Clinical Profile and outcome of Tuberculosis in Patients with Diabetes

Jiyani M. R., Vadgama P. K., Pandey A. S., Modh D. A.

ABSTRACT
BACKGROUND: The association between Pulmonary Tuberculosis (TB) and Diabetes Mellitus (DM) has been known to clinicians for a long time. DM impacts the clinical progression and treatment outcomes of patients suffering from TB. Efforts have been devoted to find the association between TB and DM as well as the concurrent effect of each co-morbidity. This study has been carried out to compare clinical and radiological presentation of PTB in DM and non DM cases, to compare treatment outcome of PTB in DM and non DM cases, and to assess the impact of glycamic control on smear conversion. MATERIALS AND METHODS: The present study includes the patient of PTB with DM and non-DM in outpatient setting as well as indoor setting of Pulmonary Medicine Department in SMIMER. The study pattern was Cohort study with statistical application of Chi-square test. The data was collected using formal proforma, which elicited demographic and clinical information. RESULT: In present study, we had 50 patients of DM with TB and 100 cases of Non DM with TB. 34% of DM with TB had cavity lesion and lower zone involvement of lung whereas 30% of non DM TB patients had upper zone involvement. Patients on insulin had better sputum Conversionat the end of 2 months as compared to those on Oral Hypo-glycolic Drugs. Patients who had good glycemic control with HB1AC level of 6 to 7 had highest rate of sputum conversion at the end of 2nd month (20%). Cure rate was 82% in CAT 1 and was 80% in CAT II cases. CONCLUSION: The early detection of diabetes in TB patients and tuberculosis in DM patients has good prognosis in the management of the co-occurrences. The optimum glycemic control helps in early sputum conversion and results in higher cure rates. Keywords: Diabetes Mellitus, Tuberculosis, HbA1c, Smear Conversion, Outcome.

INTRODUCTION
Pulmonary TB represents an important worldwide public health problem. Tuberculosis remains a leading cause of death globally. In 2005 there were an estimated 8.8 million new cases of tuberculosis worldwide. Incidence of tuberculosis is greatest among those with conditions impairing immunity, such as diabetes. In India 18% of patients with pulmonary tuberculosis have diabetes. Tuberculosis remains a major cause of mortality in developing countries, and in these countries, diabetes prevalence is increasing rapidly. With recognition of this explosive increase in number of people diagnosed with DM all over the world, a whole new field of related interaction between DM and pulmonary tuberculosis has been thrown open. Studies have noted that the risk of developing TB was 11 to 18 times greater in Diabetics than in normal population. Increased reactivation of tuberculosis lesions has also been recorded in diabetics. At the same time, tuberculosis appears to aggravate hyperglycaemia, with patients requiring higher doses of insulin. The primary objectives to carry out this study are to compare clinical and radiological presentation of PTB in DM and non DM cases, to compare treatment outcome of PTB in DM and non DM cases, and to assess impact of Glycemic control on smear conversion. There is an increased sputum positivity compared to general population in DM patients and delayed conversion to sputum negativity. This importance of hyperglycemia has to be emphasized because of an alteration in host defense and consequently increased susceptibility to infection eventually altering the clinical course of the disease. As much as 14.8% of pulmonary tuberculosis and 20.2% of smear-positive i.e. infectious tuberculosis may be directly linked to diabetes. Diabetes is also
probably responsible for the urban incidence of smear positive tuberculosis being 15.2% higher than that in rural areas. Raised fasting blood glucose more than 200 mg/dl have an impaired ability to engulf and kill opsonized tubercle bacilli.

**MATERIALS AND METHODS**

The present Study includes the patient of PTB with DM and non-DM in outpatient setting as well as indoor setting of Pulmonary Medicine Department in SMIMER. Participants who gave written informed consent were included in this study.

**Study type:** Cohort study

**Study setting:** OPD and indoor facility of Department of Tuberculosis and Respiratory Diseases, Surat Municipal Institute of Medical Education and Research, Surat City.

**Study period:** Study will be conducted for period of 1 year and 2 months, which includes 10 months for data collection and four months for data entry and data analysis.

Sample size: 150 (case-50, control-100)

Case: 43 + 10% add ~ 50

Control: 86 + 10% add ~ 100

Sample size of 150 was calculated using EPI INFO software considering relative risk of 4.3 for treatment failure in PTB cases with DM and non-DM.

**Data collection:**

Data was collected using formal proforma. Study included socio-demographic profile, clinical symptomatology, family and personal history of patient, laboratory examination, diabetes profile, sputum examination, radiological examination, anti-tubercular treatment and follow up sputum and blood sugar examination.

Inclusion criteria:

Patients in age group of more than 18 years and having sputum positive PTB with DM and without DM were included.

Exclusion criteria:

Patients in age group less than 18 years, and patients on steroids as well as thiazide diuretics were excluded. Diabetic patients with HIV infection as well as having other co-existent lung condition were excluded.

**RESULTS**

In present study, mean age of presentation in DM with TB was 48.24 years compared to Non-DM with TB was 44.85 years. Out of 50 patients of diabetes with tuberculosis, 68% of the patients were between 40 and 60 years of age compared to Non DM with tuberculosis was 41%. Males were twice more than the number of females in both diabetics and non-diabetics.

In present study, almost all the patients (96%) included in the study had cough and fever. Besides that anorexia, weight loss, breathlessness, chest pain and hemoptysis were observed in 42%, 64%, 46%, 28% and 6% respectively. Chi square test was utilized with a P value of 0.141 and degree
of freedom 6. In present study, the family history of Tuberculosis was present in 16% of the patients. The history of Diabetes Mellitus in the first-degree relatives was present in 32% cases. In present study, the mean duration of Diabetes Mellitus at the time of diagnosis of pulmonary Tuberculosis was 7.142 years. 42% of the patients had Diabetes for more than 5 years. Almost 38% of the patients in this study had DM between 1 to 5 years duration. In present study, extra pulmonary manifestations like osteo-articular involvement (6%) were more common in Diabetic than Non-Diabetic patients and Lymph node involvement more common in Non-Diabetic patients.

In present study, 66% patients were treated with Insulin and those who were not taking insulin were treated with OHA. 34% of patients were treated with OHA. In the present study, Grading of sputum on direct microscopy was done as per RNTCP guidelines for the same. The pre-treatment bacillary load in category 3+ (indicated by 1+, 2+ & 3+) was more in case of diabetic patients compared to non-diabetics. 44% of the patients had sputum graded with 1+; 40% with sputum graded 3+ and 16% with sputum graded 2+.

Table: 1 Distribution of Radiological lesions among TB patients.

<table>
<thead>
<tr>
<th>Zones</th>
<th>No. of diabetic (%)</th>
<th>No. of non diabetic (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper</td>
<td>12 (24%)</td>
<td>30 (30%)</td>
</tr>
<tr>
<td>Middle</td>
<td>10 (20%)</td>
<td>25 (25%)</td>
</tr>
<tr>
<td>Lower</td>
<td>21 (42%)</td>
<td>16 (16%)</td>
</tr>
<tr>
<td>Multi Zone</td>
<td>7 (14%)</td>
<td>29 (29%)</td>
</tr>
</tbody>
</table>

In present study, 42% of diabetic patients had lower zone involvement compared to non-diabetic wherein it was 16%. 34% diabetic patients had cavity lesion compare to non-diabetic patients. Chi square test was utilized with P value of 0.004 and degree of freedom 4. As defined by the diagnostic algorithm of RNTCP and as advised by WHO, 42% were new cases, 40% were relapse, 12% were treatment after default and 6% were treatment failure cases. P value obtained was 0.119 and degree of freedom was 3.

In present study, patient had good glycemic control with HB1AC level between 6 to 7 and had the highest rate of sputum conversion at the end of 2nd month (20%).

**Table: 2 Distribution of sputum conversion according to the type of Diabetic treatment**

<table>
<thead>
<tr>
<th>Diabetic treatment</th>
<th>Sputum conversion at 2nd month</th>
<th>Sputum conversion at 3rd month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oha</td>
<td>8 (16%)</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Insulin</td>
<td>19 (38%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Oha + insulin</td>
<td>7 (14%)</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

**Table: 3 Distribution of Sputum Conversion according To Hb1ac Level**

<table>
<thead>
<tr>
<th>HB1AC Level</th>
<th>Sputum conversion at 2nd month</th>
<th>Sputum conversion at 3rd month</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6.0</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>6.0-7.0</td>
<td>10 (20%)</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>7.0-8.0</td>
<td>7 (14%)</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>8.0-9.0</td>
<td>3 (6%)</td>
<td>12 (24%)</td>
</tr>
<tr>
<td>&gt;9.0</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

Chi square test yielded P value of 0.0179 with degree of freedom 4. At inception of the study, 21 out of 50(42%) patients treated with category-I, 27(54%) patients treated with category-II and 2(4%) patients treated with MDR regimen under RNTCP.

In present study, out of total number of DM with TB patients, 21 patients were put on CAT I, out of which 17 patients got cured (82%), 2 patients failed treatment(9%), 2 patients defaulted treatment (9%). Those who failed and defaulted treatment were put on CAT II treatment. During the course of study and at conclusion, out of 31 patients put on CAT II, 25 patients were declared cured (80%), 3 patients declared failure (4%), 3 patients defaulted treatment (16%). According to Criteria C, under RNTCP patients were subjected for CBNAAAT (cartridge based Nucleic Acid amplification Technique), 2 patients were diagnosed as Rifampicin Resistance Tuberculosis (9%) and those were put on CAT IV treatment, are still on treatment and clinically better with good glycemic control.

At the inception of study, out of 100 Non-DM TB patients, 61 patients were put on
CAT 1 ATT, 38 patients were put on CAT 2 ATT and 1 patient was put on CAT 4 ATT. Out of 61 patients put on CAT I, 53 patients got cured (88%), 2 patients failed treatment (3%), 6 patient defaulted treatment (9%). Those who failed and defaulted treatment were put on CAT II treatment. During the course of study and conclusion of study, out of a total of 46 patients put on CAT II, 36 patients (78%) were declared cured, 4 patients (8%) were declared failure, 6 patients (14%) defaulted treatment. According to Criteria C, under RNTCP patients subjected for CBNAAT (Cartridge Based Nucleic Acid Amplification Technique), 1 patient was diagnosed as Rifampicin Resistance Tuberculosis. This patient was put on CAT IV treatment and is clinically improving with good glycemic control.

**DISCUSSION AND CONCLUSION**

In the present study, 40% patients of DM with TB presented with grade +++AFB smear similar to the findings of Gupta et al study in which it was 48%. This suggests that there are more chances of high degree of infectivity in case of diabetic patients. Consolidation with or without cavitation was the most common presentation in our study similar to both Singh et al(60%) and Gupta et al (59.2%) studies. Patients of DM with TB usually have lower zone involvement with cavitations. In the present study, lower zone involvement was most common which was similar to this Patel el at. Singh et al and Gupta et al study. Lower zone involvement more common in diabetic patient because retrograde lymphatic flow from involved hilar nodes and ulceration of a bronchus by a lymph node affected by tuberculosis with spillage of tuberculosis material into the bronchus. In present study, extra pulmonary manifestations like Osteoarticular involvement (6%) more common in Diabetic than Non-Diabetic patients similar to Nissapatron et al (5.1%).

In present study, 34% were on OHA and 46% on insulin compared to Singh et al study in which 60% were on OHA and 16% on insulin at time of diagnosis of pulmonary tuberculosis. Those who were on uncontrolled diabetes during follow up treatment shifted to insulin therapy considering fact that OHA had high interaction with rifampicin drug dual therapy. Interaction of Rifampicin with OHA leads to suboptimal glycemic control and alters the prognosis. In present study, those patients who had good glycemic control with HB1AC level between 6 to 7 had highest rate of sputum conversion at the end of 2nd month (20%). Sputum conversion is slightly delayed in DM patients with TB as compared to non-DM patients.

In present study, out of total number of DM with TB patients, 21 patients were put on CAT I, out of which 17 patients got cured (82%), 2 patients failed treatment (9%), 2 patients defaulted treatment (9%). Those who failed and defaulted treatment were put on CAT II treatment. During the course of study and at conclusion, out of 31 patients put on CAT II, 25 patients were declared cured (80%), 3 patients declared failure (4%), 3 patients defaulted treatment (16%). According to Criteria C, under RNTCP patients subjecting for CBNAAT (cartridge based Nucleic Acid amplification Technique), 2 patients were diagnosed as Rifampicin Resistance Tuberculosis. 2 patients put on CAT IV treatment are still on treatment and clinically better with good glycemic control.

**REFERENCES**

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