

Assessment of Asymptomatic Coronary Heart Disease in Type 2 Diabetics with Treadmill Test and Framingham 10-Year CHD Risk Scoring System

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ABSTRACT

Background and objectives: Coronary Heart Disease (CHD) has a high prevalence in Asian Indians & is the leading cause of morbidity & mortality in patients with Type 2 diabetes due to silent myocardial ischemia. This needs early cardiovascular assessment through non invasive tests e.g. Treadmill Test (TMT) & Framingham 10-year CHD risk in addition to periodical clinical examination & resting electrocardiogram. **Methods:** 102 known north Indian diabetics without clinical & electrocardiographic evidence of CHD were evaluated for smoking, blood pressure, glycosylated hemoglobin, fasting & post-prandial blood sugar & lipid profile to calculate Framingham score system for 10-year CHD risk assessment along with exercise treadmill test. **Results:** Among 102 diabetic patients, TMT was positive in 32 (31.37%) patients; more in males (59.73%). Mean cholesterol (189.81 mg %), triglycerides (135.19 mg %) and LDL (116.28 mg %) levels were significantly high in TMT positive cases ($P < 0.001$). A significantly higher mean duration of diabetes (8.87 years) in TMT positive cases, in which 21.31%, 33.33%, 70% & 75% cases are of ≤ 5 years, 6-10 years, 11-15 years & 16-20 years of diabetes; respectively. Mean BMI (30.41 kg/m²) was significantly high in TMT positive cases ($P < 0.0001$) as well as in males (mean BMI 29.46 kg/m², $P < 0.001$). Mean Framingham 10-year CHD risk in males (18.59%) is more than females (13.47%); also significantly high (22.91%) in TMT positive cases ($p < 0.0001$). TMT positive cases 19 (82.60%), 10 (35.71%) & 3 (5.88%) were found in 23 high ($> 20\%$), 28 intermediate ($\geq 10-19.9\%$) & 51 low ($< 10\%$) Framingham 10-year CHD risk groups, respectively. **Conclusion:** A 6-fold higher incidence between low & intermediate, 2.4-fold between intermediate & high and 14-fold between low & high Framingham 10-year CHD risk groups is suggestive of higher incidence of TMT positive cases correlates with higher Framingham 10-year CHD risk & are more prone for asymptomatic CHD in north Indian diabetics.

Key words: Coronary heart disease, Electrocardiogram, Framingham 10-year CHD risk, Treadmill test, Type 2 diabetes.

INTRODUCTION

Diabetes mellitus is an 'iceberg disease' affecting 382 million worldwide and set to rise to 592 million by 2035.¹ It is the commonest endocrine disease with every fifth diabetic in the world being an Indian.^{2,3} Diabetes mellitus is an established

risk factor for cardiovascular morbidity and mortality. Framingham heart study demonstrates the increased and poor prognosis of cardiac disease in diabetes. Cardiovascular mortality is doubled in diabetic men and quadrupled in diabetic women over that in their non diabetic counterparts.⁴

Therefore, a need for early cardiovascular assessment is required; through non invasive tests e.g. Treadmill Test (TMT) and Framingham 10-year Coronary Heart Disease (CHD) risk; in addition to periodical clinical examination and resting electrocardiogram (ECG) to prevent catastrophe events.

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Table 1: Comparison of diabetic subjects with and without asymptomatic coronary heart disease

Parameters	TMT	Mean	SD	P value	Inference
Age (years)	Positive	53.84	7.35	<0.0001	Significant
	Negative	42.43	7.55		
Duration of diabetes (years)	Positive	8.87	4.61	<0.0001	Significant
	Negative	5.01	3.14		
BMI (Kg/m ²)	Positive	30.41	5.13	<0.0001	Significant
	Negative	25.01	3.68		
HbA _{1c} (%)	Positive	8.20	1.20	>0.623	Not significant
	Negative	8.10	0.78		
FBS (mg %)	Positive	159.84	23.63	>0.331	Not significant
	Negative	164.42	21.09		
PPBS (mg %)	Positive	208.13	58.56	>0.649	Not significant
	Negative	213.67	55.90		
Total Cholesterol (mg %)	Positive	189.81	25.28	<0.001	Significant
	Negative	169.59	27.82		
Triglyceride (mg %)	Positive	135.19	27.67	<0.0001	Significant
	Negative	112.71	22.31		
LDL (mg %)	Positive	116.28	22.88	<0.0001	Significant
	Negative	97.41	16.31		
HDL (mg %)	Positive	38.19	2.80	>0.598	Not significant
	Negative	38.51	2.84		
Framingham 10-year CHD risk (%)	Positive	22.91	11.54	<0.0001	Significant
	Negative	8.56	5.60		

TMT: Treadmill Test, SD: Standard deviation, BMI: Body mass index, HbA_{1c}: Glycosylated hemoglobin, FBS: Fasting blood sugar, PPBS: Post-prandial blood sugar, LDL: Low density lipoprotein, HDL: High density lipoprotein, CHD: coronary heart disease.

SUBJECTS AND METHODS

In this study, 102 known north Indian diabetics were evaluated by using exercise treadmill testing and investigated for glycosylated hemoglobin, fasting and post prandial blood sugar and lipid profile to calculate Framingham score system for 10-year CHD risk assessment. Type 2 diabetes mellitus patients; without previous evidence of CAD, cerebro-vascular accident and hypertension with normal 12 lead ECG; were included, while patients with myocardial infarction, angina, congestive heart failure, left bundle branch block, left ventricular hypertrophy, renal disorders, febrile illness, severe osteoarthritis or other disabilities and abnormal resting ECG; were excluded. We have used glucose enzymatic colorimetric (glucose oxidase/ peroxidase) method for plasma glucose, enzymatic colorimetric cholesterol (cholesterol oxidase/ peroxidase aminophenazone) method for fasting serum lipid profile and allengers Gemini –a–dx machine for TMT with modified Bruce protocol and The Framingham Global Risk Assessment Scoring System. Data were analyzed on SPSS statistics version 21 by using t-test for estimating mean, statistical significance ($P < 0.05$) and prevalence rate (%).

RESULTS

This study consisted of 102 known north Indian diabetics without clinical and electrocardiographic evidence of CAD. These patients were evaluated for the prevalence

of asymptomatic coronary artery disease by using exercise Tread mill testing and investigated for Framingham 10-year CHD risk and following observations are made:

Out of 102 patients, 73 were males and 29 females (mean age 50.11 years), 32 patients (31.37%) were overweight, 38 patients (37.25%) obese and remaining with normal body mass index. 61 patients (59.8%) were having diabetes for ≤ 5 years, 27 patients (26.4%) for 6-10 years, 10 patients (9.8%) for 11-15 years and only 4 patients (3.9%) for 16-20 years. Two patients (1.96%) were on diet control alone, 59 patients (57.8%) were on oral hypoglycemic agents, 10 patients (9.8%) were on insulin while 31 patients (30.39%) were receiving both.

In diabetic patients, mean age (53.84 years), mean total cholesterol (189.81 mg%), mean triglyceride levels (135.19 mg%), mean LDL levels (116.28 mg%) and Framingham 10-year CHD risk (22.91%) were significantly high in TMT positive case ($p < 0.0001$, $p < 0.001$, $p < 0.0001$, $p < 0.0001$, $p < 0.0001$; respectively) while mean HDL (38.19 mg%) was also low as part of dyslipidemia but statistically indifferent ($p = NS$) in both groups. Mean BMI (30.41 kg/m²) was significantly high in TMT positive cases ($P < 0.0001$) as well as in males (mean BMI 29.46 kg/m²) ($P < 0.001$). TMT positive cases had mean HbA_{1c} (8.20%), fasting blood sugar (159.84 mg%) and 2-hour post-prandial blood sugar (208.13 mg%) ($p = NS$) (Table 1).

Table 2: Relation of TMT Results with Sex

TMT	Male	%	Female	%	Total	%
Positive	19	59.37	13	40.62	32	31.37
Negative	54	77.14	16	22.85	70	68.63

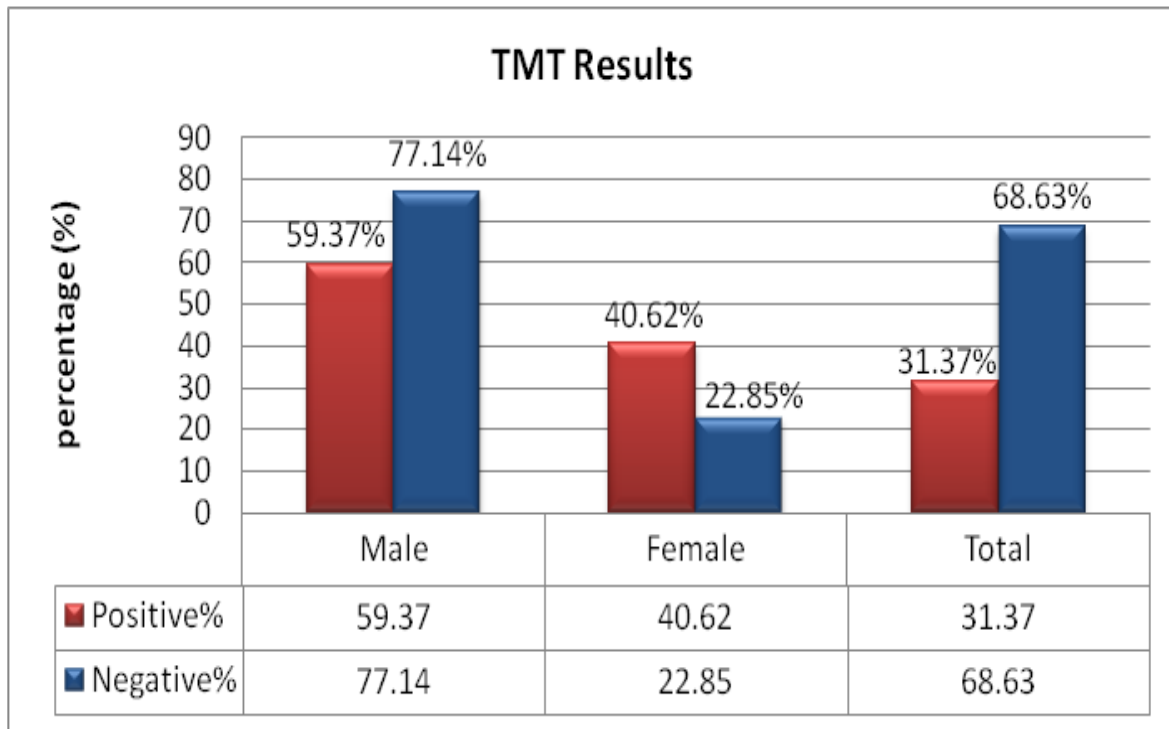


Figure 1: Relation of TMT results with sex

Table 3: Relation of TMT Results with Duration of Diabetes Mellitus

Duration of diabetes (years)	TMT Positive		TMT Negative	
	TMT Positive	%	TMT Negative	%
≤ 5	13	21.31	48	78.69
6-10	9	33.33	18	66.67
11-15	7	70.00	3	30.00
16-20	3	75.00	1	25.00
Total	32	31.37	70	68.63

In diabetic patients, the prevalence of asymptomatic coronary disease in the study population was higher in males 19 (59.37%) than females. Among 102 patients, TMT was positive in 32 patients (31.37%). (Table 2) (Figure 1) TMT positive cases were having significantly higher mean duration of diabetes (8.87 years) ($P < 0.0001$) in which 13/61 (21.31%), 9/27 (33.33%), 7/10 (70%) and 3/4 (75%) patients are of ≤ 5 , 6 to 10, 11 to 15 and 16 to 20 years of diabetes, respectively (Table 3, Figure 2).

In diabetic patients, out of 23 patients of high Framingham 10-year CHD risk ($>20\%$) 19 patients (82.60%) had positive TMT while out of 28 patients of intermediate Framingham 10-year CHD risk (10-19.9%) only 10 patients (35.71%) had positive TMT and out of 51 patients of low

Framingham 10-year CHD risk ($<10\%$) only 3 patients (5.88%) had positive TMT (Table 4) (Figure 3).

DISCUSSION

The present study was aimed at the asymptomatic presentation of coronary artery disease in north Indian diabetes mellitus patients. It consists of assessing the prevalence of asymptomatic coronary artery disease with normal resting ECG in diabetes mellitus, by seeking the TMT changes (positivity) and correlating with Framingham 10 year CHD risk.

Among 102 diabetic patients, one-third were having asymptomatic coronary heart disease as TMT was positive in 32 (31.37%) patients, more in males e.g. 19 (59.73%). A

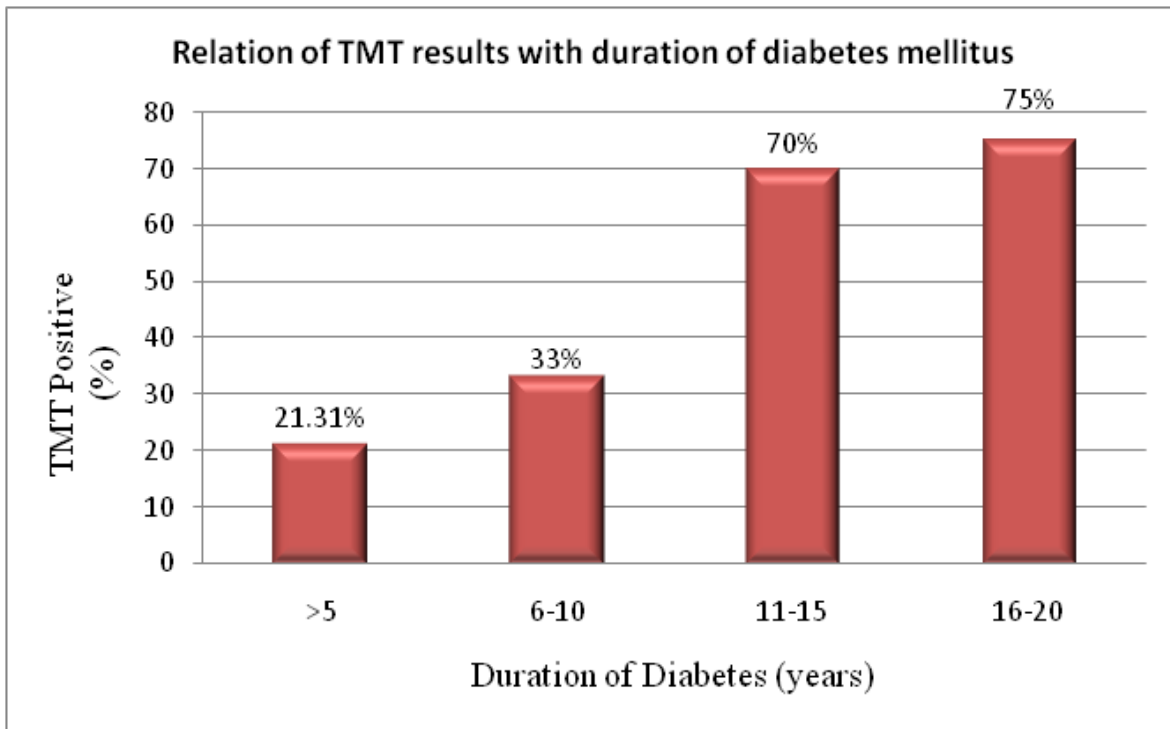


Figure 2: Relation of TMT results with duration of diabetes mellitus

Table 4: TMT Results and Framingham Risk Score 10-Year CHD Risk

Framingham Score 10-year Risk of CHD	No. of positive TMT (%)	No. of negative TMT (%)
≥20% (High risk)	19 (82.60%)	4 (17.39%)
10-19.9% (Intermediate risk)	10 (35.71%)	18 (64.28%)
<10% (Low risk)	3 (5.88%)	48 (94.11%)

similar study done by Motoji N *et al.* found 31% diabetics without prior evidence of coronary artery disease had treadmill test positive and silent myocardial ischemia was 2.2 times more common in diabetics as compared with non diabetics.⁵ Another study by Gupta SB *et al.* in India found that 38.3% of diabetics without prior coronary artery disease had silent myocardial ischemia on exercise test.⁶ Also, Ahluwalia G *et al.* from India, reported 50% incidence of silent myocardial ischemia in diabetics on exercise electrocardiogram and 35% on ambulatory monitoring.⁷ Similarly, Koistinen *et al.* found that 29% diabetics who were asymptomatic for coronary artery disease had silent myocardial ischemia on 24 hour ambulatory monitoring exercise electrocardiogram.⁸

Scheidt-Nave C *et al.* had shown higher prevalence of silent myocardial ischemia in diabetics as compared to non diabetics.⁹ Misad group found 12.1% of diabetics free of coronary heart disease, to have silent myocardial ischemia on exercise electrocardiogram testing.¹⁰ Sukhija R *et al.* found

that silent myocardial ischemia was seen in 14 (46.7%) out of 30 diabetics by using TMT.¹¹ Fornengo P *et al.* concluded that the prevalence of silent myocardial ischemia by using exercise ECG was 17% and angiographic coronary heart disease was found in 13% of middle aged subjects with Type 2 diabetes mellitus without other cardiovascular risk factors.¹² Achari V *et al.* from India, found that 51 diabetics (42.5%) had evidence of silent ischemia on TMT, of these 18 underwent coronary angiography and found to have significant coronary heart disease in 15 (83.7%).¹³ 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.¹⁴ Hence, the present study is in agreement with that diabetics have a higher prevalence of asymptomatic coronary heart disease which can be diagnosed with positive TMT.

The present study showed a significantly higher mean cholesterol (189.81 mg%), triglycerides (135.19 mg%) and LDL (116.28 mg%) levels among TMT positive cases,

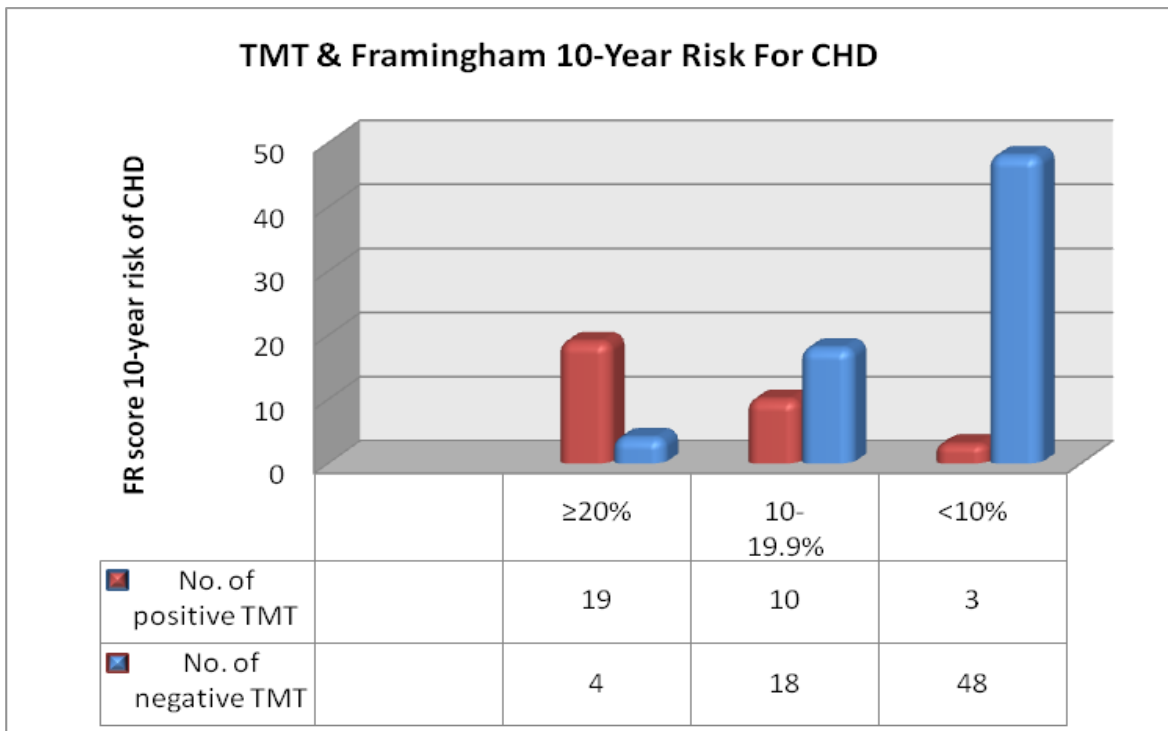


Figure 3: TMT results and Framingham risk score for 10-year CHD risk

suggestive of dyslipidemia as a risk factor for asymptomatic coronary heart disease. Although, a low mean HDL (38.19 mg%) level also seen as part of dyslipidemia in TMT positive cases ($p=NS$). Lehto S *et al.* concluded that 1059 patients with diabetes and a high serum cholesterol level had a two fold increase in the risk of CHD mortality or morbidity, independently of other cardiovascular risk factors.¹⁵ Mathura KC *et al.* found that dyslipidemia was very common in Type 2 diabetics with increased serum triglyceride levels (73.3%); decreased serum HDL and increased LDL levels both seen in 66.7%. Coronary artery disease had a stronger correlation with high levels of triglycerides.¹⁶ Barrett-Connor E *et al.* studied 358 diabetics with 4387 non-diabetics and found that hypertriglyceridemia was associated with diabetes in 29% of non-obese and 25% of obese men while 10% of non-obese and 21% of obese women.¹⁷ Pourmoghaddas A *et al.* a case control study on 272 patients showed that the LDL/HDL ratio was an important predictor of cardiovascular disease in diabetic patients and that a LDL/HDL cholesterol ratio greater than 8 was associated with a 66% higher risk of CAD.¹⁸ Agarwal R *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). Bahia L *et al.* found that frequency of hyperlipidemia in CAD was high with high cholesterol levels ($p=0.04$). Another study found that cholesterol and triglyceride levels were elevated in 28 treadmill positive cases compared to 15 treadmill negative cases ($p<0.01$).²⁰

This study showed that significantly higher mean duration of diabetes (8.87 years) in TMT positive cases, in which 21.31%, 33.33%, 70% & 75% cases are of ≤ 5 years, 6-10 years, 11-15 years and 16-20 years of diabetes; respectively, suggestive that higher incidence of asymptomatic ischemic heart disease with prolong duration of diabetes. Above 10 years of duration of diabetes has 2 fold risk of developing asymptomatic ischemic heart disease in diabetic patients. Similarly, Ahluwalia V *et al.* found that 70% subjects (7/10) with diabetes of >5 years duration had associated silent myocardial ischemia than only 30% subjects (3/10) with <5 years.²¹ Sargin H *et al.* included 500 patients with Type 2 diabetes mellitus with normal resting ECG found that, 62 (12.4%) patients had asymptomatic coronary heart disease on exercise TMT. The abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$).²²

This study showed significantly higher mean BMI (30.41 kg/m²) in TMT positive cases as well as in males (29.46 kg/m²), suggestive of association of obesity with asymptomatic ischemic heart disease; more in males.

In the present study, mean Framingham 10-year CHD risk in males (18.59%) is more than females (13.47%). Also mean Framingham 10-year CHD risk (22.91%) was significantly high in TMT positive cases ($p<0.0001$). This is suggestive of a positive correlation between treadmill test and Framingham 10-year CHD risk score system in estimating asymptomatic

coronary heart disease. Similarly, Metcalf PA *et al.* evaluated 461 diabetics with no past history of cardiovascular disease and found mean Framingham 10-year CHD risk score in male (18.5%) is more than females (13.4%).²³

In our study, TMT positive cases 19 (82.60%), 10 (35.71%) & 3 (5.88%) were found in 23 high (>20%), 28 intermediate (≥10-19.9%) & 51 low (<10%) Framingham 10-year CHD risk groups, respectively. This shows a 6-fold higher incidence between low & intermediate, 2.4-fold between intermediate & high and 14-fold between low & high Framingham 10-year CHD risk groups. Therefore, higher incidence of TMT positive cases correlates with higher Framingham 10-year CHD risk group and are more prone for asymptomatic coronary heart disease. Similarly Mora S *et al.* followed 6126 asymptomatic individuals over 20 years for enhanced risk assessment with exercise testing & Framingham risk scores and found that application of exercise testing to Framingham risk score assessment identified those at high risk (>0.5% annual CVD mortality) in 52-55% women with Framingham risk score 6 to 19% and 47% in men with Framingham risk score 10 to 19%.²⁴

CONCLUSION

Advanced age, prolong duration of diabetes, obesity and dyslipidemia are significant risk factor for asymptomatic ischemic heart disease in Type 2 diabetics. Type 2 diabetes mellitus patients have 31.37% prevalence of asymptomatic ischemic heart disease based on positive TMT, more in males. There is a significant correlation between positive treadmill test and higher mean Framingham 10 year CHD risk (22.91%) in diabetic patient to diagnose asymptomatic ischemic heart disease. A 6-fold higher incidence between

low & intermediate, 2.4-fold between intermediate & high and 14-fold between low & high Framingham 10-year CHD risk groups is suggestive of higher incidence of TMT positive cases correlates with higher Framingham 10-year CHD risk and are more prone for asymptomatic coronary heart disease in north Indian diabetics. An aggressive and early screening by both TMT and Framingham score system of patients with type 2 diabetes mellitus for the evidence of asymptomatic ischemic heart disease may prevent catastrophic cardiac events.

ABBREVIATION

BMI	: Body mass index
CAD	: Coronary artery disease
CHD	: Coronary heart disease
CVD	: Cardiovascular disease
ECG	: Electrocardiogram
FRSS	: Framingham risk scoring system
HDL	: High density lipoprotein
LDL	: Low density lipoprotein
NS	: Not significant
TMT	: Treadmill test
VLDL	: Very low density lipoprotein

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