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Original Research Article

Treadmill test as a screening tool for detecting silent myocardial ischemia in type 2 diabetes patients: a case control study from Raipur, Chhattisgarh, India

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ABSTRACT

Background: The incidence of diabetes mellitus (DM) is increasing substantially worldwide. CAD silently progresses over years in the diabetics. Diabetic individual appears to be less able to perceive some of the symptoms and signs of ischemia or may have asymptomatic 'classic silent ischemia'. Thus, screening for early detection of asymptomatic CAD in type 2 diabetes may be helpful to prevent these catastrophic cardiac events and consequent deaths. Objectives of the study was to assess utility of TMT in Type 2 diabetic mellitus subjects to detect silent myocardial infarction.
Methods: Hospital based observational analytical case control study was conducted in Department of Medicine in Dr BRAM Hospital Raipur during August 2016 to September 2018. Cases were 45 subjects of Type 2 Diabetes mellitus with normal ECG and controls were 45 subjects of Type 2 Diabetes Mellitus with abnormal resting ECG. Data analyzed using SPSS 17 version.
Results: Majority i.e. 40% were found to be in fifth decade of their life. 71 (78.9%) male subjects and 19 (21.1%) female subjects. TMT was found positive in 8(17.8%) subjects with positive ECG changes whereas in 12(26.7%) subjects with no ECG changes. No significant difference was noted between distribution of any parameters except for hypertension which was found to be significantly higher in TMT positive subjects compared to TMT negative subjects.
Conclusions: No significant difference was observed regarding TMT findings between T2DM subjects with and without ECG changes. Type 2 diabetes mellitus subjects with dyslipidemia, and hypertension are at higher risk of Positive TMT.

Keywords: Silent MI, Screening tool, Trade mill, Type 2 diabetes

INTRODUCTION

The incidence of diabetes mellitus (DM) is increasing substantially worldwide. Over the past three decades, the global burden of DM has swelled from 30 million in 1985 to 382 million in 2014, with current trends indicating that these rates will only continue to rise.[1] The latest estimates by the international diabetes federation project that 592 million (1 in 10 persons) worldwide will have DM by 2035.[2] While the rates of both type 1 DM (T1DM) and T2DM are growing, T2DM has a disproportionately

greater contribution to the rising prevalence of DM globally compared to T1DM.[1]

A close link exists between DM and cardiovascular disease (CVD). CVD is the most prevalent cause of mortality and morbidity in diabetic populations. CVD death rates in the United States are 1.7 times higher among adults (>18 years) with DM than those without diagnosed DM, largely due to an increased risk of stroke and myocardial infarction (MI).[3] This increased risk of CVD mortality in diabetic patients is found in both men and women. The relative risk for CVD morbidity and mortality in adults with diabetes ranges from 1 to 3 in men and from 2 to 5 in women compared to those without DM.[4]

CAD silently progresses over years in the diabetics. Diabetic individual appears to be less able to perceive some of the symptoms and signs of ischemia or may have asymptomatic 'classic silent ischemia'. This may eventually present with sudden death, myocardial infarction, arrhythmias or heart failure leading to premature deaths. Thus, screening for early detection of asymptomatic CAD in type 2 diabetes may be helpful to prevent these catastrophic cardiac events and consequent deaths. However, periodical thorough clinical examination and resting ECG are not useful for this purpose as many times these methods fail to detect asymptomatic coronary artery disease. Also, invasive tests are highly expensive so are not cost effective for screening purpose.[5]

Therefore, the present study is designed to demonstrate the usefulness of exercise electrocardiograph for early detection of asymptomatic CAD in type 2 diabetic individuals. If TMT is found useful and established as diagnostic test for silent ischemia in T2DM it can be used as regular non-invasive screening test for silent ischemia in subjects with T2DM.

Objectives of the study was to assess utility of TMT in Type 2 diabetic mellitus subjects to detect silent myocardial infarction.

METHODS

This is a hospital based observational analytical case control study. Study was conducted in the Department of Medicine in Dr BRAM Hospital Raipur. Duration of study was from August 2016 to September 2018. Study was performed on the subjects with type 2 Diabetes mellitus as per American Diabetes association criteria. Sample size includes 90 subjects across two groups.

- Group 1: 45 subjects of Type 2 Diabetes mellitus without any symptoms suggestive of CAD and a normal ECG.
- Group 2: 45 subjects of Type 2 Diabetes Mellitus without any symptoms suggestive of CAD and an abnormal resting ECG.

Calculation of sample size: With alpha error 5% and power of study 80% considering expected frequency of 36% positive TMT as per previously available data the need is to recruit total 90 subjects for our study. EPI info stat scale Vs 9 sample size calculator for android.

Inclusion criteria

- Study subjects with type 2 Diabetes Mellitus as per ADA criteria.
- Age >/= 30 years.
- Either gender.
- Group 1: Asymptomatic T2DM subjects without any change in the ECG.
- Group 2: Asymptomatic T2DM with any change in ECG.

Exclusion criteria

- Typical history of angina.
- Known cases of heart diseases such as congenital or acquired valvular heart disease heart failure (CCF) or arrhythmia.
- Diagnosed CAD by invasive or non-invasive procedures.
- Patient not willing to participate in the study.

Study was approved by scientific committee and institutional ethical committee and was carried out in accordance with declaration of Helsinki. Informed written consent was obtained from all study participants.

Data Collection procedure are as follows, all subjects fulfilling inclusion criteria were recruited after obtaining written informed consent. Detailed history regarding diabetes mellitus, complications of diabetes any family history of DM or CAD, personal history for risk factors of CAD was obtained. Thorough physical examination was performed. Any relevant medical records, reports and documents available with patient were assessed. Five ml blood was obtained from median cubital vein and was used for hemoglobin, lipid profile, and HbA1c levels. Hemoglobin was estimated based on Merk ™ hematology analyser, Werfen® Germany. Patients were then subjected to Electrocardiogram using Phillips Page writer TC 30™. Phillips Inc. Amsterdam Netherlands and treadmill test using a PC based stress test system with treadmill, Schiller Spandan™ Schiller® Inc Pvt Ltd Altagasse, Switzerland.

Statistical analysis

Data was expressed as percentage and mean±SD. Kolmogorove - Smirnove analysis was performed for checking linearity of data. Student's test was used to check the significance of difference between the two parameters in parametric data and Mann Whitney U test was used to check the significance of difference between frequency distribution of data, p value <0.05 was considered statistically significant. SPSS© for

windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc was used to perform statistical analysis.

RESULTS

Age distribution of study subjects was assessed. Eighteen subjects (20%) were found to be belonging to age </=40 years. Thirty-six subjects (40%) were found to be in fifth decade of their life and frequency was found to be higher in these subjects. Thirty-three subjects (36.7%) were in age group 51-60 years. Two (2.2%) and one (1.1%) subjects were present in seventh decade of their age and >70 years respectively (Table 1).

Table 1: Distribution according to age.

		Frequency	Percent
Age in years	≤40	18	20
	41-50	36	40
	51-60	33	36.7
	61-70	2	2.2
	>70	1	1.1
	Total	90	100

In our study strong male preponderance was seen in study with 71 (78.9%) male subjects and 19 (21.1%) female subjects (Table 2). TMT was found positive in 8(17.8%) subjects with positive ECG changes whereas in 12(26.7%) subjects with no ECG changes. Comparison of TMT status in study groups was performed using Chi square test. No significant difference in distribution of TMT status was observed between two groups (Table 3).

Mean age in subjects with ECG changes was 47.89±7.89 whereas in subjects with no ECG changes was 48.67±9.76 years. The difference was statistically found to be not significant (p>0.05). Mean duration of diabetes in subjects with ECG changes was 6.33±1.19 years whereas in subjects with no ECG changes was 6.4±0.99 years. The difference was statistically found to be not significant (p>0.05) (Table 4).

Table 2: Distribution according to gender.

		Frequency	Percent
Gender	Female	19	21.1
	Male	71	78.9
	Total	90	100

Table 3: Distribution according to ECG changes and TMT findings.

		ECG changes present		ECG changes absent	
		Frequency	Percent	Frequency	Percent
TMT	Negative	37	82.2	33	73.3
	Positive	8	17.8	12	26.7
	Total	45	100.0	45	100.0

Chi square-1.02, p-0.31, Not significant

Table 4: Comparison of mean age and diabetes duration between two groups.

Parameter	Group	N	Mean	SD	t	p	Inference
Age (Years)	ECG changes present	45	47.89	7.89	-0.416	0.679 (>0.05)	Not significant
	ECG changes absent	45	48.67	9.76			
Duration of diabetes (Years)	ECG changes present	45	6.33	1.19	-0.29	0.773 (>0.05)	Not significant
	ECG changes absent	45	6.4	0.99			

Table 5: Comparison of frequency distribution of various parameters between subjects with positive and negative TMT.

		ECG changes present		ECG changes absent	
		Frequency	Percent	Frequency	Percent
Gender	Female	9	20.0	10	22.2
	Male	36	80.0	35	77.8
Smoking		14	31.1	31	68.9
Alcoholism		14	31.1	30	66.7
Hypertension		22	48.9	32	71.1
Diabetes duration	1 to 5	13	28.9	8	17.8
	6 to 10	32	71.1	37	82.2
BMI	23-24.9	4	8.9	1	2.2
	25-29.9	41	91.1	44	97.8

Comparison of frequency distribution of various parameters between subjects with positive and negative TMT was perform. No significant difference was noted between distribution of any parameters except for hypertension which was found to be significantly higher in TMT positive subjects compared to TMT negative subjects (p=0.032) (Table 5).

DISCUSSION

Age and gender

Age distribution of study subjects was assessed. Eighteen subjects (20%) were found to be belonging to age </=40 years. Thirty-six subjects (40%) were found to be in fifth decade of their life and frequency was found to be higher in these subjects. Thirty-three subjects (36.7%) were in age group 51-60 years. Two (2.2%) and one (1.1%) subjects were present in seventh decade of their age and >70 years respectively. Mean age was found to be 47.89±7.89 yrs in group 1 and 48.67±9.76 years in group 2 In our study strong male preponderance was seen in study with 78.9% male subjects.

Between 2 and 4 percent of apparently healthy asymptomatic middle-aged man have a significant coronary disease. The prevalence may be up to 10 percent in asymptomatic men with 2 or more coronary risk factors (smoking, obesity, family history of heart disease, age over 45, diabetes, hypertension, and hypercholesterolemia). The data on women are inconclusive because of a higher incidence of false positive electrocardiograms. The risk of silent ischemia is increased substantially in patients with diabetes, particularly if they have other risk factors.[6]

In a study by Yoo WS et al, mean age in study subjects was found to be 57.2 ± 10.7 years. Bhatia LC et al, also included study subjects with same age distribution as ours.[7] In a study by Sarkar NC et al, also mean age was 56.2 years. Sharda M et al, also recruited the study subjects in similar age range to authors and mean age was 52.96 years.[8] Thus age distribution was found to be similar to previous studies mean age in the study was less compared to other studies.

Tread mill tests between study groups

Though in this study higher frequency of positive TMT was noted between study groups, the difference failed to reach statistical significance. Total 20 (22.2%) asymptomatic subjects were found to be having positive TMT.

Sarkar NC et al, from India, evaluated 47 asymptomatic diabetics who underwent exercise ECG and autonomic function testing.[8] 63.8% had >1 autonomic test abnormal and 46.8% had >2 autonomic tests abnormal, 38.3% had abnormal responses on TMT and those with autonomic dysfunction had a greater prevalence of silent ischemia than those without (59% vs 20%). Further, to validate the results coronary angiography was carried out in 9 patients who were TMT positive and 4 patients who were TMT negative. 8/9(88%) of the former and 1/4th (25%) of the later demonstrated significant coronary stenosis.

Gupta SB evaluated the prevalence of silent myocardial ischemia in 925 non-insulin dependent diabetes mellitus patients, aged 40 to 65 years, asymptomatic, free from known coronary artery disease, advanced diabetic retinopathy and nephropathy with exercise electrocardiogram and thallium scintigraphy.[9] The exercise tests were abnormal in 112 patients (12.1%), of whom 59 (6.4%) had perfusion defects at thallium scintigraphy. Multivariate analysis showed that the associated independent risk factors were age, total cholesterol, proteinuria and ST-T abnormalities on electrocardiogram at test.

In the Detection of Ischemia in Asymptomatic Diabetics (DIAD) study 1123 patients with type 2 diabetes, aged 50-75 years, with no known or suspected CAD were randomly assigned to stress testing.[10] The prevalence of ischemia in 522 patients randomized to stress testing were assessed myocardial perfusion imaging. A total of 113 / 522 patients (22%) had silent ischemia. The strongest predictors for abnormal tests were abnormal vasalva (odds ratio =5.6), male sex (2.5) and longer duration of diabetes (5.2).

Fuster V included 500 patients with type 2 diabetes in his study with no evidence of CAD on resting ECG found that 62(12.4%) patents exhibited abnormal changes on tread mill exercise test.[11] CAD was diagnosed in 53 individuals by coronary angiography. The abnormalities of exercise test were associated with the age of patients or the duration of diabetes.

In a study conducted by Tandon R, 33 patients with type 2 diabetes mellitus, aged 41- 72 years with no clinical history suggestive of coronary heart disease, were evaluated for silent myocardial ischemia by stress cardiac exercise tolerance test (ETT), 12 lead electrocardiography (ECG).[12] Eleven patients (26.2%) showed an ischaemic pattern on ETT, the resting ECG was suggestive of ischemia in only 2 (4.2%).

So multiple studies have given variable results in detection of silent ischemia in diabetic subjects in this case though 22.2% study subjects were found to be having silent ischemia, TMT was not able to differentiate between subjects with positive prior ECG changes.

CONCLUSION

Most common age group to be detected with asymptomatic diabetes mellitus was fifth and sixth decade of life. There was significant male preponderance in diabetics with 78.9% subjects were male. Parameters of personal history, hypertension and serum cholesterol

were significantly higher in subjects type 2 diabetic subjects with ECG changes. No significant difference was observed regarding TMT findings between T2DM subjects with and without ECG changes. Type 2 diabetes mellitus subjects with dyslipidemia, and hypertension are at higher risk of Positive TMT.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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