VOLUME - 11, ISSUE - 09, SEPTEMBER - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Community Medicine

A CROSS-SECTIONAL STUDY TO FIND THE PREVALENCE OF IMPAIRED GLUCOSE TOLERANCE IN PULMONARY TUBERCULOSIS PATIENTS

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ABSTRACT

Introduction: Higher prevalence of pulmonary tuberculosis in a diabetic patient is a well-known fact. The inverse relationship i.e. higher prevalence of impaired glucose tolerance in a tuberculous population is also being increasingly realized now and it becomes more relevant due to increased prevalence of DM in general population. **Aim/ Objective:** To find the prevalence of abnormal glucose tolerance in pulmonary tuberculosis patients and to correlate the glycaemic parameters with the grades of sputum AFB positivity. **Materials & Methods:** A hospital based prospective observational comparative study was conducted at a tertiary care hospital. A total of 100 consecutive eligible patients of tuberculosis, were included after taking informed parental consent. Data was analyzed using statistical software SPSS ver. 21. **Results:** Mean age of the study cases was 42.59 years with 78% males to 22% females. On Oral glucose tolerance test, 56% had normal results while 44% had deranged results. Out of the total 44 cases with deranged results, 13% had IGT and 31% had diabetes. A significant association was observed between deranged OGTT values and higher sputum grades ($p<0.05$). Glycemic control as measured by glycated haemoglobin was significantly associated with grade of sputum positivity. HbA1c levels were 5.98% in cases with "scanty" grade while it was 6.18%, 6.53% and 6.99% in cases with grade +1, +2 and +3 respectively ($p<0.05$). **Conclusion:** We observed high prevalence of impaired glucose tolerance and diabetes in tuberculosis patients. Impaired results were significantly associated with higher degree of sputum positivity. We thus recommend diabetes screening in all TB patients by either HbA1c or OGTT and glucose levels should be measured at least every 2 months after the initiation of anti-tuberculosis treatment.

KEYWORDS : Diabetes, Glycaemic Control, Impaired Glucose Tolerance, Tuberculosis

INTRODUCTION

Tuberculosis (TB), an infectious disease caused by Mycobacterium tuberculosis, is the second leading infectious cause of death worldwide. The World Health Organization (WHO) declared TB as a global health emergency in 1996 [1].

TB is a major public health problem in India. India accounts for one-fifth of the global TB incident cases and topping the list among high burden countries [2]. It is estimated that annually around 330,000 Indians die due to TB [3]. As per WHO estimate, 9 million people globally develop active TB and 1.7 million die of it annually. In India, it is estimated that about 2 million people develop active disease every year and about 0.5 million die from it [4].

Higher prevalence of pulmonary tuberculosis in a diabetic patient is a well-known fact. The association of diabetes mellitus and pulmonary tuberculosis was first observed by Avicenna [5] and has also been reported by other workers [6]. Diabetics are four to five times more prone to contract tuberculosis than the general population [7].

The inverse relationship i.e. higher prevalence of impaired glucose tolerance in a tuberculous population is also being increasingly realized now and it becomes more relevant due to increased prevalence of DM in general population [8].

Presently both developed and developing nations are facing epidemic of diabetes. Diabetes mellitus and tuberculosis may complicate each other at many levels so it is necessary to screen DM in patients of tuberculosis, as DM increases chances of relapse, treatment failure [9], mortality [10], delayed mycobacterial clearance [11] suggested by systematic review of multiple studies.

Dysglycaemia is best evaluated by glucose tolerance test (GTT). Abnormal GTT patterns includes impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and DM. IGT is the intermediate metabolic state between normal and diabetic glucose homeostasis. IGT thought be the precursor of DM but how it progress to overt disease is not well understood [12]. IGT may occur transiently during pulmonary tuberculosis due to stress of prevailing infection and has been shown to improve following effective anti-tubercular therapy [13].

Studies conducted after the introduction of GTT in 1950 have shown high prevalence of abnormal GTT in tuberculosis patients with rates ranging from 2% to 41% [12].

The relation of pulmonary tuberculosis and development of abnormal GGT are not well documented and data on prevalence of DM and IGT in pulmonary tuberculosis patients is limited. Very few studies are available on correlation of glycemic parameters with grades of sputum acid fast bacilli (AFB) positivity. Hence, this study is undertaken to find the prevalence of abnormal GTT in pulmonary tuberculosis patients which will help to facilitate early detection and intervention, so as to improve the prognosis of pulmonary tuberculosis patients.

MATERIALS AND METHODS

A Cross Sectional Study was conducted at Department of Community Medicine, PIMS, Jalandhar.

Inclusion Criteria

The study includes subjects:

- ≥18years of age, both male and female
- Patients with sputum positive AFB

Exclusion Criteria

Patients with

- HIV positivity
- Known case of diabetes mellitus
- Hypertension
- Thyroid or adrenal disorders
- Critical illness
- Malignancy
- Pregnant and lactating women
- On oral contraceptive pills
- On glucocorticoids, blockers, diuretics, statins.

Sample Size calculation:

The sample size was calculated using following formulae:

$\mathbf{n = (Z_{1-\alpha/2})^2 * P(1-P) / D^2}$

Where,

$Z_{1-\alpha/2} = Desired \quad confidence \quad int \; erval \quad = 1.96$

$P = \; prevalence \quad of \quad impaired \quad glucose \quad tolearanc \; e \; in \; pulmonary \quad tuberculos \; is \quad = 0.41 \, (41\,\%)$

$d = Pr \; ecision \quad = 10\,\%$

$$n = \frac{1.96^{\,2} * 0.41(1-0.41)}{.010^{\,2}}$$

$$n = \frac{0.929}{0.01}$$

$$n = 93$$

Thus by rounding off, 100 cases of tuberculosis from out-patient and in-patient department in our hospital, who satisfy the inclusion criteria were included.:

METHODOLOGY

A pre structured case record form was used to collect the data. Detailed history and thorough clinical examination was done. Following investigations was done:

- Oral glucose tolerance test: The OGTT was conducted in the morning after the patients had atleast 3 days of unrestricted carbohydrate diet (>150 g of carbohydrate daily) and usual physical activity. The test was preceded by an overnight fast of 8 hours. After the fasting, blood sample was collected, the subject drank 75g of anhydrous glucose in 150 to 300 ml of waterover the course of 5 minutes. Blood samples were drawn before (fasting), 1 hour and 2 hours after the load.
- Glycated haemoglobin (HbA1c)
- Sputum for AFB by Ziehl Nielsen technique

Statistical Analysis

The quantitative data was represented as their mean ± SD. Categorical and nominal data was expressed in percentage. The t-test was used for analysing quantitative data, or else non parametric data was analyzed by Mann Whitney test and categorical data was analyzed by using chi-square test. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 21.

RESULTS

Mean age of the study cases was 42.59 years with male preponderance (80%). Out of the total 100 cases, sputum was graded as scanty in 15% cases while grade +1, +2 and +3 was graded in 23%, 29% and 37% cases respectively (Table 1). On Oral glucose tolerance test, 56% had normal results while 44% had deranged results. Out of the total 44 cases with deranged results, 13% had IGT and 31% had diabetes. A significant association was observed between deranged OGTT values and higher sputum grades ($p<0.05$). A total of 26.7% cases with scanty report had impaired values as compared to 54.2% in cases with grade 3+ sputum. Mean fasting and blood sugar levels at 1 and 2 hours were higher in cases with grade +2/+3 sputum positivity as compared to scant/ +1 grade, the result was however not statistically significant. Glycemic control as measured by glycated haemoglobin was significantly associated with grade of sputum positivity. HbA1c levels were 5.98% in cases with "scanty" grade while it was 6.18%, 6.53% and 6.99% in cases with grade +1, +2 and +3 respectively ($p<0.05$).

DISCUSSION

Tuberculosis is prevalent in developing countries where the incidence of diabetes is also increasing. The relationship among these two diseases is well known. As tuberculosis exerts stress, it is expected that susceptible pulmonary tuberculosis patients can develop diabetes mellitus. Keeping these concepts in mind, it was aimed to find out the prevalence of diabetes mellitus and IGT among pulmonary tuberculosis patients attending a tertiary care hospital.

Study included 100 cases of tuberculosis from out-patient and in-patient in our hospital, who satisfy the inclusion criteria. Sputum AFB, OGTT and glycated hemoglobin was done in every patients and their relationship was sought.

In present study, on OGTT, 56% had normal results while 44% had deranged results. Overall 13% had impaired glucose tolerance while 31% had diabetes.

Bloom JD et al. (1969) [14] in one of the first study observed that in 34% of the TB subjects, glucose tolerance curves were abnormal. Jawad F et al. [15] in their study observed glucose intolerance in 52 (49%) patients, 31 had impaired glucose tolerance (IGT) and 21 had Diabetes Mellitus (DM).

Jain MK et al. [16] in their study observed that out of the 106 patients of pulmonary tuberculosis, prevalence of abnormal glucose tolerance test (GTT) was 16.98%. Ramesh Betal et al. [17] in their study observed prevalence of IGT and DM as 14.67% and 4% respectively. Sarker M et al. [18] studied 1910 tuberculosis patients. Out of these, 245 (12.8%) were found to have diabetes and 296 (15.5%) to have pre-diabetes. Ushanagadevi CS et al. [19] observed that total number of patients with abnormal blood sugar values (IFG, + IGT + DM) account for 53.28% of the TB population. IGT was significantly high in TB population (31%) when compared to (14%) that in normal population and p value is significant ($p<0.01$). Kavalikai SS et al. [20] reported overall incidence of impaired glucose tolerance as 17.33% in patients with pulmonary tuberculosis while Gandhimohan R et al. [21] reported the incidence of impaired glucose tolerance as 22% (11patients) while that of diabetes mellitus was 8% (4 patients).

In present study, a significant association was observed between deranged OGTT values and higher sputum grades ($p<0.05$). A total of 26.7% cases with scanty report had impaired values as compared to 54.2% in cases with grade 3+ sputum. Mean fasting and blood sugar levels at 1 and 2 hours were higher in cases with grade +2/+3 sputum positivity as compared to scant/ +1 grade, the result was however not statistically significant. Glycemic control as measured by glycated haemoglobin was significantly associated with grade of sputum positivity. HbA1c levels were 5.98% in cases with "scanty" grade while it was 6.18%, 6.53% and 6.99% in cases with grade +1, +2 and +3 respectively ($p<0.05$).

Srivatava AB et al. [22] in their study observed that majority of TB diabetics have far advanced disease and grade 3 sputum positivity ($p<0.05$). Shariff NM et al. [23] in their study observed that diabetes mellitus ($p<0.01$) is being

independently associated with the risk of persistent sputum smear positivity after 2 months of intensive treatment. Siddiqui AN et al. [24] in their study observed that TB-DM patients have observed higher sputum positivity (OR 1.247 95% CI; 0.539–2.886) at the end of 2-month treatment and poor outcome (OR 1.176 95% CI; 0.310–4.457) at the completion of treatment as compared with non DM patients. Other studies also showed a trend toward increased time to sputum conversion in TB-diabetics [25-27].

Thus to summarize, in present study, we observed a high prevalence of IGT and diabetes mellitus among tuberculosis cases. Thus association between diabetes and tuberculosis is the next challenge for global tuberculosis control. Improved understanding of the bidirectional relationship of the two diseases is necessary for proper planning and collaboration to reduce the dual burden of diabetes and TB. In people with TB, it may be appropriate to actively screen for DM. Prevention, screening, and treatment of both diseases together is more effective. Perhaps, a model similar to the TB-HIV program may be the best approach.

CONCLUSION

In present study, we observed high prevalence of impaired glucose tolerance and diabetes in tuberculosis patients. Impaired results were significantly associated with higher degree of sputum positivity. We thus recommend diabetes screening in all TB patients by either HbA1c or OGTT and glucose levels should be measured at least every 2 months after the initiation of anti-tuberculosis treatment. However, given the paucity of data on both DM screening methods and the timing of screening for dysglycaemia in TB patients, we believe that further studies are required to confirm our recommendations.

Tables

Table 1. Distribution of patients according to OGTT Results

OGTT Results	N	%
Normal	56	56.0%
IGT	13	13.0%
Diabetes	31	31.0%
Total	100	100.0%

Table 2. Association of Sputum grade with OGTT Results

Sputum Grade	Diagnosis			Total
	DM	IGT	Normal	
Scanty	3	1	11	15
	20.0%	6.7%	73.3%	100.0%
1+	6	1	16	23
	26.1%	4.3%	69.6%	100.0%
2+	9	5	13	27
	33.3%	18.5%	48.1%	100.0%
3+	13	6	16	35
	37.1%	17.1%	45.7%	100.0%
Total	31	13	56	100
	31.0%	13.0%	56.0%	100.0%
p (trend)- value <0.05				

Table 3. Mean blood sugar levels among various OGTT grades

OGTT	Group	N	Mean	SD	p- value
Fasting	Scanty	15	118.70	21.83	0.35
	1+	23	120.20	24.86	
	2+	27	128.52	26.68	
	3+	35	132.77	23.65	
1 hour	Scanty	15	156.80	23.30	0.60
	1+	23	161.60	24.22	
	2+	27	225.37	327.96	
	3+	35	177.86	33.77	
2 hour	Scanty	15	138.70	24.02	0.34
	1+	23	141.39	21.77	
	2+	27	144.15	24.32	
	3+	35	150.69	29.32	

Table 4. Mean glycated haemoglobin levels among various OGTT grades

OGTT	Group	N	Mean	SD	p- value
HbA1c	Scanty	15	5.98	0.90	<0.05
	1+	23	6.18	1.22	
	2+	27	6.53	1.14	
	3+	35	6.99	1.16	

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