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Original Research Paper

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SCREENING OF MICRO- AND MACROVASCULAR COMPLICATIONS IN NEWLY DIAGNOSED DIABETES MELLITUS PATIENTS WITH MYCOBACTERIUM TUBERCULOSIS INFECTION, AT TERTIARY CARE CENTER IN NORTHERN INDIA

Dr.Manoj Kumar Mathur	(MD) Professor, Department of Medicine, MLN Medical College, Prayagraj.
Dr.Ajeet Kumar Chaurasia	(MD) Professor, Department of Medicine, MLN Medical College, Prayagraj.
Dr. Poonam Gupta	(MD) Professor, Department of Medicine, MLN Medical College, Prayagraj.
Dr. Virey Vireshwr Goyal	Junior Resident, Department of Medicine, MLN Medical College, Prayagraj.

ABSTRACT To screen for micro- and macrovascular complications in patients with newly diagnosed diabetes mellitus and mycobacterium tuberculosis infection. Total 182 patients infected with TB were enrolled in the study. Patients of TB were selected from Medicine and Pulmonary Medicine departments in MLN Medical College Prayagraj. They were evaluated for glucose intolerance at the time of enrollment. Patients who did not have previous diagnosis of diabetes had samples drawn for A1C and on a subsequent day have an OGTT on a fasting state. In all patients diagnosed with glucose intolerance and tuberculosis infection, ECG, 2 D Echo, CIMT (carotid intima media thickness), fundus examination was done and ABPI (ankle brachial pressure index) was calculated. 18 patients who had known history diabetes and were on diabetic medications were excluded. Out of 164, total 88 (53.66%) patients had normal glucose tolerance (NGT) and 76 (46.34%) had abnormal glucose tolerance (AGT). AGT group included patients with impaired glucose tolerance (IGT) and newly diagnosed diabetes mellitus. In the AGT group 50 (30.49%) patients were diagnosed as prediabetes and 26 (15.85%) were as newly diagnosed diabetes mellitus. Seven (9.21%) newly diagnosed diabetic patients had ABPI below 0.89 and fundus abnormalities (9.21%, p=0.012). Urine microalbuminuria >300md/dl was present in seven patients (9.21%, p<0.001), ECG abnormalities with ST-T changes and 2D-Echo findings of diastolic dysfunction were found in 4 (5.26%, p=0.095), and 5 (6.58% p=0.047) in newly diagnosed DM patients. Newly diagnosed diabetic patients had micro- and macrovascular complications associated with them at time of their diagnosis

KEYWORDS : tuberculosis, diabetes mellitus, glucose intolerance, microvascular and macrovascular complications.

INTRODUCTION

According to the WHO's Global TB Report 2020, the number of persons diagnosed with tuberculosis in 2019 was anticipated to be around 10 million, with 0.25 million deaths, a figure that has been steadily dropping in recent years[1].

There is a bidirectional association between diabetes and tuberculosis. When compared to non-diabetics, diabetics are more likely to become infected with Mycobacterium tuberculosis. Screening for DM in TB patients could thus help to identify DM cases early, which could lead to earlier DM treatment and better treatment outcomes[2]. Diabetics with a long history of diabetes have a weakened host defense system, which raises the risk of infection. The growth of TB bacilli is aided by hyperglycemia. Diabetes individuals have a threefold greater risk of tuberculosis.

Diabetes-related microvascular and macrovascular problems are more likely in people with chronic hyperglycemia. Diabetes and its effects can be reduced if detected early. Insufficient or complete lack of insulin secretion, insulin resistance, altered fuel metabolism, and the development of diabetes-specific complications in the eye, kidney, and peripheral nerve characterize all forms of diabetes mellitus. Diabetes is also linked to increased atherosclerosis of the heart, brain, and lower extremities arteries[3]. Diabetic atherosclerosis is more widespread in coronary arteries, with a higher inflammatory infiltration and necrotic core size. Diabetes quadruples the risk of heart failure and doubles the rates of early and late post-myocardial infarction death[3].

MATERIALS AND METHOD:

Total 182 patients infected with TB were enrolled in the study. Patients of TB were selected from Medicine and Pulmonary Medicine departments in MLN Medical College Prayagraj. They were evaluated for glucose intolerance at the time of enrolment. All consecutive adults with TB infection determined bacteriologically, histology, clinically or radiologically were recruited after informed consent.

Patients with a known history of diabetes mellitus or on treatment were excluded from the study, as well as patients with serious life-threatening TB infection, pregnant women, on steroid therapy, patients with MDR/XDR TB, HIV and those unwilling for study.

Patients who did not have previous diagnosis of diabetes had samples drawn for A1C and on a subsequent day have an OGTT on a fasting state. In all patients diagnosed with glucose intolerance and tuberculosis infection, ECG, 2 D Echo, CIMT (carotid intima media thickness), fundus examination was done and ABPI (ankle brachial pressure index) was calculated. Treatment outcomes was determined at the end of the study.

RESULTS

Total 182 patients infected with TB were enrolled in the study. 18 patients who had known history diabetes and were on diabetic medications were excluded from the study. Out of 164, total 88 (53.66%) patients had normal glucose tolerance (NGT) and 76 (46.34%) had abnormal glucose tolerance (AGT). AGT group included patients with impaired glucose tolerance (IGT) and newly diagnosed diabetes mellitus.

Table 1: Distribution Of Mycobacterium Tuberculosis Infection Into Normal Glucose Tolerance (NGT) And Abnormal Glucose Tolerance (AGT) Group

Group	Numbers	Percentage
Normal glucose tolerance (NGT)	88	53.66

Abnormal glucose tolerance (AGT)	76	46.34
Total	164	100.00%

In the AGT group 50 (30.49%) patients were diagnosed as prediabetes and 26 (15.85%) were as newly diagnosed diabetes mellitus. The mean age was significantly more 44.65 years in AGT group as compared to 34.86 years in NGT group.

Table 2 and figure 2 showed that dyslipidemia was present in AGT group, and the result was statistically significant p=0.001. In AGT group the number of patients having high total cholesterol (≥240 mg/dl) was 18 (23.68%), serum triglycerides ((≥200 mg/dl) was 20 (26.32%), and LDL cholesterol (>160 mg/dl) was 7 (9.21%), when compared to number of patients having TB alone had 2 (2.27%), 5 (5.68%), and 2 (2.27%) respectively.

Table 2: Comparison Of Lipid Profile Of Total Cholesterol (TC), S. Triglycerides (TG), LDL-C, and HDL-C in NGT and AGT groups.

Parameters	Range	NGT group (n=88)		AGT group (n=76)		P value
		N	%	N	%	
TC	Normal (<200mg/dl)	84	95.45	48	63.16	<0.001*
	Borderline (200-239 mg/dl)	2	2.27	10	13.16	
	High (≥240mg/dl)	2	2.27	18	23.68	
TG	Normal (<150 mg/dl)	76	86.36	42	55.26	<0.001*
	Borderline (150-199 mg/dl)	7	7.95	14	18.42	
	High (≥200 mg/dl)	5	5.68	20	26.32	
LDL-C	Normal (<129 mg/dl)	86	97.73	59	77.63	<0.001*
	Borderline (130-160 mg/dl)	0	0.00	10	13.16	
	High (>160 mg/dl)	2	2.27	7	9.21	
HDL-C	Normal (≥60 mg/dl)	7	7.95	5	6.58	0.971

*=Significant (p<0.05)

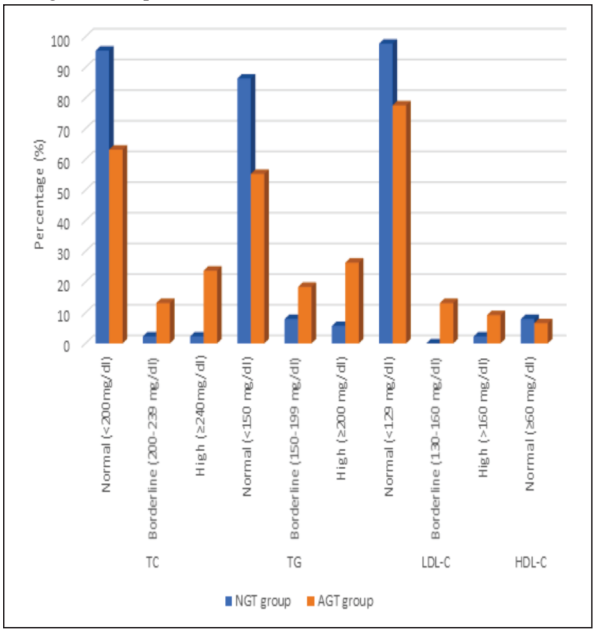

Figure 2: Comparison Of Lipid Profile Of Total Cholesterol (TC), S. Triglycerides (TG), LDL-C, and HDL-C in NGT and AGT groups.

Table 3 show the distributions of study populations according to ankle-brachial pressure index (ABPI) in groups. The percentage of >1.30, 0.90-1.30, 0.60-0.89, 0.40-0.59 and <0.040 ABPI were 0.00%, 98.86%, 1.14%, 0.00%, 0.00% in NGT group and 0.00%, 90.79%, 9.21%, 0.00%, and 0.00% AGT group, respectively. The distributions of study populations according to ankle-brachial pressure index (ABPI) were significantly different between groups.

Table 3: Distributions Of Study Populations According To Ankle-brachial Pressure Index (ABPI) In Groups

ABPI	NGT group (n=88)		AGT group (n=76)		Chi Sq.	P value
	N	%	N	%		
>130	0	0.00	0	0.00	4.12	0.042*
0.90-1.30	87	98.86	69	90.79		
0.60-0.89	1	1.14	7	9.21		
0.40-0.59	0	0.00	0	0.00		
<0.040	0	0.00	0	0.00		

*=Significant (p<0.05), [1]=Chi-square test

Table 4 show the distribution of study population according to 24-hour Urine microalbumin in groups. The percentage of <30, 30-300 and >300 Urine microalbumin were 64.77%, 35.23% and 0.00% in NGT group, 11.84%, 78.95% and 9.21% in AGT group, respectively. The distributions of study populations according to Urine microalbumin was significantly different between groups. 7 (9.21%) newly diagnosed diabetes had 24-hour urine microalbumin >300md/dl.

Fundus showed either proliferative retinopathy or non-proliferative retinopathy in 7(9.21%) newly diagnosed diabetes patients. The results were significant in AGT group having abnormal fundus as shown in Table 4.

Table 4 also show the distribution of study population according to CIMT in groups. The percentage of ≤0.9 and >0.9 CIMT were 98.86% and 1.14% in NGT group, 96.05% and 3.95% in AGT group. The distribution of study population according to CIMT was not significantly different in between groups.

The number of patients having newly diagnosed diabetes mellitus in AGT group were found to have ECG (ST-T changes) and 2D echocardiography (Left ventricular diastolic dysfunction) abnormalities associated with them. The having ECG, and 2D echo abnormalities were 4(5.26%), and 5 (6.58%) respectively. The results were significant in AGT group having abnormal fundus and 2D echo findings. ECG changes had a non-significant result. No changes were observed in the patients having TB alone or in prediabetes in the AGT group.

Table 4: Association Of 24-hour Urine Microalbumin, Fundus, CIMT, ECG, And 2D Echo Findings In AGT And NGT Group

Urine microalbumin	NGT group (n=88)		AGT group (n=76)		Chi Sq.	p-Value
	N	%	N	%		
<30	57	64.77	9	11.84	50.54	<0.001*
30-300	31	35.23	60	78.95		
>300	0	0.00	7	9.21		
Fundus						
Normal	88	100.00	69	90.79	3.63	0.012*
Abnormal	0	0.00	7	9.21		
CIMT						
≤0.9	87	98.86	73	96.05	0.43	0.512
>0.9	1	1.14	3	3.95		
ECG						
Normal	88	100.00	72	94.74	2.79	0.095
Abnormal	0	0.00	4	5.26		
2D Echo						
Normal	88	100.00	71	93.42	3.95	0.047*
Abnormal	0	0.00	5	6.58		

*=Significant (p<0.05), [1]=Chi Sq. test

DISCUSSION:

Out of 164, total 88 (53.66%) patients had normal glucose

tolerance (NGT) and 76 (46.34%) had abnormal glucose tolerance (AGT). In the AGT group 50 (30.49%) patients were diagnosed as prediabetes and 26 (15.85%) were as newly diagnosed diabetes mellitus. The mean age in AGT group was 44.65 years whereas 34.86 years in NGT group.

This study showed that the majority of patients in AGT group had dyslipidemia in comparison to NGT group with a significant result p=<0.001. The mean total cholesterol 209.74±124.89 mg/dl, serum triglycerides 165.11±77.17 mg/dl, LDL cholesterol 99.65±40.48 mg/dl, and VLDL 32.76±13.66 mg/dl was present in the AGT group (p=<0.001). Vrieling et al[4] found that DM patients had dyslipidemia, as shown by high levels of VLDL, triglycerides, and low HDL cholesterol in comparable research of 177 individuals. They concluded that patients with TB-DM had a unique plasma lipid profile with pro-atherogenic features.

The mean ankle brachial pressure index was comparable between the two group with AGT and NGT group having 0.92±0.02 and 0.93±0.01 with non-significant result p=0.161. Seven (9.21%) newly diagnosed diabetic patients had ABPI below 0.89 whereas only one (1.14%) patient with TB alone had ABPI less than 0.89. the results were significant with p=0.042 and showed that newly diabetic patients had a risk of peripheral artery disease. Cardoso et al[5] studied the impact of ankle brachial pressure index for development of microvascular and macrovascular complications in people with type 2 diabetes. ABI of 0.90 was associated with a 2.1-fold increase in all-cause mortality (95 percent CI 1.3-3.5: p0.004) and a 2.7-fold increase in cardiovascular mortality (95 percent CI 1.4-4.5; p=0.004).

In AGT group newly diagnosed diabetic patients had microvascular and macrovascular disease on being diagnosed. Urine microalbuminuria >300md/dl was present in seven patients (9.21%, p<0.001), ECG abnormalities with ST-T changes and 2D-Echo findings of diastolic dysfunction were found in 4 (5.26%, p=0.095), and 5 (6.58% p=0.047) in newly diagnosed DM patients. The results were significant for urine microalbuminuria and 2D echo findings, and non-significant for ECG changes seen. Fundus abnormalities (proliferative or non-proliferative changes) was present in seven patients (9.21%, p=0.012). This showed that newly diagnosed DM patients also had a higher prevalence of microvascular and macrovascular complications at the time of their DM diagnosis. Gedebjerg et al[6] found that in 6,958 newly diagnosed DM patients, 35% (n=2456_ had diabetic complications at time of diagnosis. 12% (n=828) had microvascular and 17% (n=1186) had macrovascular complications, and 6% (n=442) had both. Similar study by Palladino et al[7] showed that the prevalence of microvascular (retinopathy and nephropathy) and macrovascular disease. They found that 49.9% patients had at least one vascular disease, 37.4% had microvascular, and 23.5% had macrovascular complications at the time of diagnosis of type 2 diabetes mellitus.

806 patients with newly diagnosed diabetes mellitus were screened by Bonora et al[8] where he found that in 30.8% had microvascular, 9.3% had macrovascular, and 9.1% had combination of both complications. He concluded that as much as 50% of newly diagnosed diabetic patients had clinical or preclinical manifestations of microvascular and/ macrovascular complications.

CONCLUSION:

In patients with newly diagnosed DM, they were more likely to have microvascular and/ macrovascular complications at time of diagnosis. The findings of this study showed that there is higher prevalence of dysglycemia in patients with tuberculosis infection. Early detection and treatment of glucose intolerance in patients with TB is important for timely control of infection and improving treatment outcomes.

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