

A Study of Treadmill Test in Asymptomatic Type 2 Diabetes Mellitus in Guru Gobind Singh Govt. Hospital, Jamnagar

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Abstract:

Introduction: India has become country with 2nd highest diabetic population in world, which is global epidemic and ice berg disease and the most common endocrine disease in occurrence. Diabetes also affects vital organs of our body by various macro and microvascular complications, one of which is coronary artery disease and which is more often asymptomatic because of occurrence of silent myocardial ischemia.

Aims and Objective: To assess the prevalence of ischemic heart disease in asymptomatic Type 2 Diabetes mellitus by exercise treadmill test. To assess various factors related to type 2 diabetes with coronary artery disease.

Material and Methods: It was non randomized cross sectional study conducted in Guru Gobind Singh Govt. Hospital, Jamnagar between November - 2019 to November – 2020. In the study period of 12 months among the patients seen under the Department of General Medicine. 50 patients were included in this study, who had no clinical evidence of ischemic heart disease, patients known case of type 2 diabetes mellitus (DM), All the patients attending medicine OPD or admitted hospital were screened for eligibility and then after taking informed consent and enrolling them in this study, they underwent interview and through physical examination, All the patients had normal resting ECG and normal 2D ECHO. All the patients had already underwent treadmill testing. A detailed history was taken from all the patients enrolled which was specific for symptoms related to DM, duration of DM and symptoms related to complication of DM.

Results: The mean age of patients studied is 57.06 years; standard deviation (SD) of 10.0496 with range of 32 years to 70 years. Out of 50 cases, 28 males and 22 females. Among 50 patients studied, 19(36%) were TMT positive while 32(64%) were TMT negative. According to this study, following observations were made, with reference to average age (p value-0.0012), average duration of diabetes mellitus (p value -0.0001), average HbA1c(p value-0.0137), average FBS (p value-0.0181), average PP2BS (p value -0.000002), average total cholesterol (p value-0.000321), average triglyceride (p value-0.0128), average LDL (p value -0.00038), average HDL (p value-0.00425) was found to have statistically significant difference between TMT positive cases and TMT negative cases.

Conclusion: Longer the duration of diabetes, greater the risk of asymptomatic coronary artery disease. An aggressive and early screening of patients with type 2 diabetes mellitus for the evidence of asymptomatic coronary artery disease may prevent catastrophic cardiac events.

Keyword: Treadmill Test, Type 2 Diabetes Mellitus, Coronary Artery Disease, Electrocardiogram.

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Introduction

India has become country with 2nd highest diabetic population in world, which is global epidemic and ice berg disease and the most common endocrine disease in occurrence. Diabetes also affects vital organs of our body by various macro and microvascular complications, one of which is

coronary artery disease and which is more often asymptomatic because of occurrence of silent myocardial ischemia. Diabetes is very important modifiable risk factor for development of coronary artery disease. It is hyperglycaemia, classical risk factor, which in diabetes has good correlation with

risk and severity of both macro as well as micro-vascular complications of diabetes. Autonomic neuropathy developed as part of complication of diabetes mellitus plays major role in asymptomatic nature of coronary artery disease, which can present with sudden death, arrhythmias, silent myocardial infarction or heart failure.

Since routine clinical examination and periodic ECG monitoring may fail to detect early changes of coronary artery disease, so there is proposal to use another non-invasive method as treadmill test to detect the early coronary artery disease. Diabetes mellitus can be defined as a state of chronic hyperglycaemia sufficient to cause long-term damage to specific tissues, notably the retina, kidney, nerves, and arteries, but this functional label gives little insight into the long and colourful history of this disease, its clinical and scientific importance, or its immense personal and socioeconomic impact. Diabetes was recognized in antiquity, and its clinical features (with empirical treatment guidelines) were recorded over 3500 years ago in the Egyptian Ebers papyrus. Our understanding of the disease has advanced greatly, especially during the last two decades, but many aspects of its management remain imperfect [21].

This study will help detect prevalence of asymptomatic coronary artery disease in asymptomatic patients of Diabetes mellitus by exercise treadmill test.

Materials and Methods

It was non randomized cross sectional study conducted in Guru Gobind Singh Govt. Hospital, Jamnagar between November-2019 to November-2020. In the study period of 12 months among the patients seen under the Department of General Medicine, after applying inclusion criteria like, No clinical evidence of ischemic heart disease, patients known case of type 2 diabetes mellitus, Normal resting electrocardiogram, No past history of ischemic heart disease, hypertension, cerebrovascular accident, Those who had given written informed consent, 50 patients were included in this study.

Exclusion criteria were Abnormal baseline ECG, Myocardial infarction, Unstable angina, Left bundle branch block, Severe left ventricular hypertrophy, Renal disorders, Febrile illness, Severe osteoarthritis or other such disabilities and Those who had not given written informed consent.

All the patients attending medicine OPD or admitted in Guru Gobind Singh Govt. Hospital, Jamnagar were screened for eligibility and then after taking informed consent and enrolling them in this study, they underwent interview and through physical examination, Information which is present in Performa. All the patients had normal resting

ECG and normal 2D ECHO. All the patients had already undergone treadmill testing. A detailed history was taken from all the patients enrolled which was specific for symptoms related to DM, duration of DM and symptoms related to complication of DM.

Systemic examination was done and which was mainly focused on complication related to Diabetes as below.

1. Autonomic neuropathy: its presence was determined by following tests in our study

a. Heart Rate Variation During Deep Breathing - Patients were asked to take deep breath and during that patients heart rate was monitored by ECG (RR interval) and difference of heart rate >15 was considered normal, 10-15 as borderline and <10 was taken as abnormal

b. Blood Pressure Response to Standing - Presence or absence of postural hypotension was taken as marker of autonomic disturbance in present study.

2. Peripheral neuropathy: It was diagnosed based on patients symptoms which comprised of tingling and numbness over foot and pain and burning sensation over lower limb and also by means of loss of ankle jerk.

All the patients who got enrolled in this study had following investigations of recent time like Routine hemogram, Glycosylated hemoglobin, Fasting and post prandial blood sugar, Lipid profile (total cholesterol, triglycerides, LDL, HDL), Blood urea and serum creatinine, Urine routine and microscopic examination, Resting ECG, 2D ECHO.

Results

50 cases of type 2 diabetes mellitus without having clinical or electrocardiography evidence suggesting ischemic heart disease in tertiary care hospital, Jamnagar were studied and following observations are noted. The mean age of patients studied is 57.06 years; standard deviation (SD) of 10.0496 with range of 32 years to 70 years. Out of 50 cases, 28 are males and 22 females. 4 patients are in group of 31-40 year range, having 3 male and 1 female patients. Range of 41-50 year contains 11 patients in total having 6 males and 5 females, out of 15 patients in range of 51-60 year 9 are female and 6 male, and finally in group of patient with >60 years age there are total 20 patients with 13 males and 7 female patients (table 1).

Total of 50 patients were studied in current study. Out of 50, 21 (42%) patients had normal BMI (18.5-24.9), 23 (46%) patients were overweight (25-29.9), While 6 (12%) patients were obese (>30) (table 2). In this study, out of all enrolled patients, 44% patients had duration of diabetes from 0 to 5

years, 20% patients had duration of diabetes from 6-10 years, 20% patients had duration of diabetes from 11-15 years, 14% patients had duration of diabetes from 16-20 years, 2% patients had duration of diabetes more than 20 years (table 3). This graph shows average HbA1c in patients with duration of diabetes, 0-5 years, 6-10 years, 11-15 years, 16-20 years, more than 20 years which is respectively, 7.61, 8.01, 7.89, 7.9 and 8.6. (Table 4).

In patients with duration of diabetes of 0-5 years there are 22 patients having mean total cholesterol is 204.9, mean Triglyceride level is 136.36, mean LDL is 120.36 while mean HDL is 37.31. In patients with duration of diabetes of 6-10 years there are 10 patients having total cholesterol is 230, mean Triglyceride 157.2, mean LDL 137.1 while mean HDL is 34.3. In patients with duration of diabetes of 11-15 years there are 10 patients, mean cholesterol 242.2, mean Triglyceride is 162.9, mean LDL is 52.69 and mean HDL is 36.2. In patients with duration of diabetes of 16-20 years there are 7 patients, having mean total cholesterol 235.85, mean Triglyceride level 235.8, mean LDL is 169.14 and mean HDL is 35. There is only one patient having duration of DM more than 20 years having mean total cholesterol 250, mean Triglyceride level 135, mean LDL is 194 and mean HDL is 35 (table 5). Among 50 patients studied, 19

(38%) were TMT positive while 31 (62%) were TMT negative. According to this study 12 (42.85%) male are TMT positive while 7 (31.81%) females are TMT positive (table 6). Relation between duration of diabetes and TMT positive status. In this study of 50 patients, 19 (38%) had positive TMT test, and 31(62%) had negative TMT test. Patients with duration of DM less than 5 years – 13.63% had positive TMT test, 86.33% had negative TMT test, 5-10 years-40% had positive TMT test, 60% had negative TMT test, 11-15 years- 50 % patients had positive and equally had negative TMT test, 16-20 years 85.71% had positive TMT test while 14.28% had negative TMT test (table 7). out of 18 patients having autonomic neuropathy, 10 were TMT positive while out of 32 patients without autonomic neuropathy, 22 had negative result in their TMT study (table 8).

According to this study, following observations were made, with reference to average age (p value-0.0012), average duration of diabetes mellitus (p value-0.0001), average HbA1c (p value-0.0137), average FBS(p value-0.0181), average PP2BS(p value -0.000002), average total cholesterol (p value-0.000321), average triglyceride (p value-0.0128), average LDL (p value -0.00038), average HDL (p value-0.00425) was found to have statistically significant difference between TMT positive cases and TMT negative cases (table 9).

Table 1: Distribution of cases depending on their age and sex

Age(years)	Male	Female	Total
31-40	3	1	4
41-50	6	5	11
51-60	6	9	15
>60	13	7	20
Total	28	22	50

Table 2: Distribution of cases based on BMI

BMI	No. of patients	Percentage (%)
Normal (18.5-24.9)	21	42
Overweight (25-29.9)	23	46
Obese (>30)	6	12
Total	50	100

Table 3: Distribution of cases based on Duration of Diabetes Mellitus

Duration of diabetes	Male	Female	Total	Percentage (%)
0-5 year	11	11	22	44
6-10 year	4	6	10	20
11-15 year	7	3	10	20
16-20 year	6	1	7	14
>20 year	0	1	1	2
Total	26	24	50	100

Table 4: Average Glycosylated Haemoglobin and Duration of DM

Duration of Diabetes	No. of Patients	Average HbA1c
0-5 year	22	7.61
6-10 year	10	8.01
11-15 year	10	7.89
16-20 year	7	7.9
>20 year	1	8.6

Table 5: Blood Lipid Profile

Duration of Diabetes	No. of Patients	Cholesterol		Triglycerides		LDL		HDL	
		Average	SD	Average	SD	Average	SD	Average	SD
0-5 Year	22	204.9	55.97	136.36	50.47	120.36	39.07	37.31	6.85
6-10 Year	10	230	46	157.2	53.86	137.1	42.97	34.3	6.78
11-15 Year	10	242.2	50.72	162.9	74.13	135.7	52.69	36.2	7.45
16-20 Year	7	235.85	51.18	152.57	46.15	169.14	37.04	35	7.09
>20 Year	1	250		135		194		35	

Table 6: TMT Results

Sex	TMT Positive	Percentage (%)	TMT Negative	Percentage (%)	Total
Male	12	42.85	16	57.1	28
Female	7	31.81	15	68.18	22
Total	19	38	31	62	50

Table 7: TMT Results and Duration of Diabetes Mellitus

Duration of DM	TMT Positive	Percentage (%)	TMT Negative	Percentage (%)	Total
0-5 Year	3	13.63	19	86.33	22
5-10 Year	4	40	6	60	10
11-15 Year	5	50	5	50	10
16-20 Year	6	85.71	1	14.28	7
>20 Year	1	100	0	0	1
Total	19	38	31	62	50

Table 8: Diabetic Autonomic Neuropathy and Asymptomatic Coronary Artery Disease

Autonomic Neuropathy	TMT Study		Total
	Positive (%)	Negative (%)	
Yes	10 (55.55%)	8 (44.44%)	18 (100%)
No	10 (31.25)	22 (68.75)	32 (100%)
Total	20 (40%)	30 (60%)	50

Table 9: Comparison of Diabetic Subjects with and without Asymptomatic Coronary Artery Disease

	TMT	Mean	SD	P-Value	Inference
Average Age (Years)	Positive	61.84	7.63	0.0012	Significant
	Negative	54.12	10.32		
Average Duration Of DM (Years)	Positive	13.28	7.03	0.0001	Significant
	Negative	6.53	5.28		
Average BMI (Kg/M ²)	Positive	26.17	4.09	0.4420	Not significant
	Negative	26.34	3.86		
Average HbA1c%	Positive	8.05	0.65	0.0137	Significant
	Negative	7.66	0.53		
Average FBS (Mg/Dl)	Positive	175.42	58.04	0.0181	Significant
	Negative	144.74	34.08		
Average PP2BS (Mg/Dl)	Positive	287.21	56.17	0.00002	Significant
	Negative	221.12	33.97		
Average Total Cholesterol (mg/dl)	Positive	252.36	48.45	0.0003	Significant
	Negative	204.48	47.65		
Average Triglycerides (mg/dl)	Positive	171.39	65.09	0.0128	Significant
	Negative	133.93	42.85		
Average LDL (mg/dl)	Positive	169.1	38.11	0.0003	Significant
	Negative	114.22	31.76		
Average HDL (mg/dl)	Positive	32.84	7.63	0.0042	Significant

Discussion

Our study consist of 50 patients known case of type 2 diabetes mellitus of variable duration without prior evidence of coronary heart disease. It consist of assessing the prevalence of asymptomatic coronary artery disease with normal resting ECG

and 2D ECHO in type 2 diabetes mellitus, by finding the TMT changes (positivity). Among 50 patients studied, TMT test was positive in 19(31%) patients and was negative in 31(61%) patients and so prevalence of asymptomatic coronary artery disease in type 2 diabetes mellitus was found to be

31%. This study concurs with other studies done before. One study by Motoji N et al found 31% diabetics without prior evidence of coronary artery disease had treadmill test positive and silent myocardial ischaemia was 2.2 times more common in diabetics as compared with non-diabetics [4]. A study done by Gupta et al in India found that 38.3% of diabetics without prior coronary artery disease had silent myocardial ischaemia on exercise test [6].

Another study Ahluwalia et al from India, reported 50% incidence of silent myocardial ischaemia in diabetics on exercise electrocardiogram and 35% on ambulatory monitoring [7]. Another group Koistinen MJ et al found that 29% diabetics who were asymptomatic for coronary artery disease had silent myocardial ischaemia on 24 hour ambulatory monitoring exercise electrocardiogram [1]. A similar study Scheidt-Nave C et al had shown higher prevalence of silent myocardial ischaemia in diabetics as compared to non-diabetics [3]. The other group Misad et al found 12.1% of diabetics free of coronary artery disease to have silent myocardial ischaemia on exercise electrocardiogram testing [8]. One study Sukhija R et al, found that silent myocardial ischaemia was seen in 14 (46.7%) out of 30 diabetics by using treadmill test [9]. One of the study Fornengo P et al concluded that the prevalence of silent

myocardial ischaemia by using exercise ECG was 17% and angiographic coronary artery disease was found in 13% of middle aged subjects with type 2 diabetes mellitus without other cardiovascular risk factors [13]. The other study Achari V et al from India, found that 51 (42.5%) had evidence of silent ischemia on treadmill testing. Of these 18 underwent coronary angiography and found to have significant CAD in 15 (83.7%) [10]. One study Wackers FJ et al found that a total of 113/522 patients (22%) had silent ischemia using stress testing in asymptomatic patients with type 2 diabetes mellitus. Hence, the present study is in agreement with that diabetics have a higher prevalence of asymptomatic coronary artery disease. Out of TMT positive patients, 42.85% were males and 31.81% were females reflecting higher preponderance of Asymptomatic CAD towards female Type 2 Diabetics [11]. A study done by Meenaxi et al for utility of TMT for asymptomatic CAD also found significant relation of male sex with positive treadmill test [19]. G. Premalatha et al found higher prevalence among males that failed to reach statistical significance concluded that IHD is as common in female as in male diabetics [20]. In our study more positivity of males may be due to less number of female study subjects.

Table 10:

Studies	Prevalence of asymptomatic CAD
our study	31 %
Motoji N et al	31 %
Gupta et al	38.3 %
Ahluwalia et al	50 %
Koistinen MJ et al	29 %
Misad et al	12.1 %
Sukhija R et al	46.7 %
Fornengo P et al	17 %
Achari V et al	42.5 %
Wackers FJ et al	22 %

Asymptomatic coronary artery disease and associated Autonomic Neuropathy: In our study, 10 (55.55%) out of 18 patients with autonomic neuropathy had asymptomatic coronary artery disease while 10 (31.25%) out of 32 patients without autonomic neuropathy had asymptomatic coronary artery disease. Thus, it was seen that, diabetics with autonomic neuropathy had higher incidence of associated asymptomatic coronary artery disease than those without it. (55.5% Vs 32.2%). This is in agreement with majority of studies. In a study Quek DK et al the incidence of

asymptomatic coronary artery disease was found to be 37.5% who had evidence of autonomic neuropathy (76.9%) [5]. Another group Murray DP et al found that in a diabetic population of known or suspected coronary artery disease had silent myocardial ischemia much more common with autonomic neuropathy (92% Vs 39%) [2]. One study Gupta et al in India found 38.3% to have silent myocardial ischemia with a greater prevalence in those with autonomic neuropathy (59%) than those without it (20%) [6].

Table 11:

Studies	Asymptomatic CAD in patients with autonomic neuropathy
our study	55.5 %
Quek DK et al	37.5 %
Gupta et al	59 %

Dyslipidemia and coronary artery disease: Lipid profile abnormalities are very common in type 2 diabetes and it has great influence on coronary artery disease. In current study, Average total cholesterol in TMT positive and negative cases was 252.36 mg/dl and 204.48 mg/dl respectively, Average Triglyceride level in TMT positive and negative cases was 171.39 mg/dl and 133.93 mg/dl respectively, Average LDL in TMT positive and negative cases was 169.1 mg/dl and 114.22 mg/dl respectively.

Average HDL in TMT positive and negative cases was 32.84 mg/dl and 38.12 mg/dl respectively. P value found in average total cholesterol (p value-0.000321), average triglyceride (p value-0.0128), average LDL (p value -0.00038), average HDL (p value-0.00425) was statistically significant. Which was in accordance with following studies? Lehto et al conducted a study in 1059 patients with diabetes and concluded that patients with a high serum

cholesterol level had a twofold increase in the risk of CHD mortality or morbidity, independently of other cardiovascular risk factors [14].

A study Mathura et al found that dyslipidemia was very common in type 2 diabetics and the most common abnormality seen was increased serum triglyceride levels (73.3%) The next common abnormality was decreased serum HDL and LDL levels. Both seen in 66.7%. Coronary artery disease had a stronger correlation with high levels of triglycerides [15]. Barrett-Connor et al conducted a study where 358 diabetics were compared to 4387 nondiabetic and noted that hypertriglyceridemia was associated with diabetes in 29% of non-obese men and 25% of obese men, and in 10% of non-obese women and 21% of obese women. A study from India Agarwal et al, found that CAD had strong correlation with high levels of VLDL (0.76) triglycerides (0.82), LDL (0.23) and low HDL (-0.81) [17].

Table 12:

Lipid profile	our study		Meenaxi et al	
	TMT positive	TMT negative	TMT positive	TMT negative
mean Total Cholesterol mg%	252.36	204.48	197.53	176.65
mean LDL mg%	169.1	114.22	116.46	101.51
mean HDL mg%	32.84	38.12	45.71	45.29

Duration of type 2 diabetes mellitus and coronary artery disease: In our study, out of 50 patients studied, 19 (38%) had positive TMT test, and 31(62%) had negative TMT test.

Patients with duration of DM less than 5 years – 13.63% had positive TMT test, 86.33% had negative TMT test, Duration of DM from 5-10 years-40% had positive TMT test, 60% had negative TMT test, Duration of DM from 11-15 years- 50 % patients had positive and equally had negative TMT test, Duration of DM from 16-20 years 85.71 % had positive TMT test while 14.28 % had negative TMT test. Our results are similar to one study Ahuwallia V et al who found that 70% subjects (7/10) with diabetes of more than 5 years

duration had associated silent myocardial ischemia while only 30% subjects (3/10) with diabetes of less than 5 years duration had associated silent myocardial ischemia [18]. Another study Sargin H et al including 500 patients with type 2 diabetes mellitus with normal resting ECG found that, 62 (12.4%) patients had asymptomatic coronary artery disease on exercise treadmill testing.

The abnormalities of exercise test were associated with longer duration of diabetes (p < 0.005) [12]. Another study done by Meenaxi et al over 75 cases of DM 2 found significant difference between mean duration of TMT positive patients and TMT negative patients which was 4.91 years and 3.59 years respectively [19].

Table 13:

Studies	Mean duration of diabetes in TMT positive patients (years)	Mean duration of diabetes in TMT negative patients. (years)	significance
Our study	13.28	6.53	0.0001
Sargin et al	8.07	6.12	0.05
Meenaxi et al	4.91	3.59	0.0095

Conclusion

The prevalence of asymptomatic coronary artery disease in type 2 diabetes mellitus without past

history of ischemic heart disease or hypertension is 31%. Out of TMT positive patients, 42.85% were males and 31.81% were females reflecting higher

preponderance of Asymptomatic CAD towards male Type 2 Diabetics.

Average age in TMT positive and negative cases was 68.84 year and 54.12 respectively. Diabetics with autonomic neuropathy had higher incidence of asymptomatic coronary artery disease. A significant risk factor profile was prevalent in Type 2 Diabetics with asymptomatic CAD. Dyslipidemia was found to be more in diabetics who had greater prevalence of asymptomatic coronary artery disease on TMT, with high levels of Cholesterol, Triglycerides and LDL. Longer the duration of diabetes, greater the risk of asymptomatic coronary artery disease. An aggressive and early screening of patients with type 2 diabetes mellitus for the evidence of asymptomatic coronary artery disease may prevent catastrophic cardiac events.

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