co-infection, which show that the incidence of TB is significantly higher in HIV positive TB patients and also that HIV infection was found to be significantly more profound in extra-pulmonary TB patients compared to pulmonary TB patients [3,4,13,14]. Though global studies have presented DM to be a major aggravating factor of pulmonary TB [8,9,11], there is very limited data on DM/TB co-infection from India [5,7,10]. A study from Nepal, a neighboring country of India, has shown significantly higher proportion of DM in pulmonary TB patients compared to extra-pulmonary TB patients. However there were no significant differences observed in the HIV positivity between these two groups [15]. Jeon and Murray, in a systematic review of 13 observational studies, have associated DM with increased risk of TB regardless of study design and population [9]. In this study, although the number of extra-pulmonary TB patients were less, it was observed that HIV was significantly higher in extra-pulmonary TB patients while DM was significantly higher in pulmonary TB patients compared to each other (p < 0.01).

The site of extra-pulmonary TB may vary geographically. Many of the studies have observed lymph node as the most common site [8,13–15]. However, in this study, a high incidence of disseminated TB (29.7%) was observed followed by spinal (16.2%), lymph node (13.5%), osteomyelitis (8.1%), milliary (5.4%), meningitis (5.4%), genito-urinary (5.4%) and others (16.2%), which includes arthritis, shoulder joint, pericarditis, empyema, endometrial and cold abscess. Disseminated TB was found more in HIV patients (n = 6; 50%) compared to the other sites, which was similar to the findings of Sharma et al. [4].

The occupational status of the patients was also analyzed in this study to understand the socio-economic status of the TB patients. It was interesting to note that though pulmonary TB was more prevalent among the agricultural labourers, extra-pulmonary TB preponderance was observed most among housewives and the self-employed and least in agricultural labourers. Two separate studies from Chennai, Southern India and Wardha, Western India showed predominance of TB to be higher in waged worker and non-workers respectively [16,17], which is quite contrary to the observations in this study. Similar to the observations in this study, Khan et al. observed a high incidence of pulmonary TB among the agriculturists and labourers compared to business and professional groups [18]. Nissapatorn et al. has observed a high percentage of TB among unemployed patients with and without DM from Malaysia [8]. In this study DM was observed more compared to HIV in almost all the occupational groups of pulmonary TB, which is significantly different to extra-pulmonary TB, where HIV was observed to be higher than DM in all the occupational groups.

India is a developing country where the major occupation is agriculture and it was observed that a high number of the agricultural labourers suffered from DM. Most of the patients of lower socio-economic classes were more concerned about the symptoms of TB than those of DM. DM is projected to rise to 366 million globally by 2030, with 79.4 million cases in India alone, which will be the highest in the world [19]. Thus the TB-DM co-infection cannot be ignored.

Though TB control programmes are giving more importance to the HIV-TB co-infection, the rising prevalence of DM in high TB burden countries may adversely affect TB control.
Conflict of interest statement

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References