Prevalence of Diabetes in Tuberculosis Patients in Kathmandu Valley, Nepal

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PREVALENCE OF DIABETES IN TUBERCULOSIS PATIENTS IN

KATHMANDU VALLEY, NEPAL

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日本著者情報

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SUMMARY:

This descriptive cross-sectional study collected data of the prevalence of diabetes mellitus (DM) among tuberculosis (TB) at the Urban DOTS (Directly observed treatment, short-course) Centers in the Kathmandu, Bhaktapur, and Lalitpur districts of Nepal. The prevalence of DM was assessed in 67 previously treated TB cases (PTTB) and 214 new TB cases. DM was diagnosed in 8 PTTB and 20 new TB patients. Clinical interviews identified 14 cases of DM, the rapid blood glucose test diagnosed 4 cases, and the oral glucose tolerance test (OGTT) diagnosed 4 cases. Impaired glucose tolerance and impaired fasting glycemia were found in 8 and 5 cases, respectively. The 18-24 age group had the largest number of new TB cases (82; 38.3%). However, the comorbidity of DM and TB was higher in the 35 years and older age group and was found in 24.2% of PTTB and in 23.1% of new TB cases. To provide the evidence of impacts of DM screening for TB cases, larger number of samples should be analyzed. The DM screening for TB patients is expected to start in developing countries. It should be initiated by clinical interview about DM and glucose tests by rapid kits.

INTRODUCTION
The Sustainable Development Goals and the End TB strategy aim to end the global Tuberculosis (TB) epidemic (1). However, the fall in TB incidence is too slow to achieve global targets. At the same time, the prevalence of diabetes mellitus (DM) has nearly doubled since 1980, with an even faster increase in developing countries (2). DM triples the risk of TB (3) and doubles the risk of TB relapse (4). There is growing evidence that DM is an important risk factor for TB and might even affect disease presentation and treatment response (5). For successful TB treatment, the World Health Organization (WHO) recommends that TB patients undergo DM screening and receive treatment for DM when appropriate (6, 7).

TB is still a major public health issue in Nepal. The incidence of TB was estimated at 154 per 100,000 inhabitants in 2016 (8). Despite nationwide availability of the Directly Observed Treatment Short course (DOTS) at the public health centers, the decline in TB incidence is insufficient to achieve national targets. The TB case notification rate has remained constant for last five years. However, the age distribution trends show a steady rise in TB prevalence among the elderly population (9). In addition, previous research reported that DM affects approximately 8.1% of urban people over 20 years old in Nepal (10, 11). The impact of DM on TB burden may be more conspicuous in Nepal where both diseases are prevalent. Thus, the objective of the present study was to
assess the association of DM with TB patients in urban area in Nepal. This manuscript served as starting point for Nepal government interest in DM screening for TB patients.

**MATERIALS AND METHODS**

This descriptive cross-sectional study was performed to determine the prevalence of DM and clinical factors associated with PTTB and new TB cases.

The data were collected from urban DOTS centers of Kathmandu Valley from November 2014 to April 2015. TB patients from 18 to 65 years of age who met the inclusion criteria and agreed to participate were included in the study. Our exclusion criteria were pregnant women and patients with blood pressure lower than 80 mmHg.

The diagnosis of PTTB was considered definite in all patients who had previously been treated for TB and were diagnosed again via bacteriologically positive results (smear test-positive and/or culture-positive and/or Gene Xpert-positive).

New TB patients that started medication for TB were recruited for a comparison with previously treated cases. Similarly, new patients beginning treatment were chosen at random at each facility, and every three new TB cases were selected after each PTTB
was reported. If a selected patient did not meet the criteria or refused to participate in the study, the next reported case became a candidate.

The DM condition of TB patients was identified by an algorithm based on WHO recommended diagnostic criteria for DM and intermediate hyperglycemia (Figure 1).

In this study, patients who had been receiving any DM medication or insulin injections were categorized as having DM without further blood examination. Rapid tests were performed by FreeStyle Freedom Lite (Abbott Diabetes Care Inc.) in the fasting condition. DM was diagnosed in patients who not meeting fasting conditions when the results of rapid tests exceeded 200 mg/dl.

Oral glucose tolerance tests (OGTTs) were conducted on another day within 8 weeks after the initiation of TB treatment. Patients were diagnosed with DM if the first blood samples obtained under fasting conditions exceeded 200 mg/dl in the OGTT. The lower value from the rapid tests or the first blood samples were used to determine the fasting blood glucose (FBG). Patients were diagnosed with DM when their FBG exceeded 126 mg/dl. The second blood samples for the OGTT (OGTT 2 h) were examined in patients whose FBG was less than 126 mg/dl. These patients were diagnosed with DM when their OGTT 2 h exceeded 200 mg/dl. They were diagnosed with impaired glucose
tolerance (IGT) when their OGTT 2 h exceeded 140 mg/dl and with impaired fasting
glycemia (IFG) when their OGTT 2 h was lower than 140 mg/dl and their FBG exceeded 110 mg/dl. All blood samples were transported under cool conditions to be tested within 2 hours at the Krown Laboratory and Referral Centre in Tangal, Kathmandu.

This study conformed to the principles outlined by the World Medical Assembly Helsinki Declaration and ethical approval was obtained from the ethics committee of the National Health Research Council (NHRC) in Nepal and NCGM in Japan. Consent was obtained from all participants.

RESULTS

Data were collected from 42 urban DOTS centers in Kathmandu (24 centers), Bhaktapur (11), and Lalitpur (7) districts from November 2014 to April 2015.

It was difficult to classify PTTB according to the outcome and duration of the recent treatment because only 25 patients (37.3%) could answer questions on their previous treatments. The durations of previous treatments were as follows: 3 to 6
months (2 patients), 6 months (8), 6 to 9 months (12), and 9 to 12 months (1); 2 patients did not remember their previous treatments. Table 1 shows the results of DM screening in TB patients based on the diagnosis algorithm (Figure 1). Eight of the 67 PTTB (11.9%) and 20 of the 214 new TB patients (9.3%) were diagnosed with DM.

Information from the clinical interviews on medical history and DM medication could be used to diagnose DM in 4 of the PTTB (50%) and 10 of the new TB patients (50%).

Among PTTB, one was diagnosed with DM because the result of the rapid test exceeded 200 mg/dl. Two PTTB were diagnosed with DM because the results of the rapid test under fasting conditions exceeded 126 mg/dl. Among new TB patients, three were diagnosed with DM because the results of the rapid test exceeded 200 mg/dl. Four new cases were diagnosed with DM because the results of the rapid test under fasting conditions exceeded 126 mg/dl.

Among PTTB, 62 underwent an OGTT. However, two patients had only values of their first sample of OGTT and other two patients had only values of their OGTT 2h, and other one had only value of rapid kit and no value of OGTT. Five PTTB were diagnosed with IGT and 4 were diagnosed with IFG by the OGTT. Among new cases, 201 patients underwent an OGTT. However, five patients had only one abnormal value of the first
sample and 9 patients did not join to the examination which use their blood sample, 3 were diagnosed with IGT, and 1 patient was diagnosed with IFG.

Tables 2 shows the age distributions of the PTTB and new TB patients and the presence of DM. The mean age was 41 years for PTTB patients, which was, as expected, older than the mean age of 27 years for new cases. The largest age group of PTTB patients was the 18 to 24 years age group. Of the 67 PTTB patients, 8 were diagnosed with DM, the prevalence was 11.9%: none from 18 to 34 years of age, 3 from 35 to 44 years of age (15%), 1 from 45 to 54 years of age (7.1%), and 4 from 55 to 64 years of age (36.4%). In the 214 new TB patients, the 18 to 24 years age group had the highest number of patients (n = 82). Of these new TB patients, 20 had DM, the prevalence was 9.3%: No DM from 18 to 24 years of age, 2 from 25 to 34 years of age (3.7 %), 4 from 35 to 44 years of age (11.4 %), 7 from 45 to 54 years of age (26.9%), and the remaining 7 from 55 to 64 years of age (43.8%).

It was the second course of TB treatment for 63 patients, the third course for 3, and more than the third for 1.

**DISCUSSION**
Because of the shifting of TB patient age to be older, the double burden of DM and TB is becoming a more serious concern for public health programs and individual TB treatment outcomes. WHO and The International Union against Tuberculosis and Lung Disease (The Union) thus developed the *Collaborative Framework for Care and Control of Tuberculosis and Diabetes*\(^6\) to assist each countries.

The study shows, 8 DM patients among 42 PTTB and 18 DM patients among 78 new TB from 35 to 65 years of age. The comorbidity of DM was 24.2\% with PTTB and 23.1\% with new TB from 35 to 65 years of age. These rates are higher than the reported DM prevalence in the urban areas in Nepal (11, 12). The prevalence of diabetes in Nepal was estimated to be 9\% among adults aged 18 years old and above in 2014 (13). DM screening should be recommended to TB patients from 35 years old for both PTTB and new TB cases.

DM was screened using clinical interviews, random and fasting blood sugar analyses with rapid kits and blood samples, and the OGTT. The main purpose of DM screening programs is to enable diabetes control from an early stage. This approach improves long-time results by permitting blood glucose control (14). To identify early-stage DM patients, diagnosis of IGT and IFG by an OGTT is recommended. However, it is
difficult to provide OGTT to diagnose IGT and IFG at DOTS centers in Kathmandu because there was no apparatus for blood test.

To improve TB treatment, poor control of DM should be detected and DM management should be improved due to the risks of TB relapse. Examination of HbA1c is adequate to manage DM conditions. However, there was no apparatus to provide HbA1c examinations as a screening method in local setting. A clinical interview and rapid glucose tests with random and fasting condition could diagnose 87.5% among simple postprandial blood glucose measurement with a glucometer 2 hours after a meal.

This study is the first report on the DM situation among TB patients in Kathmandu valley. To introduce the DM screening for TB patients are recommended from 35 years and older age group. It should be initiated by clinical interview and glucose test by rapid kits at DOTS centers. In other developing countries, the DM situation among TB patients in the urban area might be similar with Kathmandu valley. The first targets and action to introduce DM screening for TB patients will support the TB program in developing countries.

CONFLICT OF INTEREST
The authors have no conflicts of interest directly relevant to the content of this article.

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REFERENCES


Figure 1

Algorithm of case-finding strategies for diabetes among tuberculosis patients who agreed to participate in this study.
Table 1.
The number of diagnosed diabetes by screening processes for TB patients

<table>
<thead>
<tr>
<th></th>
<th>PTTB (n=67)</th>
<th>New cases (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interview about DM medication history</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Rapid test ≥200mg/dl</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Rapid test ≥126mg/dl</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>First sample of OGTT ≥126mg/dl</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>OGTT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OGTT 2h ≥200mg/dl</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>DM</td>
<td>8</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>PTTB</th>
<th>New cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGT</td>
<td>5 (7.5%)</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>IFG</td>
<td>4 (6.0%)</td>
<td>1 (0.5%)</td>
</tr>
</tbody>
</table>

The lower value from the rapid test or the first sample of OGTT was used as data of fasting blood sugar (FBS).

PTTB: Previously treated tuberculosis

IGT: Impaired glucose tolerance

IFG: Impaired fasting glycaemia
Table 2. Age distribution of Previously treatment TB (PTTB) and new TB, and DM in PTTB and in new TB.

<table>
<thead>
<tr>
<th>Age groups</th>
<th>PTTB</th>
<th>DM in PTTB</th>
<th>New TB</th>
<th>DM in New TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-24</td>
<td>15</td>
<td>0</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td>25-34</td>
<td>10</td>
<td>0</td>
<td>54</td>
<td>2</td>
</tr>
<tr>
<td>35-44</td>
<td>15</td>
<td>3</td>
<td>35</td>
<td>4</td>
</tr>
<tr>
<td>45-54</td>
<td>14</td>
<td>1</td>
<td>26</td>
<td>7</td>
</tr>
<tr>
<td>55-65</td>
<td>13</td>
<td>4</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>67</td>
<td>8</td>
<td>214</td>
<td>20</td>
</tr>
</tbody>
</table>
281 TB patients were interviewed about diabetic treatments histories.

14 patients answered that they had diabetic medications.

Rapid glucose check under fasting condition were conducted for 267 patients who had no diabetic medication.

1st samples of OGTT with fasting conditions were tested. The lower value from the 1st samples or rapid tests were used as FBG.

4 patients were diagnose DM by rapid glucose data, FBG ≥ 200mg/dl.

2nd samples for OGTT, 75g oral glucose ingestion and sampling after 2 hours wait.

1 patients was diagnosed DM, FBG ≥ 200mg/dl. 6 patients were diagnosed DM, FBG ≥ 126mg/dl, and <200mg/dl.

OGTT 2h were < 140mg/dl

Normal FBG were < 110mg/dl 5 patients were diagnosed with IFG FBG were ≥ 110mg/dl

OGTT 2h were ≥ 140mg/dl

8 patients were diagnosed IGT OGTT 2h were < 200mg/dl