Impact of Glycemic Status in Patients with Tb Alone and Tb with Diabetes Mellitus

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ABSTRACT

India is a key nation which is endemic and epidemic to tuberculosis and diabetes. An association between diabetes and TB is biological plausible, for diabetes impairs the immune system, making it harder for the body to fight against infection. Diabetes has been associated with increased risk of TB treatment failure or relapse, and diminished 2 month and 6 month culture conversion rates. Hence this study was aimed to study the effect of anti-TB drugs in patients with TB alone and TB with Diabetes groups and also to study the prevalence and incidence rate of TB cases and Diabetes in TB cases. Prevalence of tuberculosis among diabetic is 2.5 times higher than in the non-diabetic population, and a higher rate of lower lung field involvement seen in diabetic patients[7..] In 85% of the patients, tuberculosis had developed after the onset of diabetes. The association is more common among those above 40 years of age and males appear to be at a greater risk compared with females. Diabetes may also complicate the management of tuberculosis.

Keywords: Tuberculosis, Glycemic status, Lung field.

INTRODUCTION

The global burden of disease from diabetes and tuberculosis is immense[3]. India is a key nation which is endemic and epidemic to tuberculosis and diabetes[1,15]. Tuberculosis is a major public health problem in India. India accounts for one fifth of the global burden of TB incident cases. Each year nearly 2 million people in India develop TB, of which around 0.87 million are infectious cases. It is estimated that annually around 3,30,000 Indians die due to TB[4].

An association between diabetes and TB is biological plausible, for diabetes impairs the immune system, making it harder for the body to fight against infection[5].

Clinicians have observed an association between DM and TB, although they were often unable to determine whether DM caused by TB or whether TB led to the clinical manifestations of DM. Multiple rigorous epidemiological studies, have demonstrated that DM is indeed positively associated with TB.

A causal link between DM and TB does not bode well for the future, as the global burden of DM is expected to rise from an estimated 180 million prevalent cases currently to a predicted 366 million by 2030. Experts have raised concerns about the merging epidemics of DM and TB.

Prevalence of tuberculosis among diabetic is 2.5 times higher than in the non-diabetic population, and a higher rate of lower lung field involvement seen in diabetic patients[7..] In 85% of the patients, tuberculosis had developed after the onset of diabetes. The association is more common among those above 40 years of age and males appear to be at a greater risk compared with females. Diabetes may also complicate the management of tuberculosis[8].

TB is more common in patients with diabetes, especially in those with poor glucose control. Diabetes has been associated with increased risk of TB treatment failure or relapse, and diminished 2 month and 6 month culture conversion rates.

Hence this study was aimed to study the effect of anti-TB drugs in patients with TB alone and TB with Diabetes groups and also to study the prevalence and incidence rate of TB cases and Diabetes in TB cases.

MATERIAL AND METHODS

The protocol was accepted by Institutional Ethics Committee. It was a Prospective case control study conducted at a tertiary care hospital, Tamil Nadu. Patients on DOT treatment in continuation phase of anti-TB therapy, Patients with TB and Diabetes and Patients with TB alone were included in the study. Where as HIV positive. Pregnant and lactating women, Abnormal renal functions and Abnormal liver functions were excluded from our study. Patients under went tests for Blood glucose and Lipid profile. Blood samples were collected and Fasting Blood Glucose (FBG), Post Prandial Glucose (PPG) and Glycated Hemoglobin (HbA1c) were measured to understand the glycemic status and its

impact on TB treatment outcomes. Similarly, Total Cholesterol, Triglycerides, HDL and LDL were also measured to find whether any variation in these among the test and control groups. For the Prevalence and Incidence Studies, the datas were collected from TB register and OP register of TB center, Namakkal and Erode District Government Hospitals, and grouped based on sex, class of disease, category of treatment, HIV status, sputum smear test results, type of patients, treatment outcomes and age groups.

RESULT

1. Effect of anti-TB drugs in patients with TB alone and TB with Diabetes group, 46 and 49 patients of each group were included and the following parameters were assessed (table 1).

	TBDM group	TB group	P value
Age (28-60)	49	46	0.2742
Karnofsky Performance Status Scale (60-90)	72.5	75	0.3093
Temperature (F)	98.6	98.6	0.1426
Pulse rate (bts/min)	74	74	0.3906
Systolic BP (mmHg)	123	125	0.2696
Diastolic BP (mmHg)	84	80	0.0447
FBG (mg/dl)	179	72	0.0231
PPG (mg/dl)	318	115	0.0009
HbA1c (%)	7.7	5.5	<0.0001
Total Cholesterol (mg/dl)	176	182	0.2616
Triglycerides (mg/dl)	164	158	0.1610
HDL (mg/dl)	47	44	0.2414
LDL (mg/dl)	109	104	0.2906

In the study, no statistically significant difference was found in exposure of age, vital studies and lipid profile, while the statistically significant increase was seen in FBG, PPG and HbA1c in diabetic patients with TB than in patients with TB and without diabetes.

1. **Comparison of Glycemic status among the test (TBDM) and control**
2. **(TB) groups (table 2 and figure 1)**

	TBDM Mean ± SD (SEM)	TB Mean ± SD (SEM)
FBG (mg/dl)	179.38 ± 138.03 (48.80)	71.750 ±17.393 (6.149)
PPG (mg/dl)	317.75 ± 148.25 (52.415)	115.13 ± 21.263 (7.518)
HbA1c (%)	7.738 ± 0.5397 (0.1908)	5.475 ± 0.2866 (0.1013)

The above graph (Figure 1) explains the difference in glycemic status among the test and control groups. The TBDM group had shown an extremely significant increase in FBG (P value 0.0231), PPG (P value 0.0009) and HbA1c (P value <0.0001) levels than the TB alone group.

3. **Comparison of Lipid profile (Total cholesterol, Triglycerides,**
4. **HDL and LDL) among TBDM and TB groups(table 3)**

	TBDM Mean ± SD (SEM)	TB Mean ± SD (SEM)
Total Cholesterol (mg/dl)	175.88 ± 23.333 (8.249)	181.88 ± 11.269 (3.984)
Triglycerides (mg/dl)	164 ± 8.106 (2.866)	157.75 ± 15.192 (5.371)
HDL (mg/dl)	46.750 ± 8.812 (3.115)	43.500 ± 9.212 (3.257)
LDL (mg/dl)	108.75 ± 16.202 (5.728)	103.75 ± 19.092 (6.750)

From the graph (table 3) we found a slight variation in lipid profile among the TBDM and TB groups. Total cholesterol was slightly higher in TB group where the Triglycerides, HDL and LDL values were greater in TBDM group. But no significant changes were found.

4. Comparison of Glycemic status of patients in TBDM and TB group based on the category of treatment undergone

	TBDM Median(Range)		TB Median(Range)	
	Cat. I	**Cat .II**	**Cat. I**	**Cat. II**
FBG (mg/dl)	124(57-158)	323(107-455)	67(57-105)	65(57-73)
PPG (mg/dl)	280(166-338)	448(218-611)	121(105-136)	101.5(71-132)
HbA1c (%)	8.1(6.9-8.5)	7.4(7.1-7.8)	5.65(5.1-5.9)	5.3(5.3-5.3)

Considering the category of treatment taken, the patients with diabetes along with tuberculosis were found with a higher fasting and post prandial glucose levels in Cat.II patients than in Cat.I patients, where,HbA1c (glycated hemoglobin) values were found higher in Cat.I patients than in Cat.II patients. There was not much marked inter-individual variability was observed in patients with tuberculosis and without diabetes, based on category of treatment taken.

I.   **PREVALENCE AND INCIDENCE STUDY OF TB CASES**
1.   **Sex of patients were compared for cases at Namakkal GH in 2008 & 2009.**

	2008	**2009**
Male	57.80%	65.90%
Female	27%	27.20%
Male child	9.30%	4.20%
Female child	6%	2.60%

Males were found to be more affected than females. There is a 2.5 fold greater prevalence of TB in males than in females.

2.   **Grading of slides in AFB microscopy**

Examinations	Result Grading	Number of fields to be examined
More than 10 AFB per oil immersion field	3+	20
1-10 AFB per oil immersion field	2+	50
10-99 AFB per 100 oil immersion fields	1+	100
1-9 AFB per 100 oil immersion fiels	scanty	100
No AFB in 100 oil immersion fields	0	100

3.   **Comparison of Treatment Outcome of patients in 2008 & 2009 at Namakkal District Government Hospital**

	2008	**2009**
Cured	42.90%	51.90%
Treatment completed	47.70%	30.60%
Defaulted	1.90%	4.10%
Failure	1%	3.30%
Died	6.50%	10%
> Pulmonary	77.10%	85.20%
> Extra pulmonary	22.90%	14.80%
> HIV +ve	53.10%	39.30%
> HIV –ve	46.90%	60.70%

Even the cure rate was increased in 2009, there is 3.5% and 2.3% increase in death rate and failure rate respectively.

4.   **Patients were categorized based on the category of treatment undergone in 2008 & 2009 at Namakkal GH.**

	2008	**2009**
Cat. I	69.70%	68%
Cat. II	12.40%	13.80%
Cat. III	17.90%	18.20%

Category I were given for new   smear positive cases, where Category II for relapse or failure cases in which streptomycin injection was added along with Category

I drugs. Category III were given to patients who are extra pulmonary or smear negative pulmonary tuberculosis cases.

5. Pulmonary and Extra pulmonary cases in 2008 & 2009 at Namakkal District Government Hospital were compared

	2008	2009
Pulmonary	66.10%	80.70%
Extra pulmonary	33.90%	19.30%

In the above data the pulmonary and extra pulmonary cases were classified which shows an increase in pulmonary cases about 15% in 2009 than 2008.
The above data shows that can lead to increase in the incident tuberculosis cases as they are sputum positive and can be spreaded easily through air droplets while coughing, talking, laughing etc. So preventive measures should be explained to patients and if required patients should be isolated until they becomes sputum negative.

6. The patients were categorized based on age group in 2008 & 2009 at Namakkal GH

Age in years	2008	2009
0-15	16.30%	7.70%
16-30	20.70%	20.10%
31-45	33.50%	36.20%
46-60	21.40%	27%
61-75	8%	8.40%
76-90	-	5%

The patients in 31-45 yrs. age group were found to be more affected than the other age groups. Also it is seen that 16-30 yrs. and 46-60 yrs. age group were found to be affected with tuberculosis greater than 20%. It shows that people between 16 to 60 yrs. are more susceptible to TB infection. An increase has shown in number of patients in 31-45 yrs. and 46-60 yrs. age groups that represents the risk of TB increases with age.

II PREVALENCE AND INCIDENCE STUDY OF DIABETES IN TB CASES

1. In this study, number of diabetes cases among TB patients were observed, as diabetes is an important risk factor for Tuberculosis. More than 15% of TB cases were found to be diabetic in India. Also studies had shown that diabetes increases the morbidity and mortality of tuberculosis cases. Here the tuberculosis cases for 3 months in two hospitals were studied and the details obtained were categorized in tables below.
In Namakkal District, out of 189 TB cases 19 were found to be diabetics, means more than 10% of tuberculosis patients were diabetics.

		TB cases	DM cases
Total number of cases		**N=189 (%)**	**N=19 (10.1)**
Sex	Male	109 (57.7)	13 (68.4)
	Female	80 (42.3)	6 (31.6)
Class of disease	Pulmonary	153 (81)	18 (94.7)
	Extra pulmonary	36 (19)	1 (5.3)
Category of treatment	Cat. I	118 (62.4)	11 (57.9)
	Cat. II	15 (7.9)	2 (10.5)
	Cat. III	56 (29.6)	6 (31.6)
HIV status	HIV +ve	51 (27)	4 (21.1)
	HIV –ve	138 (73)	15 (78.9)

From the above table it is clear that males were more affected with TB than females and also the same in case of TB with Diabetes. More than 94% cases were pulmonary tuberculosis among diabetics. Patients were taking treatment under Category I, II or III. More than 20% of diabetic tuberculosis patients were found to be HIV positive.

2. The sputum smear test results categorized based on the grades of positivity

Sputum smear test results	TB cases	DM cases
3+	10.10%	21.10%
2+	11.60%	10.50%
1+	19.60%	21.10%
Negative	32.80%	36.80%
Scanty	5.30%	10.50%
Not tested	20.60%	-

The above table explains that more than 60% of diabetic tuberculosis cases were sputum positive and there by that can spread TB to others.

3. Age

Age in years	TB cases	DM cases
0-15	11.60%	-
16-30	18.50%	-
31-45	37%	26.30%
46-60	24.90%	68.40%
61-75	6.90%	5.30%
76-90	1%	-

It was found that more than 68% of cases come in between 46 to 60 years. Also about 26% of diabetic TB was found among 31 to 45 year aged TB patients and the TB cases were found more about 37% in that age group.
Studies had shown that the urban population are more prone to tuberculosis due to crowded living and are susceptible to diabetes due to improper diet patterns and unhealthy conditions.

4. Distribution of patients with diabetes along with tuberculosis in different categories

Total number of cases		N=141(%)	N=15(10.6)
Sex	Male	99 (70.2)	8 (53.3)
	Female	42 (29.8)	7 (46.7)
Class of disease	Pulmonary	121 (85.8)	15 (100)
	Extra pulmonary	20 (14.2)	-
Category of treatment	Cat. I	93 (66)	13 (86.7)
	Cat. II	24 (17)	2 (13.3)
	Cat. III	24 (17)	-
HIV status	HIV +ve	15 (10.6)	5 (33.3)
	HIV –ve	126 (89.4)	10 (66.7)

From the above table, we can see that males were more affected with TB than females. But in patients with Tuberculosis along with Diabetes they were somewhat equally affected in males and females. All the tuberculosis diabetic cases were found to be pulmonary tuberculosis. The patients were under Category I, II or III for the treatment. Among TB patients greater than 10% were HIV positive and about 33% were HIV positive among tuberculosis with diabetes.

5. Sputum smear test results categorized based on the grades of positivity

Sputum smear test results	TB cases	DM cases
3+	27%	26.7%
2+	11.3%	33.3%
1+	18.5%	33.3%
Negative	25.5%	6.7%
Scanty	9.2%	-
Not tested	8.5%	-

It was given that greater than 92% of diabetic tuberculosis were sputum positive, the easily transmissible forms of TB. Precautions should be taken which are necessary in patients with sputum positive to prevent the spread of the disease to others.

6.   The DM with TB and TB cases were classified among different age groups

Age in years	TB cases	DM cases
0-15	4.3%	-
16-30	23.4%	13.3%
31-45	34%	33.3%
46-60	30.5%	53.3%
61-75	7.1%	-
76-90	0.7%	-

Patients between age of 46 to 60 yrs. were found to be diabetic (53%) among tuberculosis patients, also 31 to 45 year old patients had shown about 33% of diabetic cases in tuberculosis population. So screening for DM in TB patients above 35 years can be beneficial for control of TB and improvement of TB treatment outcome.

DISCUSSION
The global burden of disease from tuberculosis and diabetes is immense[3]. India has a large population size, and having the availability of relatively good data on both diabetes and tuberculosis, which are two major public health problems globally. India is a developing country with increasing incidence and prevalence of diabetes and tuberculosis[2,4,6,10,13]. Also, it is a nation which is endemic and epidemic to both the diseases[1,15].
Type II diabetes is a strong risk factor for tuberculosis and is associated with a slower response to TB treatment and a higher mortality rate[9,12,14,31]. Incidence of TB is greatest among those with conditions impairing immunity such as DM. Diabetes impairs the immune system, making it harder for the body to fight against infection[1,8,48].
Earlier studies show that tuberculosis and diabetes mostly affected males than females, and also the patients with DM above 40 years are vulnerable to TB[8,45,48,53]. In our study, males were found to be affected more than females and, greater than 30 year old patients were affected with DM along with TB.
In our study it was painful to note that all the patients recruited in the study were alcoholic and smokers at the onset of TB. Since they were advised to stop alcohol and smoking in order to make treatment effective they had stopped. The tobacco smoke and alcohol abuse are major risk factors which reduces the effectiveness of TB treatment and increases prevalence of TB[3,57,59].
Among the patients with DM in anti-TB therapy around 90% cases were pulmonary tuberculosis with 70% sputum positive cases. The studies done earlier had shown a high percentage of sputum positivity and a higher rate of pulmonary TB than extra pulmonary tuberculosis in diabetic patients[1,6,9,45,53,54]. It is because glucose stimulates the mycobacterial growth[55] and uncontrolled DM is responsible for poor clinical response to anti-TB therapy[56] which also increases the susceptibility to mycobacterial growth[1,8,48].
The patients with diabetes along with TB will be having a lower health performance as these disease affects the host defenses and immunity of body, and thereby unable to resist against infections and other comorbidities[1,8].

CONCLUSION
India is a developing country which is endemic and epidemic to tuberculosis and diabetes. Our study also had shown the need to improve the care of patients with concomitant DM and TB. Enhanced medical vigilance, especially in patients with diabetes, can be required in tuberculosis population. It also seems to be rational to screen for DM in patients with TB and vice versa, as these may have implications for control and treatment of both diseases. Therapeutic monitoring of anti-TB drugs along with regular monitoring of glucose levels using insulin can be recommended in patients with diabetes and tuberculosis.
Our study also recommends, TB control program should consider targeting patients with diabetes for interventions such as active case finding and treatment of latent TB and conversely that effort to diagnose, detect and treat diabetes may have a beneficial impact on TB control.

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