

Frequency of Impaired Glucose Tolerance Test in Patients with Active Tuberculosis

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ABSTRACT

Objective: To determine the frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis in tertiary care hospital, Karachi.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at Dow University Hospital (Dow University Health Sciences Karachi) from 1st June 2014 to 30th November 2014.

Materials and Methods: A total of 110 diagnosed adult cases of active pulmonary tuberculosis on the basis of sputum smear positivity were included in this study. Blood samples were drawn for investigations and sent to the same reference laboratory to minimize bias. Data was collected on a pre-tested self administered Performa.

Results: There were 59.1% were male and 40.9% were female. Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis was observed in 20.9%. Rate of impaired glucose tolerance was highly associated with above 40 years of age patients and with family history of diabetes.

Conclusion: In Pakistan DM is on the rise and TB has one of the highest incidence in the world. There is emerging evidence that one disease is fuelling the other. The interest in diabetes and TB is mounting rapidly, so the clinician & researchers should prepare themselves to meet the challenges of the two disease combined.

Key Words: Impaired glucose tolerance, pulmonary tuberculosis and diabetes mellitus

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INTRODUCTION

Diabetes is one of the major public health problems of this century. The increased prevalence of tuberculosis in diabetic patients (four times higher than non-diabetics)¹ has been well documented while conversely the prevalence of diabetes mellitus in tuberculosis patients has received scant attention². People with impaired glucose tolerance and impaired fasting glycemia are at high risk of progressing to type 2 diabetes; although this is not inevitable. Diabetes depresses the immune response, which in turn facilitates infection with Mycobacterium tuberculosis and/or progression to symptomatic disease. Underlying impaired glucose tolerance or diabetes is a recognized cause of inadequate response to chemotherapy. So it is important that In patients attending Chest Clinic for treatment of pulmonary tuberculosis belonging to the age group 45 years and above routine investigations should include exclusion of diabetes as 80% of unknown cases of diabetes could be diagnosed in this group³.

It was initially believed that the tuberculous patients do not develop diabetes with any greater frequency than non-tuberculous. This view held sway till Nichols (1957) shattered this belief when he revealed that 5 % of his tuberculous patients had diabetes mellitus and a further one third had an abnormal screening test. Subsequent studies showed glucose tolerance increases with age, with significant increase after 40 years^{4, 5, 6}. Prevalence of IGT is significantly more in males (18.67%)³ than in females (12.90%)³ and they are more prone to complicated diseases^{6,7,8}. Lower socioeconomic group is more affected, possibly because of malnutrition^{8,9}. Incidence of complications such as cavitary lesions, spontaneous pneumothorax followed by hydro and pyo-pneumothorax is also high in patients with IGT^{8, 9,10,11}.

The high prevalence of I.G.T. in patients of pulmonary tuberculosis observed in studies probably reflects an increased association between Tuberculosis & Diabetes mellitus^{12, 13}.

Operational Definition

Impaired Glucose Tolerance: OGTT have done to assess impaired glucose tolerance. Glucose tolerance will be considered impaired when blood glucose levels 2 hours after ingestion of 75gm of glucose are ≥ 140 mg/dl^{14, 15}.

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Interpretation of Results: Results of Oral glucose tolerance test interpreted according to WHO Diabetes Criteria¹⁵.

1999 WHO Diabetes criteria – Interpretation of Oral Glucose Tolerance Test

Glucose levels	NORMAL		impaired fasting glycaemia (IFG)		impaired glucose tolerance (IGT)		Diabetes Mellitus (DM)	
	Fasting	2hrs	Fasting	2hrs	Fasting	2hrs	Fasting	2hrs
(mmol/l)	<6.1	<7.8	≥6.1 & <7.0	<7.8	<7.0	≥7.8	≥7.0	≥11.1
(mg/dl)	<110	<140	≥110 & <126	<140	<126	≥140	≥126	≥200

Pulmonary Tuberculosis: Patients who are smear positive for mycobacterium tuberculosis with or without classic symptoms of chronic cough with blood-tinged sputum, fever, night sweats and weight loss were considered having active pulmonary tuberculosis¹⁶.

MATERIALS AND METHODS

The cross sectional study was conducted at the Dow University Hospital (Dow University Health Sciences Karachi) for a period of six months from 1st June 2014 to 30th November 2014.

110 sample size of non probability purposive sampling were taken.

Inclusion Criteria: Recently diagnosed adult cases of both gender (within a month of diagnosis) of active pulmonary tuberculosis on the basis of sputum smear positivity.

Exclusion Criteria: All already diagnosed cases of type1 and 2 diabetes.

Patients with significant co-morbidities like chronic renal failure, hepatobiliary disease, thyroid disease, Cushing syndrome and pregnancy.

Data Collection Procedure: A total of 110 patients presenting to the CHEST OPD& DUH(Ojha Campus) fulfilling the inclusion criteria assessed by consultant were included in the study. The purpose, procedure risks and benefits of the study were explained to the patient and a written informed consent was taken from each patient for inclusion in the study. Blood samples were drawn for investigations by a trained phlebotomist (more than one year experienced) and sent to the same reference laboratory to minimize bias.

Data was collected on a pre-tested self administered Performa after taking permission from ethical committee of hospital. The socioeconomic data including age, sex, occupation, family monthly income was recorded. BMI was calculated by measuring height and weight of patient. Patients were interviewed regarding the family history of tuberculosis and diabetes. Confounding variables were controlled by strictly following exclusion criteria. The patients fulfilling inclusion criteria were instructed to fast for 8-12 hours prior to the test. A baseline blood sample was drawn for fasting blood glucose level. Then patient was given a measured (75 grams) dose of glucose solution to drink within 5 minutes time frame. Blood sample

was drawn at 2 hour interval for measurement of glucose level with auto analyzer method. Blood samples were drawn for investigations by a trained phlebotomist (more than one year experienced) and sent to the same reference laboratory to minimize bias. The results of oral glucose tolerance test were interpreted according to 1999 WHO Diabetes criteria. Glucose tolerance was considered impaired as per operational definition. All data was collected by the researcher on structured Performa attached with synopsis.

Data Analysis Procedure: The data was analyzed with the help of SPSS Program version 16.0. Mean and standard deviation were computed for numerical variables like age groups, height, weight whereas frequency and percentages were employed to assess the categorical variable like gender and presence or absence of impaired glucose tolerance. Results were described and also presented in the form of tables and graphs. Stratification was done with regard to age, gender, family history of DM, BMI to control the effect modifier through Chi-Square test. P-value ≤0.05 was taken as significant.

RESULTS

A total of 110 diagnosed adult cases of active pulmonary tuberculosis on the basis of sputum smear positivity were included in this study. Most of the cases were 31 to 60 years of age as presented in figure 1. The average age of the patients was 43.41 ± 5.41 years. Similarly average weight, height and BMI of the patients were also presented table 1. There were 59.1% were male and 40.9% were female (figure 2). Family history of diabetes was observed in 42(38.2%) cases (figure 3) and family history of tuberculosis was 45.5% cases as presented in figure 4.

Table No.1: Descriptive statistics of the patients
n=110

Variables	Mean ± SD	Max-Min
Age (Years)	43.41 ± 5.41	70-20
Weight (kg)	52.45 ± 7.84	65 – 35
Height (cm)	159.48±8.95	152-185

Table No.2: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis

Age Groups	Impaired glucose tolerance		Total
	YES n=23	NO n=87	
20-30 Years	1(5.6%)	17(94.4%)	18
31-40 Years	2(8%)	23(92%)	25
41-50 Years	8(22.2%)	28(77.8%)	36
51-60 Years	9(36%)	16(64%)	25
>60 Years	3(50%)	3(50%)	6

Chi-Square =11.636 p=0.020

Linear by linear association = 10.922 p=0.001

Table No. 3: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis with respect to gender

Gender	Impaired glucose tolerance		Total
	YES n=23	NO n=87	
Male	15(31%)	50(76.9%)	65
Female	8(14.7%)	37(82.2%)	45

Chi-Square =0.452 p=0.502

Table No.4: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis with respect to family history of diabetes

Family History of Diabetes	Impaired glucose tolerance		Total
	YES n=23	NO n=87	
Yes	13(31%)	29(69%)	42
No	10(14.7%)	58(85.3%)	68

Chi-Square =4.144 p=0.042

Table No.5: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis with respect to family history of tuberculosis

Family History of Tuberculosis	Impaired glucose tolerance		Total
	YES n=23	NO n=87	
Yes	12(24%)	38(76%)	50
No	11(18.3%)	49(81.7%)	60

Chi-Square = 0.53 p=0.467

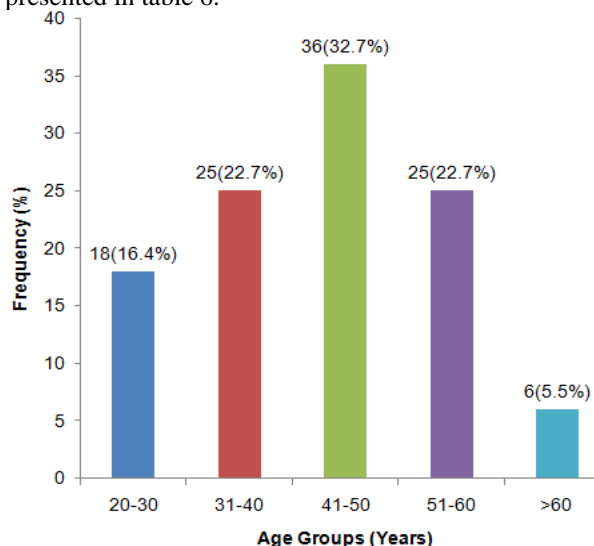
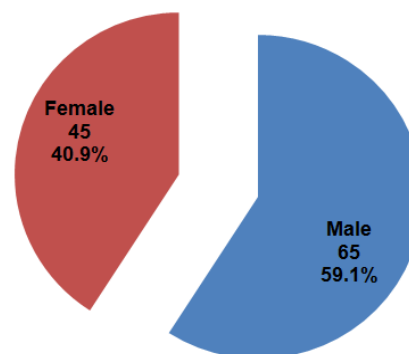
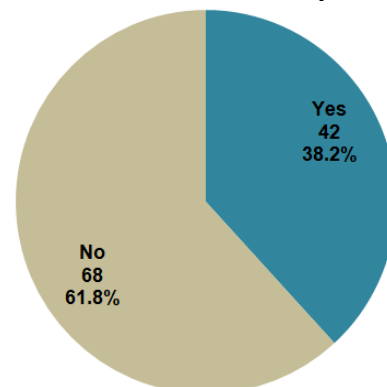
Table No.6: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis with respect to BMI of patients

BMI	Impaired glucose tolerance		Total
	YES n=23	NO n=87	
Under weight	8(32%)	17(68%)	25
Overweight	5(16.7%)	25(83.3%)	30
Normal	8(17.8%)	37(82.2%)	45
Obese	2(20%)	8(80%)	10

Chi-Square =2.458 p=0.48

Regarding categories of body mass index, 27.3% cases were overweight, 9.1% obese, 20.7% were under weight and 40.9% were normal as shown in figure 5. Abnormal GTT was observed in 26.36% (29/110) cases in which 1.8%(2/110) with impaired fasting glycemia and 3.6%(4/110) were frankly diabetic while frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis was observed in 20.9% (23/110) cases as presented in figure 6. Frequency of impaired glucose tolerance was high in above 40 years of age and significant difference was observed in percentage of IGT among the age groups ($p=0.001$) as shown in table 2. Rate of IGT was 31% (15/65) in male 14.7% (8/45) in female but statistically

significant difference was not observed between male and female (table 3). Rate of IGT was high in those patients who had family history of diabetes than those who had family history of tuberculosis (31% vs. 14.78%; $p=0.042$) while rate of IGT was not significant in those patients who had family history of tuberculosis than those who had not. (24% vs. 18.3% $p=0.467$) as shown in table 5. Rate of IGT was high in underweight but not statistically significant with other BMI groups as presented in table 6.

**Figure No.1: Age Distribution Of The Patients****Figure No.2: Gender distribution of the patients n=110****Figure No.3: Family history of diabetes of the patients n=110**

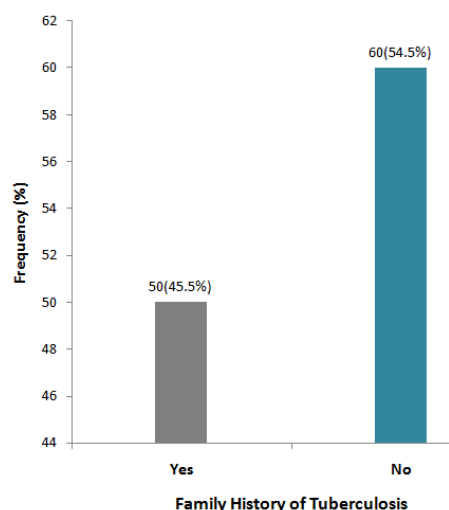


Figure No.4: Family history of tuberculosis of the patients n=110

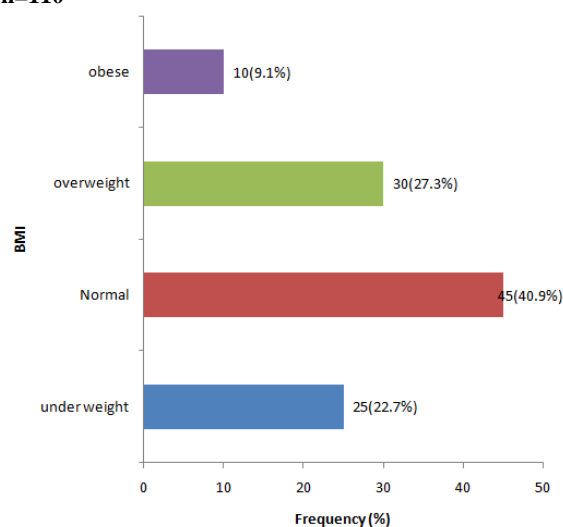


Figure No.5: Distribution of body mass index of the patients n=110

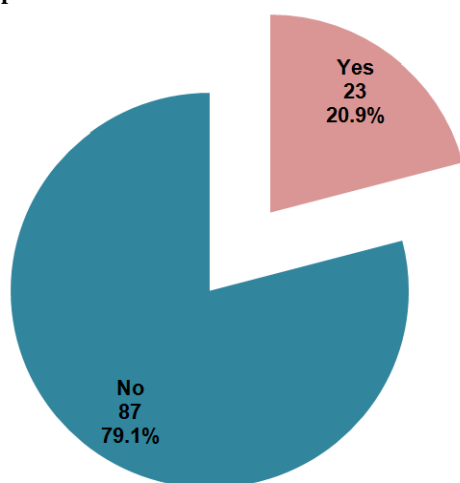


Figure No.6: Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis

DISCUSSION

Diabetics mellitus had noticed with a higher than usual risk of developing tuberculosis¹⁷. The frequency of tuberculous patients having diabetes concurrently tends to increase, and the relative risk of diabetics having tuberculosis is also high, a three to four times higher prevalence of tuberculosis had been observed in diabetic patients compared with non-diabetics¹⁸. Conversely, it is also possible that TB can induce glucose intolerance and also deteriorate glycemic control in subjects with diabetes¹⁹. The present study showed that there were 59.1% were male and 40.9% were female. Family history of diabetes was observed in 38.2% cases and family history of tuberculosis was 45.5% cases. Frequency of impaired glucose tolerance in patients presenting with active pulmonary tuberculosis was observed in 20.9% (23/110) cases. It was also observed in another study⁵ that the glucose intolerance was detected in 52 (49%) patients, 31 Impaired Glucose Tolerance (IGT), 21 Diabetes Mellitus (DM).

In Jain et al³ study the prevalence of abnormal GTT result was 18 (16.98%) which included 2 (1.88%) with impaired fasting glycemia, 11(10.34%) with impaired glucose tolerance and 5 (4.7%) were frankly diabetic. This result was statistically significant and compares to those found in the studies of Kishore et al²⁰ 20.9%, Singh et al²¹22.0 %, Mugusi et al⁹ 19 % and Yamagishi et al⁶&Parez JC²²14.1%. The present study revealed that while with the increasing age the number of tubercular patients declined, the prevalence of IGT increased. Frequency of impaired glucose tolerance was high in above 40 years of age and significant difference was observed in percentage of IGT among the age groups ($p=0.001$). The earlier exposure to pulmonary tuberculosis in our country and the development of resistance to the disease in later life accounted for involvement of younger population from tuberculosis. The higher prevalence of impaired glucose tolerance in the elderly was also observed by Kishore et al²⁰, who found that the prevalence of IGT was higher among patients aged 40 years or more. Yamagishi et al^{6,22} and Roy choudhary and Sen⁵ also had similar observations. In some recent studies done by Basugloet al⁴ and Lin et al⁷ a higher prevalence of IGT was found among the elderly. Patel et al²³, showing that 40-60 year old age group is the major affected group with about 57% of that study sample (251 diabetic patients with pulmonary tuberculosis) were 40-60 year old²⁴. many other studies showed that relative risk of having pulmonary tuberculosis is higher among diabetics aging less than 50 year old, specifically 30-49 year old with a relative risk of 9.88 and 4.72 in the 30-39 year and 40-49 year age group respectively, compared to somewhat lower relative risk in older age groups, 1.76 relative risk in those over 49 year old²⁴. In this study rate of IGT was

31% (15/65) in male 14.7% (8/45) in female but statistically significant difference was not observed between male and female. In another study the prevalence of IGT was significantly more in males (14/75-18.67%) than in females (4/31-12.90%). Out of the 18 patients with IGT majority i.e.14 (77.78%) were males. Yamagishi⁶ found the complication twice in males than in females. Fernandez et al⁸ found the prevalence in 6.2% in males and 3% in females. In present study the rate of IGT was high in underweight but not statistically significant with other BMI groups. Fernandez et al⁸ in another Indian study found that BMI was lower in both the IGT and Normal Glucose Tolerance Test (NGTT) groups, while Zack et al²⁴ and Mugusi et al⁹ found no significant differences in BMI in the two groups. Several theories have been put forward to explain why tuberculous patients develop glucose intolerance. Bloom²⁵ suggested that occult glucose intolerance predisposes to diabetes. Zack et al²⁴ suggested that glucose intolerance was not merely a reaction to acute tuberculous infection but rather a pre diabetic state. Hadden²⁶ suggested malnutrition in tuberculosis as a possible cause. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon and cortisol which raise the blood sugar level²⁷. Roychoudhary and Sen⁵ suggested tuberculosis of pancreas as the possible cause. Similarly, higher incidence of chronic calcific pancreatitis occurs in patients of diabetes and pulmonary tuberculosis leading to absolute or relative insulin deficiency state. Clinical and subclinical hypoadrenalism has been described in these patients²⁸. Plasma levels of IL-1 and TNF- α are also raised in severe illness, which can stimulate anti-insulin responses. Age, co-existing illness and alcoholism also influence the host response⁶. Physician giving diagnosis and treatment of diabetes mellitus should understand that diabetics belong to the high risk group of developing tuberculosis and perform chest X-ray examination periodically^{16,29}. There is evidence that diabetes is associated with a progressive shift of male predominance pulmonary tuberculosis. Perez et al³⁰ showed that in the non-diabetic population, male incidence of about 51%, compared to 75% frequency of tuberculosis among male diabetics.

Nakamoto found that 13 of 19 patients included in his study (68.4%) had poor glycemic control³¹. This study revealed that 8 patients (32% of the sample) had previous history of tuberculosis which is a percentage that can be considered as being higher than what is seen in non diabetic patient³². Diabetes is associated with high risk of recurrent tuberculosis. The important idea is that many of those with recurrent tuberculosis will have infection with resistant strains of mycobacterium. Studies conducted in regions with dual burden had reported that the prevalence of DM ranged from 14–40%³³. A case control study conducted in Bangalore,

South India, during 2001– 2003 reported that chronic disease particularly diabetes was a significant risk factor for developing TB. The prevalence rates of diabetes in TB and non-TB subjects were 22.2% and 15.9% respectively³⁴. Based on secondary analysis of countrywide data, another research group estimated that 18.4% of subjects with PTB also have DM in India. A retrospective analysis of 2 years data on TB subjects from Saudi Arabia in 1998 revealed that 27% had DM³³. Another study from Taiwan reported 16.9% of DM among TB patients³⁵. All these reports indicate that routine screening for DM among TB patients should be encouraged in areas with high TB burden. Alisjahbana et al³⁶ reported prospective data from a cohort of patients with TB in Indonesia, where the prevalence of confirmed DM among patients with TB is 14.8% compared with 3.2% in general population. A nationwide INDIAB study³⁷ conducted in the general population of Tamil Nadu, South India, showed that the prevalence rates of diabetes and pre-diabetes were 10.4% and 8.3% respectively, substantially lower in comparison with the estimated prevalence of DM and pre-diabetes in the current study among TB patients conducted in the same period.

CONCLUSION

In Pakistan DM is on the rise and TB has one of the highest incidence in the world. There is emerging evidence that one disease is fuelling the other. The interest in diabetes and TB is mounting rapidly, so the clinician & researchers should prepare themselves to meet the challenges of the two disease combined.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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