

# Prevalence of Silent Coronary Artery Disease (CAD) in Asymptomatic T2DM – A Prospective Study

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## ABSTRACT

**Introduction:** To detect the coronary artery disease at an early stage and also to correlate the various risk factors (age, sex, duration of diabetes mellitus, glucose lowering drugs, FBS, PPBS, HBA1C, Lipid profile, BMI and abdominal waist to hip circumference ratio) leading to coronary artery disease in asymptomatic Type 2 diabetic patients, in relation with treadmill test.

**Material and Methods:** The present study was a cross-sectional, prospective study conducted between 2016-17 on 82 asymptomatic T2DM patients, age >18yrs, with no clinical and ECG evidence of CAD.

**Results:** Out of 82 cases of asymptomatic Type 2 diabetics patients, 32.9% were positive for TMT. The risk factors like age between 56 to 65 yrs (46%), males (36%), duration of diabetes > 15yrs (50%), cases on sulfonyureas and metformin combination (33%) and on insulin therapy (45%), BMI between 30 to 34.9 (70.83%), abdominal waist to hip ratio between 0.86 to 0.99 (30%), HbA1C more than 10% (44%), FBS more than 200mg/dl (42%) and, PPBS more than 350mg/dl (58%), Total Sr. cholesterol level more than 240mg/dl (58%), T.G level more than 200mg/dl (53%), HDL levels less than 30mg/dl (47%) and HDL level between 31 to 45 mg/dl (23%), LDL level more than 160mg/dl (45%), VLDL more than 40mg/dl (50%), showed high percentage of positive treadmill test.

**Conclusion:** Treadmill test being a non-invasive sophisticated screening test should be performed on all asymptomatic T2DM patients with high risk factors for early detection of asymptomatic CAD, to prevent catastrophic cardiac events and consequent deaths.

**Keywords:** Coronary Artery Disease; Risk Factors; Asymptomatic T2DM; Treadmill Test

is more frequent in diabetics than in non-diabetics because of diabetic neuropathy.<sup>5</sup> Thus screening for early detection of asymptomatic CHD in Type 2 Diabetes Mellitus (T2DM) may be helpful to prevent these catastrophic cardiac events and consequent deaths.

Periodical thorough clinical examination and resting ECG are not always useful for this purpose as many times these methods fail to detect asymptomatic CHD. On the other hand invasive tests are highly expensive, so, not cost effective for screening purpose.<sup>3</sup> In this scenario treadmill test (TMT) has an advantage of being a non-invasive sophisticated test. It can identify the majority of patients likely to have significant ischemia during their daily activities and remain the most important screening test for significant CAD.<sup>6</sup>

Yet, the question is, should we perform treadmill test on all asymptomatic T2DM patients? or should we perform on T2DM patients having certain associated risk factors?

Recently there have been few studies guiding us towards the association of traditional and emerging cardiac risk factors with positive treadmill test. Yet, they emphasize on need for further studies. Hence the present study was conducted to detect the CAD at an early stage in asymptomatic diabetic patients and also to correlate the various risk factors leading to coronary artery disease in relation with treadmill test (age, sex, duration of diabetes mellitus, glucose lowering drugs, FBS, PPBS, HBA1C, Lipid profile, BMI and abdominal waist to hip circumference ratio).

## MATERIAL AND METHODS

The present study was a cross-sectional, prospective observational study conducted between 2016-17 on asymptomatic T2DM attending the outpatients and inward patient, at Medicine Department of S. Nijalingappa Medical College, HSK hospital and Research Center, Bagalkot.

**Sample Size:** Sample size was calculated using the formula  $n=4pq/l2$

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## INTRODUCTION

The prevalence of coronary heart disease in India earlier varied from 15- 65/1000 population, but now it has increased about 80- 120/1000, making it a major cause of morbidity and mortality.<sup>1</sup> Diabetes Mellitus (DM) is an important independent and modifiable risk factor for development of the Coronary Heart Disease (CHD). Mortality related to cardiovascular disease is doubled in diabetic men and quadrupled in diabetic women over that in their non-diabetic counter parts.<sup>2</sup> CHD silently progresses over years in diabetic patients and may eventually have asymptomatic classic silent ischemia causing catastrophic cardiac events and consequent deaths.<sup>3</sup>

Silent MI is defined as the presence of objective evidence of myocardial ischemia in the absence of chest discomfort or other angina equivalents.<sup>4</sup> Silent Myocardial Ischemia (SMI)

n - sample size, p-prevalence, l-allowable error,  $q=100-p$   
Using above formula the sample size found out to be 82.  
Patients were identified as diabetic if they met any of the following criteria: atleast one prescription of anti - diabetic drug, ongoing anti - diabetic treatment or elevated HbA1C  $\geq 7$ . Among the identified diabetic patients of both gender, those with age  $>18$  yrs, no clinical and ECG evidence of CAD were included and those with uncontrolled HTN, Type1 Diabetes Mellitus, haemodynamically unstable patients, previous history of MI, heart failure, evidence of angina pectoris, anemia, severe aortic stenosis, HOCM (Hypertrophic cardiomyopathy), renal disease, ECG evidence of Q wave MI, ischemic ST-segment or T wave abnormality or complete LBBB (Left Bundle Branch Block), any chronic illness because of cancer and ESRD (End stage renal disease) or liver disease, patients unable to perform TMT, any known absolute/relative contraindications of TMT, inconclusive test result and women with gestational DM were excluded. From all the selected participants informed consent was obtained. All participants were interviewed in detail to obtain demographic information like name, age, sex, residence, occupation and detailed personal history with special emphasis on duration of Diabetes mellitus and current drug history for Diabetes mellitus.

### LABORATORY INVESTIGATIONS

The participants were further evaluated for routine haemogram, glycosylated haemoglobin (HbA1C), fasting and post prandial blood sugar (FBS, PPBS), lipid profile, along with exercise tread mill test (TMT).

BMI (body mass index) using Quetelet's formula and abdominal waist to hip circumference ratio was calculated for all the patients undergoing treadmill test.

#### Exercise treadmill test

The exercise treadmill test was performed in each participant according to the Bruce protocol. The Bruce multistage maximal treadmill protocol has 3 minutes period to allow achievement of steady state before workload is increased. Participants if taking beta-blockers and CCB's were asked to stop these medications 72 hrs before and discontinued smoking 1 day before the TMT test schedule. It was considered positive if following criteria were satisfied:

1. Horizontal or down sloping ST segment depression more the 1mm lasting for 0.08sec after the J point (1.5mm if it is up sloping)
2. ST segment elevation of 1mm or more than the control tracing in any lead except aVR
3. In the presence of ST depression in the control tracing, additional depression of 1mm more than the rest.
4. ST segment depression for greater than 5mm during recovery period
5. Abnormal BP response
6. Ventricular arrhythmias

Participants with positive screening were sent for cardiology consultation.

### STATISTICAL ANALYSIS

The observations of this study are represented in the tables. The descriptive statistics were used to interpret the data.

### RESULTS

In the present study, 82 asymptomatic T2 DM patients were studied. Their preliminary data is represented in Table 1. In the present study, out of 82 cases of asymptomatic diabetics patient 27 (32.9%) subjects were positive and 55 were negative for TMT (Table 2). In the present study, we found majority of cases that were positive were between 56 to 65 yrs of age, 12 out of 26 cases with 46% positivity for TMT. (Table 3)

In the present study, out of 50 males 18 (36%) cases were positive for TMT, while out of 32 female cases 9 (28%) were positive (Table 3). In the present study, we found 15 (44%) out of 34 cases with diabetes for 6 to 10 years and 5 (50%) cases out of 10 cases with diabetes for more than 15 years, were TMT positive. (Table 3)

In the present study, we found 14 (33%) cases out of 42 cases on sulfonyureas and metformin Combination, 11 (45%) cases out 24 cases on insulin therapy with positive TMT test (Table 3). In the present study, 17 (70.83%) cases out of 24 cases to have BMI between 30 to 34.9; While only 10 (21.27%) cases were positive out of 47 cases with BMI between 25 to 29.9. (Table 3)

In the present study, we found majority of cases had abdominal waist to hip ratio between 0.86 to 0.99 i.e. 13 (30%) cases out of 43 cases with TMT positive. (Table 3)

Variables	Mean	Standard Deviation	Minimum	Maximum
Age(years)	52.74	9.816	9	75
Duration of diabetes(years)	5.25	4.592	1	20
BMI(Kg/m <sup>2</sup> )	30.44	21.98	2	60
Waist hip ratio	0.91	0.12	0.09	1.2
HbA1C(%)	8.29	1.64	1.48	12.3
Fasting Blood Sugar (mg/dl)	131.72	44.27	24	234
Post Prandial Blood Sugar(mg/dl)	248.35	69.94	68	388
Serum Cholesterol(mg/dl)	199.21	43.6	40	362
Triglyceride (mg/dl)	145.45	34.54	33	239
HDL(mg/dl)	33.65	6.34	6	48
LdL(mg/dl)	131.76	24.17	21	189
VLDL(mg/dl)	21.87	13.95	6	68

**Table-1:** Preliminary data of 82 patients

In the present study, we found 13 (44%) cases out of 29 cases with HbA1C more than 10%; while 10 (45.45%) cases out of 22 cases with HbA1C between 8.9 to 9.9% positive TMT. (Table 4)

In the present study, we found 15 (42%) cases out of 35 cases with FBS more than 200mg/dl and

9 (31%) case out of 29 had fasting sugars between 127 to 199mg/dl with positive TMT. (Table 4)

In the present study, 14 (58%) cases out of 24 cases with PPBS more than 350mg/dl and 6 (52%) cases out of 17 with PPBS between 301 to 349mg/dl had positive TMT. (Table 4)

In the present study, 11 (58%) cases out of 18 cases with total cholesterol level more than 240mg/dl and 11 (34%) out of 32 cases had cholesterol between 201 to 239mg/dl had positive TMT. (Table 4)

In the present study, 12 (53%) out of 23 cases with T.G level more than 200mg/dl and 13 (44%) cases out of 34 cases had T.G level between 151 to 199mg/dl had TMT positive. (Table 4)

In the present study, that 18 (47%) cases out of 38 with HDL levels less than 30mg/dl and 9 (23%) cases out of 48 with HDL level between 31 to 45 mg/dl had positive TMT. (Table 4)

In the present study, 10 (45%) cases out of 22 cases with LDL level more than 160mg/dl and 13 (39%) cases out of 33 cases with LDL level between 131 to 150mg/dl had positive TMT. (Table 4). In the present study, 8 (50%) cases out of 16 cases with VLDL more than 40mg/dl and 13 (34%) cases

out of 31 cases with VLDL level between 21-39mg/dl had positive TMT.(Table 4)

## DISCUSSION

Coronary Artery Disease detection in asymptomatic Type 2 DM is often delayed. Silent CAD is an important cause of premature death of patients. In approximately 18% of patients with CAD, sudden death is the first and the only manifestation.<sup>7</sup> The prevalence of coronary artery disease in Type 2 DM is variable and ranges from 9 to 75%. The present study was based on detection of Coronary artery disease in an asymptomatic Type 2 DM patients with use of treadmill test, associated with various risk factors, there by utilizing it for preventive aspect of IHD.

In our study, 32.9% subjects were positive for TMT. Similar results pertaining to prevalence of CHD in asymptomatic T2DM was demonstrated in various studies like Anil et al 24% (12 out of 50),<sup>3</sup> Swaminathan et al 30% (15 out of 50),<sup>8</sup> Meenaxi Sharada 37.3%,<sup>9</sup> Ajaykumar et al 23.6%<sup>10</sup> and Rajeshkumar et al 31.37%.<sup>11</sup> A study was conducted at Selva Institute of Medical Sciences on 161 asymptomatic T2DM patients and found 34 (21.1%) were positive for TMT, of these 27 underwent echo and presence of RWMA was confirmed in 20 patients.<sup>12</sup> In Sarkar Chandra et al 136 asymptomatic T2DM patients were enrolled prospectively for treadmill test and subsequent coronary angiography was performed on 96 (70.87%) TMT positive patients.<sup>13</sup> These data suggests that, silent MI is not an uncommon entity in T2DM, and hence its early detection can be a preventable measure for unwanted cardiac events.

In our present study, 46% (12 out of 26 cases) positive for TMT were between 56 to 65 yrs of age. Similar result was found in Anil et al, wherein 33.33% of the asymptomatic T2DM patients, who had TMT positive were aged between

Interpretation	No of cases	Percent	Valid Percent
Positive TMT	27	32.1	32.9
Negative TMT	55	65.5	67.1
Total	82	97.6	100

**Table-2:** Interpretation of result of TMT

S.No	Variables	Range	TMT Results (No of Patients)	
			Positive	Negative
1	Age of patients(yrs)	35-45	0	15
		46-55	7	27
		56-65	16	12
		>65	4	1
2	Gender	Male	18	9
		Female	32	23
3	Duration of Diabetes(yrs)	0-5	3	25
		06-10	15	19
		11-15	4	5
		16-20	5	5
4	Glucose lowering drugs	Metformin	1	12
		Sulfonylureas	1	2
		Metformin +Sulfonylueas	14	27
		Insulin	11	13
5	BMI (kg/m2)	20-24.9	1	11
		25-29.9	10	25
		30-34.9	16	19
6	Abdomen waist to hip circumference ratio	<0.85	4	19
		0.86-0.99	13	24
		1/>1	10	16

**Table-3:** Outcome of TMT results with vaious clinical risk factors

S.NO	Variables	Range	TMT Results(No of Patients)	
			Positive	Negative
1	HbA1C(%)	<6.6	0	3
		6.7-8.8	4	24
		8.9-9.9	10	12
		>10	13	16
2	Fasting Blood sugar (mg/dl)	<126	3	15
		127-199	9	20
		>200	15	20
3	Post Prandial Blood sugar (mg/dl)	<200	2	14
		201-300	7	18
		301-349	6	11
		>350	14	10
4	Total Sr.Cholesterol(mg/dl)	<200	5	27
		201-239	11	21
		>240	11	7
5	Triglyceride (mg/dl)	<150	6	26
		151-199	15	19
		>200	6	10
6	HDL (mg/dl)	<30	18	20
		31-45	9	39
		46-60	0	6
7	LDL(mg/dl)	<130	4	23
		131-159	13	20
		>160	10	12
8	VLDL(mg/dl)	<20	6	26
		21-39	13	18
		>40	8	11

**Table-4:** Outcome of TMT results with biochemical parameters

56 - 65yrs.<sup>3</sup> In Gerald et al the mean age of asymptomatic T2DM patients with eventful TMT was 67 ±9 years.<sup>14</sup> Also, in Kim et al a similar result was seen, wherein significant TMT events recorded in mean age group of 63.1±9.4 years.<sup>15</sup> In the present study, male preponderance (36%) was seen in positive TMT results compared to female cases (28%) among the asymptomatic T2DM patients. Similar result was recorded in Anil et al, where in prevalence of silent MI was higher in male sex (28.56%) compared to female sex (18.8%).<sup>3</sup>

In the present study, 44% cases with diabetes for 6 to 10 years and 50% cases with diabetes for more than 15 years, showed positive TMT. In Anil et al, out of 12 cases of positive TMT, 9 were with diabetes for duration of more than 10 years.<sup>3</sup> In other studies like Swaminathan showed 71.4% with duration between 11-15years and 80% with duration between 16-20 years<sup>8</sup>; Gupta et al,<sup>16</sup> Ahuwalia et al<sup>17</sup> have recorded around 70% patients with duration of diabetes for more than 5 years being associated with silent MI. Meenaxi Sharada et al,<sup>9</sup> Mathura KC et al<sup>18</sup> have also demonstrated a strong association between duration of diabetes and abnormalities in exercise test. Sarkar Chandra et al<sup>13</sup> had concluded that long standing asymptomatic T2DM (more than 10years) with family history of CAD should be done TMT for early detection of CAD.

In the present study, majority of the patients with positive TMT, were in class II (21.27%) and class III (70.83%) obesity. Similar results was found in Anil et al<sup>3</sup> wherein

positive TMT was associated with BMI of class II obesity 23.07% and class III obesity 25%. In another study Blandine et al<sup>19</sup> had noticed that average BMI in patients with abnormal TMT was 26.4 ± 3.0.

In the present study, we found 44% cases with HbA1C more than 10% and 45.45% cases with HbA1C between 8.9 to 9.9%, had positive TMT. Swaminathan et al<sup>8</sup> had shown statistically significant positive TMT in asymptomatic T2DM patients with HbA1C more than 9.7%. Goutham Ravipeth et al<sup>20</sup> found silent MI in 27 out of 54 patients i.e. 50% whose HbA1C levels were ≥ 7.6%. In a study conducted at Selva Institute of Medical Sciences,<sup>12</sup> had found a high HbA1C associated with positive TMT.

In the present study, among the asymptomatic T2DM patients, Total Sr. Cholesterol of >200mg/dl, Sr.TG of >150mg/dl, LDL levels of >130mg/dl, VLDL of >20mg/dl and HDL level of <45, had higher prevalence of positive TMT. Anil Shrinivasrao et al<sup>3</sup> documented that 25% of asymptomatic T2DM patients with positive TMT had Total Sr. Cholesterol >240mg/dl and LDL>160mg/dl. Swaminathan et al<sup>8</sup> found statistically significant average values of TG in positive and negative cases of TMT in asymptomatic T2DM to be 176.6mg% and 130.5mg% respectively, Total Sr.Cholesterol 174.4mg% and 180.9mg% respectively in negative and positive cases of TMT. De Luca et al<sup>21</sup> and Gautam Ravipathi et al<sup>20</sup> also found association between elevated levels of TG and positive TMT. In a study conducted at Selva institute of Medical Sciences,<sup>12</sup> had found TC, TG and LDL showed

marginal increase of odds in favor of TMT positive result. In Rajesh kumar et al<sup>11</sup> the mean cholesterol (189.81mg%), TG (135.19mg% and LDL (116.28mg%) levels were significantly high in TMT positive cases. Anil Shrinivasrao et al<sup>3</sup> found that number of positive TMT were higher in patients with HDL levels of < 30 (35%), TG levels of >200 (40%), with LDL levels of >160mg (50%) and with Total Sr Cholesterol levels of >240 (33.33%). In Agarwal et al<sup>22</sup> the prevalence of dyslipidemia was high in diabetic population with high Sr. Cholesterol of >240mg/dl (15%), Sr. TG of >160 (42.41), LDL of >130 (45.26%), VLDL >40mg/dl (24.09%) and low HDL levels of <40mg/dl (52.27%).

In the present study, we found 30% of asymptomatic T2DM cases with abdominal waist to hip ratio between 0.86 to 0.99 to be TMT positive. In the present study, we also found 33% cases on sulfonylureas and metformin combination, and 45% cases on insulin therapy with positive TMT. In the present study, we found 42% cases with FBS more than 200mg/dl and 31% cases with FBS between 127 to 199mg/dl had positive TMT. In the present study, we found 58% cases with PPBS more than 350mg/dl and 52% cases with PPBS between 301 to 349mg/dl had positive TMT. There were no literatures available for the same.

## CONCLUSION

CHD detection in asymptomatic Type 2 DM is often delayed. Silent CAD in Type 2 DM is an important cause of premature death of patients, as it silently progresses over years and eventually cause classic silent ischemia and catastrophic cardiac events, especially in those with associated risk factors. It can be recommended that TMT should be a part of routine investigation in asymptomatic patients with type II DM without previous clinical and electrocardiographic signs of ischemic heart disease, especially with age >55 years, duration >10 years, impaired long term sugar control and dyslipidemia.

Further large numbers of studies are recommended in this regard on large number of study populations, also considering other risk factors like hypertension, smoking and alcoholism.

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