

Research Article**Comparative Study of Oral Glucose Tolerance Test in Sputum Positive Pulmonary Tuberculosis Category I and II RNTCP Regimens****Dr. S.S. Antin. M.D.¹, Dr Mohan Kashinkunti*², Dr. Sowmya.T.V³, Dr Dhananjaya M³, Dr Shruthi.Alevoor⁴**¹Prof & Head, Dept of Medicine Navodaya Medical College, Raichur. Karnataka, India.²Professor, Department of Medicine, SDM College of medical sciences and hospital, Sattur, Dharwad-580009, State-Karnataka, India.³Postgraduate student, ⁴Intern. SDM College of medical sciences and hospital, Sattur, Dharwad-580009, State-Karnataka, India.***Corresponding author**

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Abstract: The present study was conducted to determine the impairment of glucose tolerance in sputum positive pulmonary tuberculosis patients under category I and II regimens. The study comprised of 100 sputum smear positive pulmonary tuberculosis patients grouped under category I and II based on the previous history of tuberculosis and intake of ATT. Patients were subjected to Oral Glucose Tolerance Test as per WHO guidelines. Patients were classified as having impaired glucose tolerance or Diabetes mellitus based on ADA guidelines. The study revealed that most of the cases were aged between 41-50 years with majority of the patients being males (70%). Most of the patients were underweight(BMI <18.5) as compared to controls. The study revealed that 4 patients (8%) had diabetes mellitus. The impairment of glucose tolerance was evident in both categories with a statistical significance (p<0.001). There is a high degree of association between impaired glucose tolerance and tuberculosis. Universal screening for diabetes mellitus among people with tuberculosis is recommended. Detection of impaired glucose tolerance in TB patients and timely intervention may reduce the risk of potential effects of the deadly duo.**Keywords:** Sputum, Positive pulmonary tuberculosis, Category I and Category II regimens, Impaired glucose tolerance

INTRODUCTION

Tuberculosis is an infectious disease worldwide caused by Mycobacterium tuberculosis. Tuberculosis is recognized as the single biggest killer [1]. In 1993, the WHO declared it as a global emergency due to increased prevalence worldwide [2]. India has the highest prevalence worldwide, accounting for an estimated 1/5th of all patients. One of the chief components affected is the blood. Hence this work of our puts in an effort to correlate the changes in blood worldwide [3]. Diabetes mellitus is a metabolic disorder due to defective insulin secretion and/or insulin action. 347 million people have diabetes mellitus with 7 million new cases being added every year.

It is predicted that the global prevalence of diabetes mellitus will increase by 2/3rd by 2030 with the number deaths doubling between 2005-30 [1]. India leads the world with the largest number of diabetics earning the dubious distinction of the world's diabetes capital. Studies have shown that Indian are inherently more insulin resistant when compared to other world population groups and develop diabetes at a younger age.

There is rising concern about the merging epidemics of tuberculosis and diabetes mellitus in low and middle income countries like India [3]. Higher prevalence of pulmonary tuberculosis in diabetic patients is a well known fact. The inverse relationship i.e. higher prevalence of impaired glucose tolerance in a tuberculosis population is also being increasingly recognized.

The present study is aimed at assessing the impairment of glucose tolerance category I and II tuberculosis patients attending the OPD and IPD of Navodaya Medical College Hospital, Raichur, Karnataka.

MATERIALS AND METHODS

The present study consists of 100 subjects (79 males, 29 females) who presented with clinical symptoms suggestive of TB like cough lasting for 2 weeks or more, evening rise of temperature, malaise, weight loss. Patients who were known diabetics, on known diabetogenic drugs, with liver diseases and pregnant women were excluded. They were interviewed and

detailed data regarding their socioeconomic conditions, age, family history, past history, household contact of TB, addictions and other details were collected and complete clinical examination was done. These patients were subjected to sputum smear examination for acid fast Tubercle bacilli (AFB). Patients were diagnosed as having pulmonary tuberculosis if at least one sputum sample was smear positive for AFB using Ziehl-Neelson stain as per the guidelines of RNTCP6. Patients who were sputum smear positive for AFB were grouped into Category I and II based on the history of previous intake of ATT under RNTCP regimen. Smear positive patients were subjected to oral glucose tolerance test as per WHO guidelines.

Statistical Analysis

Analysis of variance has been used to find the significance of study parameters between 3 or more groups of patients. Chi-square/Fisher Exact test has been used to find the significance parameters on categorical scale between two or more groups. The statistical software, namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for analysis of the data.

Significant figures: ⁺Suggestive significance (P value: 0.05 < P < 0.10), ⁰Moderately significant (pre-value:0.01 <P ≤ 0.05), ^{**}Strongly significant (p value: P ≤ 0.01)

RESULTS

A total of 100 patients were studied(71 males, 29 females). 35 of the cases under category I were males and 15 were females. In category II 36 were males and 14 were females. Out of 50 patients in category I, maximum number of patients(19) were in the age group 41-50 years. In category II, 12 were in the age group of 31-40 years and 14 were in the age group 51-60 years. Samples were age matched with P=1.00. 15(30%) under category I were underweight with BMI<18.5 vs 30(60%) in category II. The variables weight and BMI in category I(19.42±1.31) and category II(18.25±1.04) were strongly significant with P<0.001.

The FBS was below 110mg/dl in 38(76%) in category I, 30(60%) in category II as compared to controls where all the subjects had FBS<110mg/dl(100%). In category I 11(22%) had impaired fasting glucose with FBS 110-125mg/dl vs 15(30%) in category II. Under category I , 1(2%) had FBS greater than 126mg/dl as compared to 5(10%) in category II. The mean FBS value in Category I was 97.92 ± 11.32 vs 108.12±12.58 in category II as compared to control's 86.58 ± 6.38 with a statistical significance P<0.001. In category I, there were 19(38%) with 2 hours PPBS values <140mg/dl, 31(61%) with PPBS 140-199mg/dl. In category II, there were 19(38%) with 2 hours PPB<140mg/dl, 27(54%) were with PPBS 140-199 mg/dl, 4 with PPBS> 200mg/dl. In control's, all 50 had PPBS<140mg/dl. The mean PPBS value under category I was 142.62±13.44 vs 151.60±24.36 in category II as compared to controls with a statistical significance P<0.001.

Table 1: Distribution of sugar parameters in 3 groups of cases and controls studied

Sugar parameters	Category I (n=50)		Category II (n=50)		Control(n=50)		P value
	No	%	No	%	No	%	
FBS mg/dl							
<110	38	76	30	60	50	100	<0.001**
110-125	11	22	15	30	0	00	
>126	1	2	5	10	0	00	
PPBSmg/dl							
<140	19	38	19	38	50	100	<0.001**
140-199	31	62	27	54	0	00	
>200	0	0	4	8	0	00	

Mean age in male patients with tuberculosis being 45.55±14.14 vs mean age in female patients being 44.00 12.41 with a p value of 0.608. Mean BMI among male patients is 18.75 1.25 compared to BMI 19.05 1.49 found in females patients with a p value of 0.305. Mean FBS value among male patients is 102.92 13.17mg/dl in female patients with a p value of 0.900. Mean PPBS value in male patients is 146.46 21.37mg/dl compared to 148.69 16.79mg/dl in female patients with a p value 0.618.

DISCUSSION

Pulmonary tuberculosis is a deadly bacterial disease. Tuberculosis, like other bacterial infections alters the carbohydrate metabolism. Mycobacterium can metabolise fatty acids and use it as their carbon source causing lipid metabolism derangements which were shown to be the driving force into the pathogenesis of insulin resistance⁸. Impairment of glucose tolerance in pulmonary tuberculosis patients worsens the disease. Hyperglycemia affects the cellular immunity and host resistance with further worsening of the disease. Hyperglycemia favours the growth, viability and

propagation of tubercle bacilli nitrogenous substances which aid the growth of tubercle bacilli [5].

In the present study the mean age of patients suffered by tuberculosis was 45.1 yrs. The mean age distribution among the males was 45.5 yrs. Lincoln A Sargeant *et al* [11]. showed the mean age of 46.3 yrs in males and 44.6 in females. Study done in Tanzania showed a mean age of 34.8yrs in males and 33.8 in females. Vijay *et al* [10] showed a mean age of 43.6 in males and 35.6 yrs in females. Age distribution in our study has shown 19 patients (38%) in the age groups of 41-50 years in category I patients and 14 patients (28%) in the age groups of 51-60 years in the category II patients. The higher prevalence of impaired glucose tolerance in the elderly is noted in our study and same was also observed by Kishore *et al* [13] who was the prevalence of IGT was among the higher among patients aged more than 40 years. Yamagishi *et al*, [14] and Basuglo *et al* [15] also found a higher prevalence of IGT among patients aged more than 40 yrs. The cause of IGT in elderly needs further evaluation [6,7].

Sex distribution in our study has shown the prevalence of tuberculosis was more in males with 35 patients in category I and 36 patients in category II as compared to females with 15 patients in category I and 14 patients in category II. The prevalence of IGT was significantly more in males (40/58) than in females (18/58) in both categories. This is in accordance with Yamagishi *et al* [14], Fernandez *et al* [16] And M.K.Jain *et al* [17] The mean BMI in Tanzanian study was 14.4 study done by Vijay *et al* showed a mean BMI of 18.54 4 Our study showed a mean BMI of 18.8 1.32 BMI among males was 18.75 1.24 Mean BMI among females was 19.05 1.49 with women having BMI more than that in males in accordance with Vijay *et al* in category I patients BMI was < 18.5 in 15 (30%) VS 30(60%) In category II patients with a statistical significance ($p < .001$) which was similar to the findings of M.K.Jain *et al* [17] indicating malnutrition fever and stress as the factors leading to the weight loss. Present study showed 4 (8%) patients with type II DM in category II overall prevalence of IGT was 58% In category I had 35 patients (62%) and category II had 27 patients (54%) prevalence of impaired glucose tolerance in both cat I and cat II were statistically significant ($p < 0.001$) has compared to controls. Our findings are in accordance with the findings of Kishore *et al* (20.9%) [13] Zack *et al* (41%) [18] Oluboyo and Erasmus (3.7%) [19] Mugusi *et al* (49%) (20) Yamagishi *et al* (14.1%) [14] M K Jain (16.98%) [17] Vijay *et al* (16.3%) [6-9].

Patients who were found to be diabetic were started on appropriate oral hypoglycemic agents. Patients with impaired glucose tolerance were advised appropriate lifestyle and diet modifications the results of which are beyond the scope of this study.

Several theories are put forward to explain why tuberculosis patients developed glucose intolerance. Zack *et al* [18] suggested that glucose intolerance was not merely reaction to acute tuberculosis infection but rather a pre diabetic state. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine glucagon and cortisol which raise the blood sugar levels. Clinical and sub clinical hypoadrenalism has been described in TB patients has reported by Guptan *et al* [22] Plasma levels of IL 1 and TNF alpha are raised in severe illness like TB which can stimulate the anti insulin hormones has reported by Fong *et al*. Pulmonary TB is secondary to infection as suggested by Olubuyo *et al* [19] increased prevalence and increase degree of Hyperglycemia observed in category II patients could be due to the effect of anti tuberculosis therapy on the functioning of pancreas or due to pancreatic calcification effecting insulin secretion or insulin resistance. TB of pancreas has also been suggested as a cause of IGT. Rifampicin has been shown to produce to show early phase hyperglycemia possibly by augmenting intestinal absorption of glucose [10]. It has been shown that glucose intolerance during active pulmonary TB improves or normalizes after adequate therapy. Co existence of both TB and impaired glucose intolerance compounds the negative effects of one another adversely affecting the prognosis and results in delayed sputum conversion increased risk of mortality and morbidity multi drug resistance and takes long time to respond to treatment. Preliminary screening of all suspected and diagnosed TB patients for OGTT helps to detect diagnosed and to intervene with proper medical treatment to prevent the co-morbid spread of diseases.

CONCLUSION:

Given the a high association between TB and dysglycemia, recommendation for universal screening for DM amongst people with TB and subsequent glycaemic control would not seem out of place in a country like India with huge double burden. There is a need for greater collaboration between RNTCP and national program for prevention and control for cancer. Diabetes, CVD and stroke in India to ensure that protocols and guidelines are in place to address the dual burden.

In site into the basic mechanism of these disorders early screening co ordinate treatment better management is the primary dictum to prevent the risk of spread of diseases and at least to aim for eradication of the deadly disease TB.

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