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Original Article

Frequency of glucose intolerance in patients with tuberculosis- A Comparative Study

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Abstract

Background: Diabetes mellitus (DM) is one of the important morbidity known to affect the outcome of tuberculosis (TB). The rising prevalence of DM in TB patients in endemic areas may adversely affect TB control. Speeding up the diagnostic, curative and preventive services are required to address DM.

Methods: This cross-sectional observational study was conducted to determine the frequency of glucose intolerance among patients with TB attending the Medicine Department of BIRDEM General Hospital, Dhaka. Total 59 patients were selected according to eligibility criteria. Demographic data were collected from individual patient by investigator with an aid of a semi-structured questionnaire. Results of OGTT were also included during data collection of the patients. Edited and encoded data were analyzed with a computer software Statistical package software system (SPSS) version 22.

Results: Total 59 cases were taken for this study. Out of which 35 (59.32%) cases were diagnosed as having pulmonary TB and rests 24 (40.78%) cases were diagnosed as having extra pulmonary tuberculosis. Mean age was found 35.8 ± 19.7 years with range from 18-65 years. Out of the 59 patients with TB, 10 (16.95 %) had glucose intolerance of which 2 (3.39%) had impaired fasting glucose (IFG), 05 (8.47 %) had impaired glucose tolerance (IGT) and 3 (5.08%) were frankly diabetes. It was observed that majority 35 (59.32%) patients belonged to 36-55 years. But the frequency of abnormal OGTT was more 3, (23.07%) out of 13 in 55-65 years age group. The number of cases of pulmonary TB decreased with increasing age and the relative number of those with glucose intolerance increased. The frequency of glucose intolerance was more in male 8, (23.52%) out of 34. But there were no significant difference in different ages and sex. Majority of patients belonged to the rural population (39, 66.10% out of 59) while most of them were of lower socioeconomic class (24 of 59). The frequency of glucose intolerance was interestingly more among the rural 08 (20.51%) and those was in the low socioeconomic class. 7, (29.17%) and 8 (41.9%) cases were employed, self-employed patients but the results were not statistically significant. Out of 59 patients, glucose intolerance was more common in pulmonary TB (7/35, 20%) cases than extra pulmonary TB (3/24, 12.5%). Glucose intolerance was more common in smear positive pulmonary TB 3/10 (30%) patients and low 4/25 (16%) in smear negative patients. On radiological findings, the most common was cavitary lesion and glucose intolerance was found in 2/4, 50% patients. Glucose intolerance was 2/10 (20%) and 1/10 (10%) who had pleural effusion and consolidation respectively. Among patients with peritoneal TB glucose intolerance was 1 (12.5%) out of 8 patients who have ascites but no glucose intolerance was found in ileo-caecal TB and on fluid study there were increased glucose intolerance in tubercular pleural effusion 2 (20%) out of 10 patients and in ascites 1 (12.5%) cases out of 8 but no glucose intolerance in CSF study and found non-significant difference.

Conclusion: Glucose intolerance was 10/59 (16.95%) in patients with tuberculosis and more common in pulmonary TB patients than Extra Pulmonary TB and more in smear positive pulmonary tuberculosis patients than smear negative patients.

Key words: Pulmonary tuberculosis, Extrapulmonary tuberculosis, Glucose intolerance

Introduction: Since ancient time, physicians have been aware of the association between DM and TB. In 19th century, tuberculosis was recognized as a leading cause of death in diabetic patients with post-mortem studies finding evidence of tuberculosis in over 50% of diabetic autopsies.[1] It has been already established that diabetic patients are 2 to 3 times more prone to develop tuberculosis than non diabetic individual.[2] In the

early part of this century, Root, however, considered that the association of diabetes and tuberculosis was a 'one sided association' and stated that "tuberculosis patients do not develop diabetes with any greater frequency than non-tuberculous".[3] But Nicholas in 1957, changed this view when he found evidence of glucose intolerance using an Oral Glucose Tolerance Test (OGTT) in 22% of 178 subjects with tuberculosis, at least 5% had diabetes.[4] Glucose tolerance was assessed, according to WHO criteria, in 505 consecutive African patients admitted with sputum-positive pulmonary tuberculosis to tuberculosis wards of Muhimbili Medical Centre, Dares Salam.[9] (1.8%) patients were known to have diabetes. Following OGTT diabetes was diagnosed in a further 25 (4.9%) patients giving an overall crude diabetes prevalence rate of 6.7%. Impaired glucose tolerance (IGT) was present in 82 (16.2%) subjects. A repeat OGTT was carried out in the 25 patients after the first test, 8(28%) of the 25 patients reverted to normal glucose tolerance after the second test, 6 (24%) to IGT, and 11 (48%) remained with blood glucose values in the diabetic range, giving a crude diabetes prevalence rate of 4%. Diabetes is therefore at least four times as common in the tuberculosis patients ($p < 0.001$, IGT twice as frequent ($p < 0.0001$) 5.In Bangladesh, a study conducted by BIRDEM hospital on tuberculosis patients admitted in NIDCH found that the frequency of diabetes among TB patients was 16% compared to 6% in non-tubercular chest disease patients.[6]

It is attractive to speculate on whether occult glucose intolerance predisposes to tuberculosis or whether some underlying tissue or endocrine abnormality predisposes to both latent diabetes and tuberculosis. A multitude of factors determine a given person's glucose intolerance. Several theories have been put forward to explain why tuberculosis patients develop glucose intolerance. Bloom suggested that occult glucose intolerance predisposes to diabetes.[7] Zack suggested that glucose intolerance was not merely a reaction to acute tubercular infection but rather a prediabetic state.[8] Hadden suggested malnutrition in tuberculosis is a possible cause.[9] Roychoudhary and Sen have suggested that tuberculosis of pancreas may give rise to glucose intolerance.[10] Higher incidence of chronic calcific pancreatitis occurs in patients of diabetes and pulmonary tuberculosis (PTB) leading to absolute or relative insulin deficiency.[11] Clinical and subclinical hypoadrenalism has been described in these patients.[12] Mugusi and Guptan have suggested the possibility of stress diabetes.[11] Acute severe stress, infection, inactivity and malnutrition stimulate the release of stress hormones–epinephrine, glucagon and cortisol; which raise the blood glucose level. Plasma levels of IL-1and TNF-∞ are raised in severe illness, which can stimulate anti insulin responses. Age, co-existing illness and alcoholism also influence the host response.[13]

Materials and Method:

The study was carried out in the department of Internal Medicine and DOTS center, BIRDEM over the period of 12 months, dated from July 2017 to June 2018. After departmental approval and obtaining informed written concepts from the patients between 18 to 60 years of age of either male or female and diagnosed as any type of tuberculosis at the time of diagnosis and 2 weeks before antitubercular treatment were enrolled in the study. Patients were excluded from the study if they had known case of diabetes mellitus, pregnant and lactating woman and having history of gestational diabetes, any autoimmune disease such as hypothyroidism/ hyperthyroidism, Addison's disease or associated with genetic syndrome such as Klinfelter, Turner syndrome etc., pancreatic disease such as (pancreatitis, pancreatectomy, neoplastic diseases, cystic fibrosis, haemochromatosis, fibro calculou pancreatopathy) received steroid or beta blocker, thiazide diuretics or phenytoin for long duration or unable to co-operate adequately.

The study group were consist of 59 patients of tuberculosis, who had either positive or negative sputum smear for Acid Fast Bacilli (AFB) and an OGTT was performed before starting of anti-tubercular drugs or taking anti-tubercular drugs for less than 2 weeks duration. The results were evaluated according to the criterion laid down by WHO for diabetes. A standard patient record form was designed for each subject that included name, age, sex, occupation, family history of diabetes mellitus, duration of illness, primary disease causing hospitalization and detailed treatment history. Height without shoes and weight was measured and BMI was calculated. All patients was undergo OGTT according to WHO guidelines.

Results:

Table-I: Socio-demographic information of patients by age and sex

Characteristics	Frequency	Percentage
Age group in years		
18-24	3	5%
25-35	5	8.72%
36-45	19	32.2%

Characteristics	Frequency	Percentage
46-55	19	32.2%
56-65	13	22.03%
Mean age 35.8 ± 19.7		
Sex		
Male	34	57.62%
Female	25	42.37%
Total	**59**	**100%**

Table-II: Socio-demographic distribution by residence, socio-economic status and occupation

Characteristics	Frequency	Percentage
Residence		
Rural	39	66.10
Urban	20	33.10
Socio-economic status		
Lower Class	24	40.6%
Middle Class	22	37.88%
Upper Class	13	22.03%
Occupation		
Unemployed	15	25.42%
Employed	14	23.73%
Self employed	30	50.85%

Table-III: Categorical distribution of tuberculosis (n=59)

TB Category	Frequency	Percentage
PTB	35	59.32
Extra PTB	24	40.78

Table-IV: Distribution of the PTB patients by sputum for AFB (n=35)

Sputum for AFB	Frequency	Percentage
Positive	10	28.57
Negative	25	71.43

Table-V: Distribution of the patients by fluid study (n=20)

Fluid study	Frequency	Percentage
Pleural effusion	10	16.95
Ascites	08	13.56
CSF	02	3.39

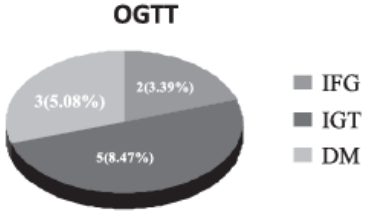

Figure I: Pattern of OGTT (n=59)

Table-VI: Age and Sex Specific glucose intolerance among TB patients (n=59)

Age group in years	No of subject (n=59)	Abnormal OGTT/ (IFG/IGT /DM) (n=10)	P-Value
18-25	3	0 (0%)	
26-35	5	1 (20%)	0.90
36-45	19	2 (10.52%)	
46-55	19	4 (21.05%)	
56-65	13	3 (23.07%)	
Total	**59**	**10 (16.95%)**	
Sex			
Male	34	8 (23.52%)	0.44
Female	25	2 (8%)	
Total	**59**	**10 (16.95%)**	

Test done by Chi-Square test

Table-VII: Glucose intolerance among TB patients in residence and socio-economic status and occupation. (n=59)

Residence	Number of Subjects	Abnormal OGTT	P-Value
Rural	39	08 (20.51%)	0.38
Urban	20	02 (10.00%)	
Socio-Economic Status			
Lower Class	24	07 (29.17%)	
Middle Class	22	02 (9.09%)	0.22
Upper Middle	13	01 (7.69%)	
Occupation			
Unemployed	15	02 (13.33%)	0.55
Employed	14	04 (28.57%)	
Self employed	30	04 (13.33%)	

Test done by Chi-Square test

Table-VIII: Glucose intolerance among TB patients in relation to sputum AFB, radiological findings and aspirated fluid study

Variable	Number of Subjects	Abnormal OGTT	P-Value
TB (n=59)			
PTB	35	07 (20%)	0.522
Extra PTB	24	03 (12.5%)	
Sputum for AFB (n=35)			
Positive	10	03 (30%)	0.61
Negative	25	04 (16%)	
Radiology			
Chest X Ray (n=24)			
Cavitary Lesions	04	02 (50%)	0.7
Pleural effusion	10	02 (20%)	
Consolidation	10	01 (10%)	
USG (n=10)			
Ascites	08	01 (12.5%)	0.621
Ileo-Caecal TB	04	00 (0%)	
Aspirated fluid study			
Pleural effusion	10	02 (20%)	0.88
CSF	02	00 (0%)	
Ascites fluid	08	01 (12.5%)	

*Chi-square test

Discussion:

Total 59 cases were taken for this study, 35 (59.32%) cases were diagnosed as having PTB and and 24 (40.78%) cases had extra PTB. In this study, Mean age of the 59 cases were 35.8 ± 19.7 years with range from 18-65 years. It was observed that 35 patients (59.32%) belonged to 35-55 years group. The frequency of glucose intolerance 3 (23.07%) were more in 55-65 years age group and the present study revealed that with increasing age the number of tubercular patients declined and the frequency of glucose intolerance was increased . This result was similar to those found in the studies Jain et al., 2006.[15] Here the mean age of glucose intolerance was in the range of 30-65 years. Higher prevalence of glucose intolerance in the elderly was also observed by Kishore et al., 1973,[16] who found that prevalence of IGT was higher among patients aged 40 years or more. Yamagishi et al., 2000[17] and Roychoudhary and Sen in 1980[10] also had similar observations. The earlier exposure to PTB in our country and the development of resistance to disease in later life accounted for involvement of younger population from TB. The frequency of glucose intolerance was more in males 08 (23.52%) out of 34 patients than in females 2 (8%) out of 25 patients. The finding is supported by another study. MK Jain et al., 2006[15] found that the prevalence of glucose intolerance was significantly more in male (14/75-18.65%) than in female (4/31-12.90). Yamagishi et al., 2000[17] found the glucose intolerance was twice in male than female. Fernandez et al., 1997[13] was found glucose intolerance in 6.2% males and 3% in females. Majority of patients belonged to the rural population (39 out of 59) . The frequency of glucose intolerance was interestingly more among the rural 08 (20.51%) which was also slight similar to Jain et al., 2006[15] where majority of people belongs to the rural population (69 out of 108) but glucose intolerance was more among the urban 12 (33, 44%). Socioeconomic status is particularly one such variable affecting the prevalence of tuberculosis. Two-third of patients in our study also belonged to lower & lower middle class families while most of them belong to lower socioeconomic class (24 of 59). Glucose intolerance was found more in low socioeconomic class 07 (29.17%) which was also similar to Jain et al., 2006 where majority of the patients studied were from the low socioeconomic class (76/106-71.70%) and glucose intolerance was more among them (14/76-18.42%) as compared to middle class (4/30-7.13%). The common factor of malnutrition and poor access to medical facilities may account for above observation. Glucose intolerance was more common in PTB 7 (20%) cases out of 35 cases than extra PTB 3 (12.5%) out of 24 patients. The study was similar to Magee et al., 2015 in which glucose intolerance was 116 (12.1%) out of 956 (72.1%) in patients with PTB and 27 (10.5%) out of 258 (19.5%) in extra PTB and in Kottarath et al., 2015 20 study in which diabetes were more in PTB 21 (29.57%) out of 71 cases in comparison with extra PTB, 8 (10.5%) cases out of 76.

Glucose intolerance is more common in smear positive patient, 3 cases (30%) out of 10 patients and low in smear negative patients 4 (16%) cases out of 25 patients. The study was also similar to Kottarath et al., 2015 20 in which number of sputum positive PTB was high in diabetes as 15 out of 29. The higher number of sputum positive in diabetes individuals indicate public health importance of screening and identified PTB sufficiently early so that the spread of the tuberculosis in the community can be contained.

On chest x-ray findings, the most common was cavitary lesion and glucose intolerance was found in 2/4 (50%) patients who had cavitary lesion. Glucose intolerance

was 2/10, 20% and 1/10, 10% who had pleural effusion and consolidation respectively. Similar type of result found in Venkateswara et al., 2013entitled a comparative study of Diabetes Mellitus in PTB patients. Here among 8 (36.4%) had cavitary lesion out of 22 diabetes patients. Cavitary lesions were seen as the predominant lesion in studies by Mugusi et al., 1990;[5] Morris et al., 1992;[18] Fernandez et al., 1997[13] and Parez et al., 2000. Two of 6 patients (33.33%) had exclusive lower zone involvement. On USG of abdomen, glucose intolerance was found on 1 (12.5%) case out of 8 patients who had ascites but no IGT was found in ileo-caecal TB. No further study are available to find out the frequency of glucose intolerance in pleural effusion, consolidation, ascites and ileo-caecal TB. On fluid study there was increased glucose intolerance in tubercular pleural effusion 2 (20%) out of 10 patients and in ascites 1 (12.5%) cases out of 8 but no glucose intolerance in CSF study and found non-significant difference. Out of the 59 patients of tuberculosis, glucose intolerance was positive in 10 (16.95%) patients out of them 2 (3.39%) had IFG, 05 (8.47%) had IGT and 3 (5.08%) were frankly diabetes shown in figure 6. This result was also similar to those found in the studies of Kishore et al., 1973 (20.9%);[16] Singh et al., 1978 (22.0%);[19] Mugusi et al., 1990 (6.7%)5 and Yamagishi et al., 2000 (14.1%).[17]

Conclusion: The frequency of glucose intolerance in TB patients in our study is 16.95%. Out of the 59 tuberculosis patients, 2 had IFG, 05 had IGT and 3 were frankly diabetic. The frequency of glucose intolerance was more among elderly, male and rural population. The lower socioeconomic groups were significantly more affected and there was significantly increased glucose intolerance among the elderly patients, the most common lesion was cavity in those with glucose intolerance and lower zone was significantly more affected. The rising burden of DM may adversely affect TB control and effective utilization of the TB control program could be beneficial in early detection and treatment of DM.

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