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Prevalence of Diabetes Mellitus in Newly Diagnosed Subjects with Sputum +Ve, Pulmonary Tuberculosis and A Literature Review

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Abstract

The co-morbid diabetic-tuberculosis (DM-TB) patients are often encountered in the clinics. Both the diseases complicate each other at many levels. The idea of the current observational study is to find out the incidence of DM in newly diagnosed TB patients among a study group of 396 patients in Hindu non-tribal and Muslim, low to middle socio economic strata group. And also to review the literature and future strategies to combat such co–morbid conditions.

Keywords: Diabetic-tuberculosis co-morbidity, DM-TB; Diabetes mellitus; Glycemic control; Risk factors for tuberculosis; Tuberculosis; Prevelance.

Introduction

Diabetes mellitus is known to double or triple the incidence of active tuberculosis and increases the risk of tuberculosis treatment adverse outcome, worsen the symptoms and fasten the mortality.[1,2,3] Approximately 15% cases of pulmonary tuberculosis are linked with DM worldwide.[4] It is also true that the tuberculosisincreases insulin resistance and causes stress induced hyperglycemia, which may lead toa false diagnosis of diabetes mellitus during the initial phase of active tuberculosis.[5] The idea of the current observational study is to find out the incidence of DM in newly diagnosed TB patients among a study group of 396 patients in Hindunon-tribal and Muslim, low to middle socio economic strata group. Diagnostic criteria of DM by the American Diabetes Association (ADA) includes a fasting plasma glucose (FPG) level of 126 mg/dL (7.0 µmol/L) or higher, or a 2 hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or higher during a 75g oral glucose tolerance test (OGTT), *or* a random plasma glucose of 200 mg/dL (11.1 µmol/L) or higher in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis. Whether a hemoglobin A1c (HbA1c) level of 6.5% or higher should be a primary diagnostic criterion or an optional criterion remains a point of controversy.[6] The socio economic strata of the patient is calculated based on modified Kuppuswamy scale which includes 3 parameters those are the head of families educational status, occupational status and overall aggregate income of the whole family, pooled from all sources. The total score of Kuppuswamy SES ranges from 3-29 and it classifies families into 5 groups, "upper class, upper middle class, lower middle class, upper lower and lower socio-economic class. All the patients in the study group belonged to lower middle class to lower class as per the scale.[7]

Materials and Methods

The study was conducted at two different Centers, namely All India Institute of Medical Sciences, New Delhi and at Chest clinic and TB hospital at Nehru Nagar, New Delhi from September 2018 to January 2019.

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The inclusion criteria werenewly diagnosed; smear positive, drugsensitive, pulmonary tuberculosis patients without extra pulmonary involvement, in the age group of 18–60 years. Patients with raised blood glucose levels or with a positive history of diabetes mellitus were included in the study. Patients with any morbidity other than newly diagnosed TB and DM were excluded from the study. A meticulous detailed history was taken including the socioeconomic status, nature of occupation, family history and personal history including the determinants of disease like age, gender, alcohol abuse, cigarette smoking, drug addiction, for both TB and DM, history of present illness, history of co-morbid diseases, and history of diabetes mellitus (type, duration, medication and treatment compliance, and complications). On day 1, the purpose of the study was explained to the patient and informed written consent was obtained. Physical parameters like height, weight, body mass index (BMI), waist circumference; hip circumference and waist-hip ratio were recorded.

Current usage of tobacco or alcohol; number of cigarettes smoked perday and number of years of smoking; average daily quantity and frequency of alcohol consumed were ascertained. The height, weight, waist circumference and hip circumference were measured. BMI was also measured through Bio–scale. The participants were called the very next day after overnight fasting. The fasting blood glucose levels of the patient were measured using a standardized glucometer. Patients with abnormal fasting blood sugar values or presence of two or more risk factors were subjected to further blood investigations and send to the laboratory in the center itself for blood investigations including PP blood sugar and HbA1c. Data were statistically analyzed.

Results

A total of 396 patients were screened. Of these, 28 patients were alreadyknown to have Type II diabetes and were on anti-hyperglycemic treatment. Additional 26 patients were detected having increased blood glucose levels and glycosylated hemoglobin (HbA1C) at the time of screening (Table 1). These patients were unaware of their raised blood glucose levels and only 7 out of 26 patients gave a positive family history of DM. Patients were considered to be diabetic if they had fasting plasma glucose > (126 mg/dl). Or with a glucose tolerance test, two hours after the oral dose of plasma glucose > (200 mg/dl) or Glycosylated hemoglobin (HbA1c) of greater than 6.5%.[8] Among these 54 diabetic patients, 24 were male and 30 were female. Patients of DM who developed TB were all found to have poor glycemic control. In the present study all the 24 males falls in working category involved in semi-skilled to unskilled works. Many of the males were into tobacco chewing, smoking and were having regular alcohol intake. Among all the males 18 of the males were alcoholics, 12 were found to be smoking tobacco, 12 were smokeless tobacco chewers and none of them was a drug addict. All the 30 females were non-alcoholic and non-tobacco chewers. Only 4 of the females were enrolled in unskilled household activities, rest of the females was householders.

The present study has found a 13.6% prevalence of diabetes mellitus in newly diagnosed TB patients. This study has not found any significant association between patients mean weight, height orBMI with the outcome of disease, in the literature also no such association has been found.[13] This study has reported a significant number of male subjects involved in some form of substance abuse. The current study does not, have sufficient data to establish sex predilection among the DM-TB patients. In the current study the mean age of (DM-TB) co-morbid group was (f43.14 ± 9.75) that fall in forth and fifth decade of life. The result is also consistent with the study conducted in Mexicoon 561 DM-TB subjects with a mean age group of 53 years, the DM-TB patients are found to be older than patients having TB alone.[8] The mean weight and height of the patients in DM-TB patients is found to be (48.88 ± 11.67)and mean height is calculated to be (157 ± 5.96) which means DM-TB are less obese than patients of DM alone, as TB is known to cause anorexia in these patients (Figs. 2-9).

Table 1: Presenting the mean and standard deviation of fasting blood glucose, PP and HbA1c in the study group

DM + TB patients	Age (years)	Weight (kg)	Height (cm)	Fasting (mg/dL)	PP (mg/dL)	HbA1C
Study group (All 54 patients)	43.14 ± 9.75	48.88 ± 11.67	157 ± 5.96	136 ± 40.71	178.38 ± 54.77	7.33 ± 1.22
Known cases of DM (28 patients)	44.92 ± 9.86	52.10 ± 13.15	156.60 ± 5.47	132.42 ± 36.93	159.92 ± 46.26	7.28 ± 1.47
Newly diagnosed DM (26 patients)	41.23 ± 9.45	45.42 ± 8.81	157.42 ± 6.53	141.11 ± 44.71	198.26 ± 57.06	7.38 ± 0.90

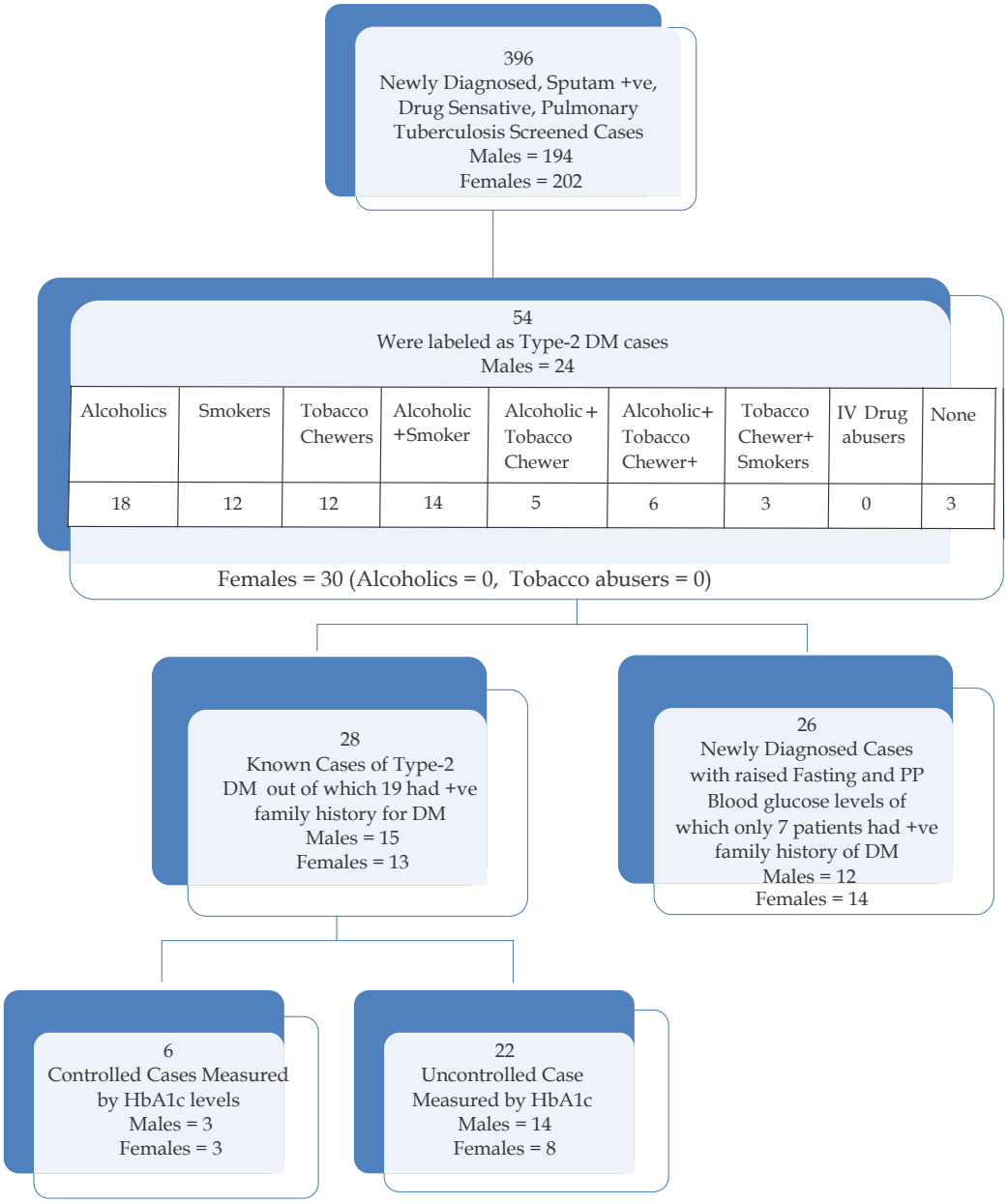

Fig. 1: The study methodology flow chart.

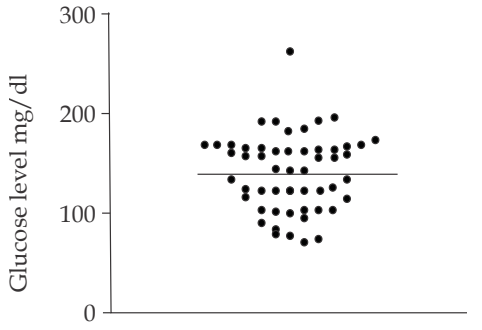

Fig. 2: Fasting blood glucose levels at baseline of the study group.

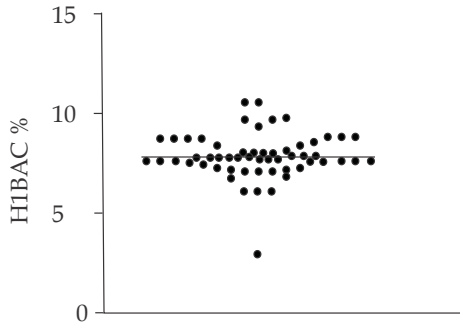

Fig. 3: HbA1c levels in the study group at baseline.

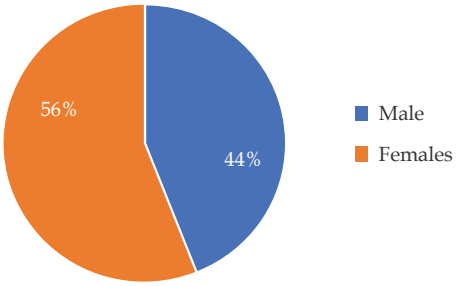

Fig. 4: Sex distribution graph in DM-TB patients.

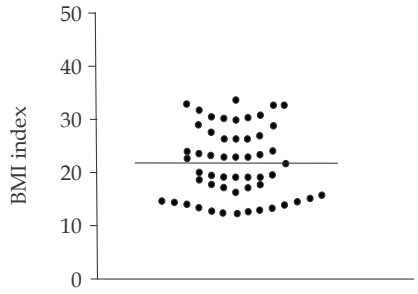

Fig. 5: BMI distribution graph of DM-TN patients.

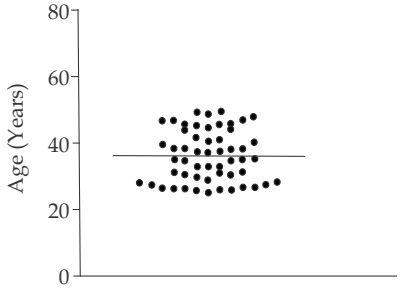

Fig. 6: Age distribution graph of DM-TB patients

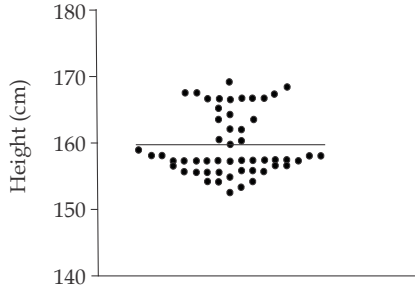

Fig. 7: Height distribution graph of DM-TB patients.

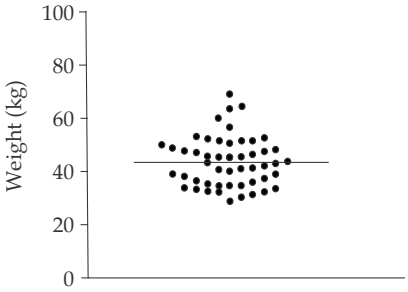

Fig. 8: Weight distribution graph of DM-TB patients.

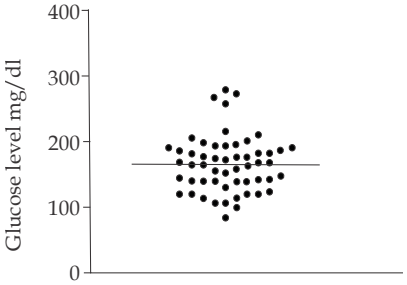

Fig. 9: PP blood gulcose levels at baseline of the study group.

Discussion

DM is linked to TB in 15% of cases worldwide from other countries like Indonesia, Malaysia, Saudi Arabia, Taiwan and Mexico.[9–12] A large number of studies have associated DM with an increased risk of relapse rates in TB patients, raised blood glucose levels are also a cause of treatment failure and high mortality in TB patients.[14] Diabetes mellitus is an important risk factor for reactivation of tuberculosis.[15] A systemic review says that DM triples the risk of developing tuberculosis and worsens the symptoms to a significant patient discomfort.[7]

The Relation of Glycemic Control and Development of Tuberculosis

The hazard of TB in diabetic patients with good glycemic control (FPG 130 mg/dl) did not differ significantly from that in non-diabetic individuals.[9] In the linear dose-response analysis, by one study the hazard of TB increased with poor glycemic control. Assuming the observed association between glycemic control and TB was found to be causal.[16,17]

Tuberculosis patients with DM show more pronounced clinical presentation in terms of symptoms, weight loss, fever, dyspnea, and night sweats.[18] Radiologically also DM-TB patients have more extensive lesions, more often have multilobar disease, more frequently present with cavitation and with predominant involvement of the Lower-lung.[19] The bacterial burden at presentation is higher in patients with DM as DM can lead to multiple complications like increased susceptibility to infection, hyperglycemia and insulinopenia which may further alter the function of lymphocytes and

macrophages.[20,21] On the other hand tuberculosis can also cause transient hyperglycemia by causing impaired glucose tolerance. Which is a risk factor for occurrence of DM.[22] Therefore in the current study the newly diagnosed 26 patients may or may not have developed true Diabetes mellitus. The raised blood glucose levels could be due to transient hyperglycaemia caused by tuberculosis infection.[16] Therefore glucose levels should be rechecked after 4 weeks of start of ATT, or after the patient is afebrile to establish a frank diagnosis of DM.[4,1,23]

A person with tuberculosis has significantly higher mortality if the person also has DM.[21] Studies have shown that, in patients with pulmonary tuberculosis the mortality rate is 6.5–6.7 times higher than patients of Tuberculosis alone.[24] In a study by Baker et al. it has been concluded that patients with tuberculosis and DM have a nearly 4-fold higher risk of relapse than do those with tuberculosis alone.[25]

Cigarette smoking is known to be an independent risk factor for tuberculosis. The role that cigarette smoke plays in the pathogenesis of tuberculosis is related to ciliary dysfunction, and majorly due to altered immune response. Many systemic reviews and meta-analyses of observational studies have shown an unfavorable association between the global epidemics of tuberculosis and smoking.[26]

Literature in the past has shown a significant association between alcohol consumption and use of tobacco in the prevalence of TB in diabetes.[4] P Alcohol abuse has also been associated with tuberculosis as an independent risk factor. It has been estimated by literature in the past that approximately 10% of all tuberculosis cases are attributable to alcohol use.[27] Alcohol use disorder or AUD is a chronic, relapsing brain disease characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences. The prevalence of AUD among tuberculosis patients varies among different ethnic groups.[28] The association between alcohol use and tuberculosis has been known since ages, but it is not known if the increased risk of tuberculosis is due to the use of alcohol per say or because of the sequel of AUD, which attributes to liver damage and nutritional deficiency, or may be due to social factors, such as crowding, malnutrition, homelessness, and imprisonment, independently of the alcohol consumption.[29]

Conclusion

With the increase in life expectancy, improvements in provision of health services worldwide, progressing sedentary life styles, the absolute numbers of cases of diabetes is likely to increase exponentially in future. The World Health Organization (WHO) collaborative framework for tuberculosis and DM currently recommends bidirectional screening—screening for DM in all patients with tuberculosis and vice versa.[30] The collaborative framework for care and control of TB and DM has already started many pilot studies and projects globally. The WHO Non-communicable disease global action plan 2013–2020 aims to reduce the impact of diabetes under the new sustainable development goals which also puts a spotlight on TB-DM cases.[22] Glycemic control in DM patients may also be an important strategy for global TB control. It is hypothesized that adequate management of blood glucose would reduce the risk of TB among diabetic patients.[9] Further studies are needed to differentiate true diabetes mellitus patients from patients having transient hyperglycemia during early stage of tuberculosis.

Future Strategies

Metformin an oral hypoglycemic drug is found to has an inhibitory effect on cellular mitochondrial Complex I, inhibition of which has been found to alter the cellular energy status in immune cells. It promotes phagocytosis, phagolysosome fusion and autophagy in macrophages. Metformin may stimulate macrophages to produce large number of nitrous oxide for oxidative killing and promote higher bactericidal capacity attributed to increased mitochondrial reactive oxidative species (ROS) production required for bacterial killing.[31] Approximately 90% of the newly diagnosed sputum-positive patients are sensitive to isoniazid (H) and rifampicin (R), adding the drug metformin would have a beneficial effect in the early killing of intracellular bacteria by influencing the host immunity.[32] As per the study it should also reduce the overall burden on the health care system.[32,33]

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