

**A STUDY OF IMPAIRED GLUCOSE TOLERANCE TEST IN PULMONARY TUBERCULOSIS**Devpriya Lakra<sup>1</sup>, M. K. Minj<sup>2</sup>, Rashmi Dewangan<sup>3</sup>, S. P. Kujur<sup>4</sup>, R. C. Arya<sup>5</sup>, A. K. Bhardwaj<sup>6</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT:** The link between Diabetes mellitus & Tuberculosis has been recognizing for centuries. Recently Tuberculosis has re-emerged as a major health concern. There is growing evidence that Diabetes mellitus with Tuberculosis may affect disease presentation and treatment. The Tuberculosis also influences glucose intolerance and influences the glycaemic control in the people with Diabetes mellitus. Approximately 2 Million persons worldwide died of Tuberculosis and 9 Million become infected each year. (CDC, 2007)<sup>1</sup>. With the convergence of tuberculosis and diabetes Mellitus epidemic, co-affliction with the two diseases is on the rise. The observational study was conducted with 100 patients. The patients with Pulmonary Tuberculosis sputum positive/negative with radiological lesions was admitted in medicine wards of our hospital between years 2009-2011. The aim of our study is to find out the prevalence of GTT in patients of Pulmonary Tuberculosis Age, sex distribution of impaired Glucose Tolerance Test (GTT) in Patients with pulmonary tuberculosis and study the correlation between impaired GTT with Sputum positivity and also radiological extent of disease. The patients were subjected to oral GTT and results were evaluated according to the WHO criteria and the statistical analysis was done to determine the P value and significance on the basis Chi-square test. The results found in the studied patient were that prevalence of abnormal GTT in Pulmonary Tuberculosis patients was found to be 22% (P=0.07). Abnormal GTT was more common in males as compared to females and this was found to be significant (P=0.692). Sputum positive Pulmonary Tuberculosis is strongly associated in patients with abnormal GTT (P=0.03), and bilateral lung involvement was more common among Pulmonary Tuberculosis patients with abnormal GTT.

**KEYWORDS:** Pulmonary Tuberculosis, Impaired Glucose tolerance.

**INTRODUCTION:** Tuberculosis has recently re-emerged as a major health concern. The Global burden of diabetes mellitus is expected to rise from an estimated 180 Millions to prevalent cases currently to a predicted 366 million by 2030 with the greatest increase projected in the developing world. (WHO, 2006).<sup>2</sup> With the convergence of Tuberculosis and Diabetes Mellitus epidemic, co affliction with the two diseases is on the rise. (Stevenson CR et al, 2007).<sup>3</sup> Studies conducted after the introduction of glucose tolerance test in 1950 have shown high prevalence of impaired glucose tolerance test in patients with Tuberculosis with rates ranging from 2 % to 41%. There have been reports of high prevalence of diabetes in cases of Tuberculosis (4 to 20%) & rates are higher for impaired glucose tolerance test (16 to 29%) (Mboussa J et al, 2003).<sup>4</sup>

Impaired fasting Glucose & impaired Glucose tolerance referred to the intermediate metabolic state between normal and diabetic glucose homeostasis. One or both of these conditions are thought be the precursors of diabetes mellitus, but how they progresses to overt

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disease is not well understood. The risk for both macro & micro vascular complications increases across the distribution of blood glucose concentration well below the level for overt diabetes mellitus and is more strongly associated with post challenge hyperglycaemia than fasting glucose level.

Diabetes has been associated with increased risk of all Tuberculosis treatment failure or relapse (Morsy AM et al, 2003)<sup>5</sup> and diminished 2 months and 6 months culture conversion rates (Guler M et al 2007).<sup>6</sup> Diabetes mellitus have been associated with increased risk of all causes mortality in Tuberculosis patients & more specifically death related to Pulmonary Tuberculosis (Wang CS et al 2009).<sup>7</sup> It has also been found that Tuberculosis patients are more prone to develop Diabetes mellitus. Probable causes of higher prevalence of Diabetes mellitus in Tuberculosis may be reciprocal worsening of the two process by each other; Malnutrition and low BMI; Pancreatic Tuberculosis in rare cases; stress induced Diabetes mellitus due to Tuberculosis and pituitary and adrenocortical hyper-reactivity; and vitamin D deficiency (Banerjee S JIMA 2005).<sup>8</sup>

Sputum examination is of great value in making the diagnosis of Pulmonary Tuberculosis and in following the patient's response to treatment. Sputum smear examination is usually positive in advanced disease but may be negative in less advanced disease. Sputum smear examination has a sensitivity of about 50% and a specificity of greater than 99% in two reported studies, with a positive predictive value of 91–98.5%.

**METHODS:** The study was conducted in patients of Pulmonary Tuberculosis attending outdoor patients department and those admitted in medicine ward in our hospital during the year 2009-2011. The study group consisted of 100 patients of Pulmonary Tuberculosis, who had either sputum positive or negative smear for Acid Fast bacilli and had clinical or radiological features of Tuberculosis. All the patients were subjected to Oral Glucose Tolerance Test & results evaluated according to criteria laid down by WHO for diabetes.

The patient included in our study were of age above 18 years, were Sputum +ve AFB patients or Sputum -ve AFB with clinical or radiological features of Pulmonary Tuberculosis. The patients excluded were, below 18 years of age, Diabetes Mellitus Patients, Pregnancy, Critically ill patients and HIV positive patients.

OGTT (Oral Glucose Tolerance Test) was done in all the patients and results evaluated and interpreted as per the WHO guidelines.

The Sputum examination of the patients was done by Ziehl Neelsen's stain method to visualize acid-fast bacilli (e.g. Mycobacterium tuberculosis and mycobacterium leprae). Three Sputum specimen preferably early morning sample was collected for AFB smear and mycobacterium culture.

All the patients were subjected to radiological examination chest x-ray and the film was evaluated for infiltrate or consolidation, any cavitary lesion, pleural effusion, hilar or mediastinal lymphadenopathy, infiltration of one side of lungs or both sides were studied. (CDC guideline 2009).

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**OBSERVATIONS:** The observations made taking various points of study are as follows:

Category	Total No. of cases	Abnormal GTT		Normal GTT	
		Number	%	Number	%
Cases	100	22	22	78	78

Table 1: Prevalence of abnormal GTT cases

Chi square value-4.01 Significant Level, P=0.07.

In our study, (table no.1) the total 100 patients were studied, all patients were subjected to the standard Oral Glucose Tolerance Test. Out of 100 patients, 22% patients were found having abnormal Glucose Tolerance Test and remaining 78% patients were having normal Glucose Tolerance. Hence the results were significant.

Sex	Abnormal GTT N=22		Normal GTT N=78		Total
	No.	(%)	No.	(%)	
Male	15	68.2	50	64.165	65
Female	07	31.8	28	35.9	35
<b>Total</b>	<b>22</b>		<b>78</b>		<b>100</b>

Table 2: Sex wise distribution of cases

Chi square value-0.756 Significant Level, P=0.692.

In this study, (table no.2) out of 100 patients, 65 were male and 35 were female. The 22 patients were found having abnormal GTT and 78 were having normal GTT. In patients with abnormal Glucose Tolerance Test (i.e. N=22), the 15 patients were Male and 07 patients were female, which were 68.2% and 31.8% of the total patients with abnormal GTT respectively. Thus in this study the number of Male patients were found to be more than female patients both in case of normal as well as abnormal GTT.

Category	Abnormal GTT N=22		Normal GTT N=78		Total
	No.	(%)	No.	(%)	
18-30	2	9.1	36	46.1	38
31-40	3	13.6	15	19.2	18
41-50	3	13.6	10	12.8	10
51-60	10	45.5	10	12.8	20
>60	4	18.2	7	8.9	11
<b>Total</b>	<b>22</b>		<b>78</b>		<b>100</b>

Table 3: Age wise distribution of cases

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In this study, (table no. 3) the patients were categorized and evaluated on different age group slabs. The patients with abnormal GTT, 2(9.1%) patients were between 18 to 30 years age group, 3 (13.6%) were in the age group between 31-40 years, 3(13.6%) were in the age group 41-50 years and 10 (45.5%) patients were in age group between 51-60 and remaining 4(18.2%) patients were in the age group greater than 60 years. In patients with normal GTT 36(46.1%) patients were in age group 18-30 years, 15(19.2%) patients were in age group between 31-40 years, 10(12.8%) patients were in age group between 41-50 years, 10(12.8%) patients were in age group between 51-60 years and remaining 7(8.9%) patients were in age group above 60 years. Thus most of the patients with abnormal GTT were in the age group 51-60 years followed by greater than 60 years age group.

Sex	Abnormal GTT N=22		Normal GTT N=78		Total
	No.	(%)	No.	(%)	
Male	05	22.7	04	5.1	09
Female	04	18.2	02	2.6	06
<b>Total</b>	<b>09</b>	<b>40.9</b>	<b>06</b>	<b>7.7</b>	<b>15</b>

**Table 4: Prevalence of sputum positive pulmonary. Tuberculosis with Normal & Abnormal GTT**

Chi square value-4.01 Significant Level, P=0.03.

In this study, (table no. 4) out of 22 patients with abnormal Glucose Tolerance Test, 9(40.9%) patients were found having sputum positive. Out of 9 patients 5(22.7%) patients were Male and 4(18.2%) patients were Female. Out of 78 patients with normal GTT, 6 patients were found sputum positive. Out of which, 4(5.1%) patients were male and 2(2.6%) were female. Thus in this study, it is found that male patients were more sputum positive as compared with female patients. Further from above study, it is found that patients with abnormal GTT (N=22) were having 40.9% case of sputum positive while the patients with normal GTT (N=78) were having only 7.7% of cases of sputum positive. Hence results found in the study are significant.

Side of Lungs affected	Abnormal GTT N = 22		Abnormal GTT N = 22	
	No.	(%)	No.	(%)
Right	02	9.1	27	34.6
Left	02	9.1	16	20.5
Bilateral	18	81.8	35	44.9

**Table 5: Chest Radiograph finding in pulmonary tuberculosis patients with Abnormal & Normal GTT**

Chi square value-6.37 Significant Level, P=0.01.

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In above study, (table no. 5), it is found that out of 22 patients with abnormal GTT, 22 patients (9.1%) had right side lung affected with pulmonary tuberculosis, 2 patients (9.1%) had left side lung affected with pulmonary tuberculosis and 18 patients (81.8%) had bilateral affected with pulmonary tuberculosis. On the other hand, out of 78 patients with normal GTT, 27 patients (34.6%) had right side lung affected with pulmonary tuberculosis, 16 patients (20.5%) had left side lung affected with pulmonary tuberculosis and 35 patients (44.9%) had bilateral affected with pulmonary tuberculosis. By comparing with both figures of abnormal GTT and normal GTT cases, it is clear bilateral involvement of lung is more common, so the study is significant.

**DISCUSSION:** In our study, the prevalence of abnormal GTT was 22% in TB patients. In Study done by M K Jain et al, 2006<sup>9</sup> out of 106 patients, the prevalence of abnormal GTT results was 18(16.98%) which was statistically significant and compares to those found in the studies of Kishore et al, (1973),<sup>10</sup> 20.9%, Singh et al(1978),<sup>11</sup> 22.0%, Mugusi et al, 1990,<sup>12</sup> 19% and Yamagishi et al, 2000,<sup>13</sup> 14.1%.

The results found in the other studies were Khanna (1968),<sup>14</sup> 6.6%, Zack et al, (1973),<sup>15</sup> 41%, Roychaudhary et al (1980),<sup>16</sup> 27.25%, Marais, (1980),<sup>17</sup> 2.1%, Oluboyo and Erasmus(1980),<sup>18</sup> 3.7%, Fernandez et al (1997)<sup>19</sup> 9.3%, Basuglu et al(1999),<sup>20</sup> 19%, Firsova et al(2000),<sup>21</sup> 10.8%.

According to the study done by M K Jain et al, (2006)<sup>9</sup> with the increasing age the number of TB patients decline, the prevalence of IGT increase. In our study the prevalence of Impaired Glucose Tolerance is more in elderly group aged between 51 -60 years. The higher prevalence of IGT in the elderly was also observed by Kishore et al (1973),<sup>10</sup> who found that, the prevalence of IGT was higher among patient aged 40 years or more. Yamagishi et al (2000)<sup>13</sup> and Roychaudhary and Sen (1980)<sup>16</sup> also had similar observations. In some other studies done by Basuglo et al (1999) and Lin et al (1998),<sup>20</sup> a higher prevalence of IGT was found among elderly. In this study, the prevalence of IGT was more in male as compared to female. In study done by Fernandez et al (1997),<sup>19</sup> found the prevalence 6.2% in male and 3% in female. According to M K Jain et al (2006)<sup>9</sup> out of 18 patients with IGT majority i.e. 14 (77.78%) were Males.

In our study, the prevalence of Diabetes was 5 % among patients with abnormal GTT. In Cohort study, the presence of underline illness (DM, COPD, renal failure) and immune suppression were important predictors of survivors for patients with TB.(Oursler KK et al,2002).<sup>22</sup> In patients with TB, the most common underline disease was DM. Studies that screened for DM among patients with TB also reported a wide range of DM prevalence ranging from 1.9% to as high as 30%. For example in Veracruz, Mexico were the base line DM prevalence is relatively high at 7.6%, 35% of the screened TB patients were found to have DM. (Ponc De Leon et al 2004).<sup>23</sup>

In recent study in Taiwan, DM was the most common underline commodity in patients with culture confirmed TB, present in 21.5% of patients.(Wang JY et al, 2005).<sup>7</sup> DM prevalence in TB according to various studies are Nichols 1957<sup>24</sup> -5.1%, Kishore et al 1973<sup>10</sup>-5.6%, Singh et al 1984<sup>11</sup> 1.9%, Oluboyo& Erasmus 1990<sup>18</sup>, 1.9%, Golsha et al 2009<sup>25</sup> 2.3% and Balde et al 2006<sup>26</sup> 3.4%.

In our study, most commonly bilateral lung involvement seen in 18 patients (81.8%) with lower zone involved in 16(72.7%) patients in cases of abnormal GTT. Most common lung lesion was infiltration 10 (45.4%) patients, followed by pleural effusion 6 (27.3%) patients and cavitary

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lesion 5 (22.7%) among patients with abnormal GTT. In the study by Perez-Guzman C et al, 2001<sup>27</sup> lower lung field involvement was the most frequent change, with upper and middle changes less common. Bilateral changes were present half of the patient and as associated effusion were present in one third. In comparative study of TB patients with and without DM, being diabetic was found to be the most important factor determining lower lung field lesion. In a second study the lower lung TB was only seen in older diabetic patients above 40 years and female sex.(Bacakoglu F et al, 2001)<sup>28</sup>. Other studies have however failed to show any differences in localization of TB lesions. (AI Waben AH et al, 1997<sup>31</sup>, Ikezeoe J et al, 1992)<sup>30</sup>.

Cavitation was seen in 26% of patients, a higher rate multiple cavitations has been reported in studies (Perez-Guzman C et al 2001,<sup>29</sup> Bacakoglu F et al, 2001<sup>28</sup> Ikezeoe J et al, 1992)<sup>30</sup> but not in study done by AI Waben AH et al, 1997.<sup>31</sup> Lower field involvement was very frequent (less than 70%) among diabetics at any age group. (Perez-Guzman C et al, 2001).<sup>27</sup> According to M K Jain et al, 2003<sup>9</sup> unilateral lung involvement was seen in 11 out of 18 (61.11%) cases with IGTT while bilateral involvement was seen in 7 out of 18 (38.89%) cases. Most common lesion was infiltration in 7 (22.58%) while cavitary lesion with fibrosis was seen in 4(20.0%) with IGT. Lower zone was significantly more commonly involved among those with impaired glucose tolerance. Similar observations was seen in the studies by Mugushi et al 1990<sup>12</sup> and Marais et al 1980<sup>17</sup> who found lower zone involvement in 27% and 29% cases respectively.

Mugushi et al, 1990<sup>12</sup> found bilateral lung involvement in 47.2% of cases. Lung infiltration was seen as the most common lung lesion in 22.58% cases while cavitary lesion with varying amount of fibrosis was seen in 20% of cases. Cavitary lesions were the predominant lesion in studies by Mugushi et al 1990,<sup>12</sup> Fernandez et al 1997<sup>19</sup> and Parez et al 2000.<sup>27</sup>

The greater association between Diabetes and sputum smear positive TB compared to smear negative Pulmonary TB has been found in most, but not all studies. (Stevenson C R et al 2007)<sup>3</sup> A recent large retrospective study involving the Texas –Mexico border region revealed significantly higher rate sputum smear positivity during the first month of treatment among patients with self-reported DM. (Restrepo BI et al, 2007).<sup>31</sup> Several studies indicate that patients with TB who have DM, present with a higher bacillary load in sputum. (Singla et al, 2006), delayed micro bacterial clearance (Gullar M et al, 2007)<sup>04</sup> and higher rates of MDR infections (Basher M et al 2001).<sup>32</sup> In our study sputum positive found in 9 patients (40.9%) in patients with abnormal GTT and 6 patients (7.7%) with normal GTT.

**CONCLUSION:** To conclude the high prevalence of impaired glucose tolerance in patients of pulmonary tuberculosis observed in this study probably reflects an increased association between TB and DM. Further evidence is provided by the fact that correlation between extent of radiological lesion and IGT achieves statistical significance. The results are highly suggestive of positive association with bilateral lung involvement, infiltration of lung lesion and lower zone involvement more common among patients with impaired glucose tolerance.

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