Detection of Asymptomatic Coronary Artery Disease (CAD) in Newly detected Type 2 Diabetes Mellitus (DM) by Exercise Treadmill Test

Amit Daphale[1], Sourya Acharya[2], Samarth Shukla[3]

ABSTRACT

Introduction: Diabetes mellitus is one of the leading and main threats to human health in the 21st century. Study aimed to detect the prevalence of asymptomatic coronary artery disease (CAD) in newly diagnosed cases of type 2 diabetes mellitus by exercise tread mill test (TMT).

Material and Methods: This cross sectional study was conducted in the department of Medicine, Acharya Vinoba Bhave Rural Hospital and Jawaharlal Nehru Medical College, Sawangi (M) Wardha. Two hundred newly detected diabetic cases were selected from patients coming to medicine OPD and admitted in medicine ward. All cases went through a detailed history, physical examination and tread mill test (TMT) to detect silent ischemia. Hundred age and sex matched healthy controls were taken for comparison.

Results: In this study, the prevalence of asymptomatic CAD in newly detected cases of type 2 DM was 11%. Uncontrolled HTN, raised BMI (>23 kg/m^2), raised waist circumference (>90 cm in males/>80 cm in females), raised total cholesterol levels and raised triglycerides were significantly associated with cases of newly detected type 2 DM ($p<0.05\%$).

Conclusion: Newly detected cases of type 2 DM form a vulnerable population for asymptomatic CAD. Cases of newly detected type 2 should be thoroughly screened for other co -morbid conditions like hypertension, obesity, abdominal obesity and dyslipidemia. The exercise stress test is a simple, noninvasive, cost effective and comparatively less complicated tool to diagnose asymptomatic CAD.

Keywords: CAD, TMT, silent Ischemia, Dyslipidemia, Type 2 DM

INTRODUCTION

The number of individuals with diabetes globally in 2014 was estimated to be 422 million. This amounts of 8.5% of global population. In the year 2015, around 1.6 million deaths resulted directly from diabetes. WHO predicts that diabetes will be 7th leading cause of death by the year 2030. Diabetes is one of the major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.[1].India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the ‘’diabetes capital of the world’’. World health organization (WHO) reports show that 32 million people had diabetes in the year 2000.[1]

Diabetes and cardiovascular diseases are rapidly gaining pandemic proportions in south East Asian subcontinent, and India is leading the race. There are 33 million diabetics in India presently and this number is expected to reach 79.4 million in 2030. This means by that time India will contribute to more than one fifth (20%) of the total diabetic population of the world. One of the important factors contributing to increased prevalence of type 2 diabetes in Asian Indians is the fact that they have a greater degree of insulin resistance compared to Caucasians.[2-4] Asian Indians have higher insulin levels to a glucose load than European was first demonstrated by Mohanetal(1986).[5]The euglycemic clamp studies later demonstrated and confirmed that insulin resistance is greater among Asian Indians compared to age, sex and body mass index matched Europeans.[6] The Framingham study pointed out a previously unknown factor in diabetic patients that causes much higher incidence of cardiovascular complications.[7] Diabetic individuals have higher serum concentration of lipid, more hypertention and obesity and thus the pathogenesis of advanced atherosclerosis. The type 2 diabetics are also prone to asymptomatic coronary artery disease(CAD) even before the development of its overt symptoms.[8] This reflects the accelerated coronary atherosclerosis, although autonomic neuropathy has also been implicated in its causation.[9] Such silent coronary artery disease appears to be associated with an adverse outcome in asymptomatic patients.[10]

Coronary artery disease is the leading cause of death in patients with type2 DM and is often asymptomatic because of silent myocardial ischemia. Silent ischemia may delay or mask the diagnosis of CAD making it asymptomatic and contributing to more advanced disease when it is finally discovered. Diabetic patients are more prone to development of autonomic neuropathy and this can be histologically characterised and physiologically demonstrated[11-17]and is postulated as mechanism responsible for defective angina warning system attributed to diabetic patients. Periodical clinical examination and resting electrocardiogram may fail to detect coronary artery disease. Exercise electrocardiogram can identify the majority of patients likely to have significant ischemia during their daily activities and remains the most important screening test for significant CAD[18]. Attempt have been made to elucidate the risk factors that can help us predict the subgroup of diabetics who are at risk for development

[1]Resident, [2]Professor, Department of Medicine, [3]Professor, Department of Pathology, J.N. Medical College, DMIMS (DU), Sawangi (Meghe), Wardha, Maharashtra, India

Corresponding author: Dr. Sourya Acharya, Professor, Department of Medicine, J.N. Medical College, DMIMS (DU), Sawangi (Meghe), Wardha-442001, Maharashtra, India

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of asymptomatic CAD by many studies but no consistent results have been found[19]. Exercise treadmill testing is one such diagnostic tool for the diagnosis and risk stratification of coronary heart disease whose diagnostic and prognostic value has been studied extensively[20]. The predictive value of the exercise stress test is greatest when test results are combine with family history, current symptoms and underlying risk factors. Combining clinical information with test data yields 94% sensitivity and 92% specificity[20].

Studies about asymptomatic CAD in Indian population with type 2 DM have been done previously and this study is undertaken to add to the current part of data regarding the prevalence of CAD. Further this study will include only the newly detected type 2 DM (DM diagnosed since 6 months) [21]. Thus, it will estimate the risk at the early stage of the disease.

Study was done with the aim to estimate the prevalence of asymptomatic coronary artery disease in newly detected cases of type 2 diabetes mellitus by exercise stress test with objectives to co-relate various risk factors in newly detected case of type 2 diabetes mellitus in patients having asymptomatic coronary artery disease and to establish trade mill test as effective diagnostic tool to diagnose asymptomatic coronary artery disease.

MATERIAL AND METHODS

The present cross sectional study entitled "Detection of asymptomatic coronary artery disease in patients with newly detected type 2 diabetes mellitus by exercise stress test" was conducted in department of Medicine, Acharya VinobaBhave Rural Hospital and Jawaharlal Nehru Medical College, Sawangi (M) Wardha. It is a 1200 bedded tertiary care center and teaching hospital. The study was carried over a period of 24 months from September 2015 to September 2017. The study consisted of 200 newly detected diabetic cases (less than 6 months)[21] and 100 control cases who attended medicine OPD, diabetic clinic and/or admitted in medicine wards.

Definition of Cases: Newly diagnosed cases of Type 2 diabetes mellitus, [21] as per as per WHO criteria:

- Symptoms of diabetes plus random blood glucose concentration more than or equal to 11.1 mmol/L (200 mg/d L) or;
- Fasting plasma glucose more than or equal to 7.0 mmol/L (126 mg/dL) or ;
- Hemoglobin A1C more than or equal to 6.5% or;
- 2-hour plasma glucose more than or equal to 11.1 mmol/L (200 mg/d L) during an oral glucose tolerance test

Exclusion criteria

- Long standing cases of type 2 Diabetes mellitus (more than 6 months)
- Patients who had symptoms of angina, evaluated by "Rose criterion." [22-24]
- Patients having ECG changes suggestive of ischemia – (ST depression. > 1mm in leads I and avL, V1 – V6 or in leads II, III, avF and T wave inversion in leads I and avL, V1 – V6 or in leads II, III, avF.)
- Person who cannot walk on treadmill and or didn't consent
- Known coronary artery disease.
- Patients already on cardio selective drugs
- Patients of CKD, hepatic disorders or patients with any physical disability

A clearance was obtained from the ethical committee of Acharya Vinoba Bhave Rural Hospital and Jawaharlal Nehru medical college by submitting the synopsis of the study prior to the start of the study.

Study protocol

A detailed medical history was taken from all the cases with emphasis on any evidence of CAD and DM. Drug history was taken to rule out use of any cardioactive drugs. History was also taken regarding duration and treatment of diabetes, hypertension, smoking or alcohol intake. Family history of CAD if any was recorded. A detailed clinical examination was carried out in all cases and included

Anthropometric measurements

1. Weight in kilograms was recorded with the subject standing motionless on the standard weighing machine, without footwear.
2. Height in centimeters was measured with patient standing without foot wear, against a wall mounted scale with the head positioned so that the top of the external auditory meatus was in level with the inferior margin of the bony orbit.
3. Body mass index (BMI) was calculated using the formula;
   BMI = weight in kg/ (height in meters)
   The cases were said to have normal BMI when it ranged Between 18.5 – 22.9 kg/m^2
   Overweight when BMI ranged Between 23 – 24.9 kg/m^2
   And obese when BMI was 25 -29.9 kg/m^2[25].
4. Waist circumference: The waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a stretch-resistant tape that provides a constant 100g tension.

Abdominal obesity was defined was waist circumference of more than 90 cm in men and 80 cm in women as per the modified NCEP ATP III guidelines for Asian population[26]. Systemic examination included a detailed examination of the cardiovascular, respiratory and abdominal systems.

Laboratory investigations

All the cases were then subjected to a battery of investigation. Fasting and post meal.

blood sugar was estimated in all cases by GOD/POD method using span kit. Lipid profile (Total cholesterol, HDL, triglycerides) was estimated by using the COD/POD method by Bayers kit. LDL was calculated using the Friedewald formula.

The samples for fasting blood sugar and lipid profile were taken early morning after a fasting period of 8 hours and the post prandial blood sugar were collected two hours after

major meal.

Tread mill test

Instrumentation

All the subjects had a treadmill test performed on a motor driven with tread mill software NASAN ST+ VERSION 6.0 analyzed by computer. Each case and control had a test exercise before starting the actual exercise. The inclination and speed of treadmill was calibrated according to the standard Bruce protocol. All the cases and control were made to run up to 9 minutes 3rd stage of standard Bruce protocol.

Peak exercise

The peak exercise on TMT was defined when the subject attained predetermined heart rate (220- age in years) or exhaustion, whatever had attained earlier.

Ischemic response to exercise to treadmill was said to be present when there was flat or downsloping depression of the ST segment > 0.1 mV below baseline (i.e. the PR segment) and lasting longer than 0.08s.Upsloping or junctional ST segment changes are not considered characteristic of ischemia.Negative tests in which the target heart rate (85% of maximal predicted heart rate for age and sex) is not achieved are considered non diagnostic. The development of angina was said to be present when there was >0.2 mV ST depression and/ or that persisted for >5 min after the termination of exercise, i.e. during recovery.

STATISTICAL ANALYSIS

Statistical Analysis was performed with help of Epi Info (TM) 3.5.3. EPI INFO is a trademark of the Centers for Disease Control and Prevention (CDC). Using this software, basic cross-tabulation, inferences and associations were performed. Means along with the standard deviations were calculated under descriptive analysis.

Chi square (χ^2)test was used to test the association of different study variables with the study groups. Z-test (Standard Normal Deviate) was used to test the significant difference between two proportions. t-test was used to compare the means. Odds ratio (OR) with 96% confidence intervals was calculated to find the risk factors. Fisher exact test also was used. $p< 0.05$ was considered statistically significant.

RESULTS

The risk of asymptomatic coronary artery disease was 3.99 times more among the patients with T2DM as compared to the patients without T2DM and the risk was significant [OR-3.99 (1.16, 13.69;p=0.018]. The prevalence of asymptomatic coronary artery disease among the patients with T2DM was 11% (table 1,2). Chi-square (χ^2) test showed that there was significant association between T2DM and asymptomatic coronary artery disease (p=0.018).

The risk of asymptomatic coronary artery disease was 7.90 times more among the patients with age>60 years as compared to the patients with ≤60 years and the risk was significant [OR-7.90 (3.03, 20.56);p<0.0001]. Chi-square (χ^2) test showed that there was significant association between age and asymptomatic coronary artery disease (p<0.0001).

The risk of asymptomatic coronary artery disease was 3.12 times more among the patients with Obesity as compared to the patients without Obesity and the risk was significant [OR-3.12 (1.01, 9.62);p=0.037]. Chi-square (χ^2) test showed that there was significant association between Obesityandasymptomatic coronary artery disease (p=0.037). Fisher Exact test showed that proportion of patients with asymptomatic coronary artery disease was significantly higher for level of triglyceride>150 mg/dl (p<0.00001).

DISCUSSION

The present cross sectional study entitled "Detection of

Parameters	Patients with T2DM (n=200)	Patients without T2DM (n=100)	Test statistic	p-value
Age	46.20±12.20	44.43±14.37	t_{298}=1.11	>0.05 NS
Sex(Male:Female)	125:75	59:41	=0.27	0.62 NS
Family history of CAD	62(31.5%)	21(21.6%)	Z=1.58	>0.05 NS
History of Hypertension	94 (47.0%)	30 (30.0%)	Z=2.47	>0.05 NS
History of tobacco consumption	89 (44.5%)	18 (18.0%)	Z=4.04	<0.001*
History of alcohol consumption	74 (37.0%)	26 (26.0%)	Z=1.67	>0.05 NS
HTN	55 (27.5%)	14 (14.0%)	Z=2.35	<0.05*
SBP(mmHg)	128.66±21.59	126.02±14.57	t_{298}=1.10	>0.05 NS
DBP(mmHg)	76.93±11.01	76.92±7.89	t_{298}=0.08	>0.05 NS
BMI (kg/m^2)	24.00±2.74	22.79±2.98	t_{298}=3.50	<0.001*
Waist circumference (cm)	79.34±6.02	77.77±7.18	t_{298}=1.99	<0.05*
FBS (mg/dl)	151.61±36.72	98.82±11.87	t_{298}=14.00	<0.001*
PMBS (mg/dl)	203.61±52.91	124.52±18.35	t_{298}=14.50	<0.001*
Total cholesterol (mg/dl)	208.09±18.03	167.08±36.32	t_{298}=13.08	<0.001*
HDL (mg/dl)	38.85±3.77	35.76±4.64	t_{298}=6.18	<0.001*
LDL (mg/dl)	143.69±14.50	97.94±27.72	t_{298}=18.77	<0.001*
VLDL (mg/dl)	25.55±11.55	23.04±8.70	t_{298}=1.91	>0.05 NS
Triglycerides (mg/dl)	159.63±24.87	115.64±40.08	t_{298}=11.67	<0.001*
Silent ischemia on TMT	22(11.0%)	3(3.0%)	Z=2.21	<0.05*
*Statistically significant				

Table-1: Baseline characteristics study of case and control group.

T2DM	Patients with asymptomatic coronary artery disease (n=25)	Patients withoutasymptomatic coronary artery disease (n=275)	Total	P value	Odd's ratio
Yes	22	178	200	p=0.018	3.99
Row%	11.0	89.0	100.0		
Col%	88.0	64.7	66.7		
No	3	97	100		
Row%	3.0	97.0	100.0		
Col%	12.0	35.3	33.3		
TOTAL	25	275	300		
Row%	8.3	91.7	100.0		
Col%	100.0	100.0	100.0		
$\chi 2$ =5.58; p=0.018; S-Significant					

Table-2: Showing Risk factors associated with asymptomatic coronary artery disease for the patients with T2DM:

Age (in years)	Patients with asymptomatic coronary artery disease (n=22)	Patients withoutasymptomatic coronary artery disease (n=178)	Total	P value	Odd's ratio
>60	11	20	31	p<0.0001	7.90
Row%	35.5	64.5	100.0		
Col%	50.0	11.2	15.5		
≤60	11	158	169		
Row%	6.5	93.5	100.0		
Col%	50.0	88.8	84.5		
Total	22	178	200		
Row%	11.0	89.0	100.0		
Col%	100.0	100.0	100.0		
$\chi 2$ =22.46;p<0.0001 S-Significant					

Table-3: Age and asymptomatic coronary artery disease

BMI (kg/m^2)	Patients with asymptomatic coronary artery disease (n=22)	Patients withoutasymptomatic coronary artery disease (n=178)	Total	P value	Odd's ratio
>23	18	105	123	p=0.037	3.12
Row%	14.6	85.4	100.0		
Col%	81.8	59.0	61.5		
≤23	4	73	77		
Row%	5.2	94.8	100.0		
Col%	18.2	41.0	38.5		
Total	22	178	200		
Row%	11.0	89.0	100.0		
Col%	100.0	100.0	100.0		
$\chi 2$ =4.30;p=0.037 S-Significant					

Table-4: Obesity and asymptomatic coronary artery disease

asymptomatic coronary artery disease in patients with newly detected type 2 diabetes mellitus by exercise stress test" was conducted in department of Medicine, Acharya VinobaBhave Rural Hospital and Jawaharlal Nehru Medical College, Sawangi (M) Wardha.

The case and control groups were matched for age and gender but when further age (in years) was analyzed to study its association with asymptomatic CAD among the cases, it was observed that cases with age more than 60 years were 7.90 times more prone for asymptomatic CAD as compared to cases with age less than 60 yrs and was statistically significant) [p<0.0001]. this was similar to other studies. M. Sharda Et al (2016)[27]and G. Premlata et al.[28]

BMI

In our study the mean BMI for cases was 24.00±2.74 and for the controls it was 22.79±2.98. when the mean BMI between the cases and controls was compared it was found to be statistically significant for the cases group[<0.001]. J. Mokta et al.(2017)[29] in there study carried among the Indian population stated that mean BMI among the diabetic population was 24.26 ± 2.56. H. E. Bays, R. H. Chapman, S. Grandy for the SHIELD Investigators Group[30] in there state conclude that there is positive relationship between the increase in BMI and prevalence of type 2 DM.

Triglycerides

In this study, the mean triglyceride among the case group was 159.63±24.87 and among the control group was 115.64±40.08. This difference between the two groups was statistically very significant.[<0.001] In a study conducted by M. Sharda Et al (2016)[26] the mean triglyceride levels

Triglyceride (mg/dl)	Patients with asymptomatic coronary artery disease (n=22)	Patients with asymptomatic coronary artery disease (n=178)	Total	P value	Odd's ratio
>150 Row% Col%	11 100.0 50.0	0 0.0 0.0	11 100.0 5.5	p<0.00001	
≤150 Row% Col%	11 5.8 50.0	178 94.2 100.0	189 100.0 94.5		
Total Row% Col%	22 11.0 100.0	178 89.0 100.0	200 100.0 100.0		

Table-5: Triglyceride and asymptomatic coronary artery disease

Studies	Prevalence of asymptomatic CAD
Walia et al,[33]	15.57%
Mohan V, Premlatha G, Sastry NG [34]	17.8%
Wackers F. Et al(2004)[35]	22%
M. Sharda Et al (2016)[26]	37.3%
Boras J., Briklijacic N., ljubicc A.(2010)[36]	10% to 20%
Jayshankar et al(2012)[37]	31.37%
AK Agrawal et al (2008)[38]	28.9%
Gupta et al (1993)[39]	38.3%
Sukhija et al (2000)[40]	46.7%
Achari et al (2002)[41]	42.5%
Motoji et al (1991)[42]	31%
Koistinen et al (1990)[43]	14%
Blandine et al (1999)[44]	16%
Lee et al(2001)[45]	38%
Bacci et al, (2002)[46]	19%
Kim et al,(2011)[47]	14%
The Milan Study on Atherosclerosis and Diabetes (MiSAD) (2002)[48]	13%
Present study	11%

Table-6: Showing the prevalence of asymptomatic CAD in cases of type 2 DM by various studies along with the present study.

varied from 150 mg/dl to 165 mg/dl across the 3 groups. The mean triglyceride in our study also falls in the similar range from which it may be stated that triglyceride level among the type2 DM population comes around 160 mg/dl. Guang-Yu Chen et al(2015)[31] and Amit Kumar Dixit, et al (2014)[32] aslo concluded a positive relationship between isolated hypertriglyceridemia and type 2 DM.

When raised levels of triglycerides among the diabetic population was analysed for its association with type 2 DM, it was found that proportion of patients with asymptomatic coronary artery disease was significantly higher for level of triglyceride>150 mg/dl (p<0.00001)

Along with the above discussed risk factors, history of hypertension was also found to have a statistically significant association with asymptomatic CAD among the diabetics. Coronary artery disease was 2.68 times more among the patients with history of hypertension as compared to the patients without history of hypertension and the risk was significant [p=0.034].

Type 2 DM and Asymptomatic CAD

In the present study, it was observed that, 11% cases with type 2 DM tested positive for asymptomatic CAD on exercise stress test whereas only 3% of the non diabetic control group tested positive for asymptomatic CAD on exercise stress test. This difference was found to be statistically significant [p <0.05].

When the association of type 2 DM as an independent risk factor for was asymptomatic CAD analysed it was observed that the risk of asymptomatic coronary artery disease was 3.99 times more among the patients with T2DM as compared to the patients without T2DM and the risk was significant. [OR-3.99 (1.16, 13.69;p=0.018].

Thus, considering the data from various studies it can be interpreted that prevalence of asymptomatic CAD in patients of type 2 DM is variable. Our study differed from most the previous studies in such a way that we included only newly detected diabetic cases (<6 months). This factor can be a possible explanation of only 11% prevalence of asymptomatic CAD in diabetic cases in our study which was low as compared to other studies on similar subjects that were reviewed (table-5).

To add to above explanation, it is also a matter of concern, that prevalence of 11% is too much of a burden because of the same reason that the study has taken only newly detected cases suggesting that this prevalence of 11% is only the tip of the ice berg. This emphasizes the magnanimity of the pathophysioloic processes that predispose to CAD very early in the disease course. Nonetheless, a strong statistical significance was observed between type 2 DM and asymptomatic coronary artery disease.

Utility of TMT as effective tool to diagnose asymptomatic CAD

Rubler et al,(1987)[49] found that exercise ECG testing had a 50% sensitivity and 83% specificity for predicting subsequent cardiac events (cardiac death, MI, or angina) over an average of 41 months of follow-up. From the studies done by Blandine et al.,1999[44] and Bacci et al.,2002;.[46] it can be concluded that the mean positive predictive value of exercise ECG for predicting angiographic coronary disease varies between 70 and 90%.

The sensitivity of the exercise test among diabetic patients was 47%, and the specificity was 81%, with a positive

predictive value of 85% and negative predictive value of 41% in study conducted by Lee et al(2001).[45] M. Sharda Et al (2016)[28]concluded that TMT in diabetic patients had a significant role in detection of silent myocardial ischemia.
Undoubtedly, tools such as coronary angiography is more reliable in detection of ischaemia with good accuracy but TMT as a screening method can be an effective means of diagnosis of asymptomatic CAD in type-2 DM patients in areas where angiography is not easily available.

CONCLUSION

Asymptomatic coronary artery disease or Silent myocardial ischemia is defined as objective documentation of myocardial ischemia in the absence of angina or angina equivalent.[50] The pathophysiology of silent ischemia remains controversial, and other factors may also play role, including differences in plasma opioid receptors, ischemic damage to nerve endings, and psychological factors.[51]
In this study, the prevalence of asymptomatic CAD in newly detected cases of type 2 DM was 11% as compared to 3% in non diabetics. When the case and control group were compared for baseline parameters it could be concluded that prevalence of Uncontrolled HTN, raised BMI (>23 kg/m^2), raised waist circumference (>90 cm in males/>80 cm in females), raised total cholesterol levels and raised triglycerides were more in cases of newly detected type 2 DM and this was statistically significant.
Age more than 60 years, history of hypertension, BMI>23 kg/m^2, hypertriglyceridemia have statistically significant association with asymptomatic CAD among the diabetic cases.
Thus, from the results of our study we conclude that cases with newly detected type 2 DM are not only more prone for asymptomatic CAD but other co morbidities like uncontrolled HTN, obesity, abdominal obesity, hypercholesterolemia and hypertriglyceridemia. On sub group analysis it was again concluded that cases with any of the studied risk factors had more number of chances to have asymptomatic CAD and precisely factors like, age more than 60 years, history of hypertension, BMI>23 kg/m^2, hypertriglyceridemia have statistically significant association with asymptomatic CAD among the diabetic cases as compared to controls. We also conclude that the exercise stress test is a simple, noninvasive, cost effective and comparatively less complicated tool to diagnose asymptomatic CAD.

REFRENCES

1. Mathers CD, Loncar D Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med, 2006;3;:e442.
2. International Diabetes Federation. IDF Diabetic Atlas 7th Edition. http://www.idf.org/idf-diabetes-atlas-seventh-edition. Accessed 30 Aug 2017
3. Chandalia M, Abate N, Garg A, et al. Relationship between generalized and upper body obesity to insulin resistance in Asian Indian men. J Clin Endocrinol Metab 1999;84:2329-35.
4. Misra A, Vikram NK. Insulin-resistance syndrome (metabolic syndrome) and Asian Indians. Current Sci 2002;83:1483-96.
5. Mohan V, Sharp PS, Cloke HR, et al. Serum immuno-reaction insulin responses to a glucose load in Asian Indian and European type 2 diabetic patients and control subjects. Diabetologia 1986;29:235-7.
6. Sharp PS, Mohan V, Levy JC, et al. Insulin-resistance in patients of Asian Indian and European origin with non-insulin dependent diabetes mellitus. Horn Metab Res 1987;19:84-5.
7. Gorcia MJ, McNamara PM, Gordon T, et al. Morbidity and mortality in diabetics in the Framingham population: Sixteen year follow up study. Diabetes 1974;23:105-11.
8. Weiner D A, Ryan T J, Parsons L, et al. Significance of silent myocardial ischaemia during exercise testing in patience with diabetes mellitus: a report from Coronary Artery Surgery Study (CASS) registry. Am J Cardiol 1991;68:729-734.
9. Airaksiran K E J. Silent coronary artery disease in diabetics – A feature of autonomic neuropathy or accelerated atherosclerosis. Diabetologia 2001; 44:256-66.
10. Ekelund, LG, Suchindran, CM, McMahon, RP, et al. Coronary heart disease morbidity and mortality in hypercholesterolemic men predicted from an exercise test: the Lipid Research Clinics Coronary Primary Prevention Trial. J Am Coll Cardiol 1989;14:556.
11. Langer A, Freeman MR, Josse RG, Steiner G, Armstrong PW. Detection of silent myocardial ischemia in diabetes mellitus. Am J Cardiol. 1991;67:1073-1078.
12. Murray DP, O'Brien T, Mulrooney R, O'Sullivan DJ. Autonomic dysfunction and silent myocardial ischemia on exercise testing in diabetes mellitus. Diabet Med. 1990;7:580-584.
13. Niakan E, Harati Y, Rolak L, Comstock J, Rokey R. Silent myocardial infarction and diabetic cardiovascular autonomic neuropathy. Arch Intern Med. 1986;146:2229-2230.
14. Ewing DJ, Campbell IW, Clarke BF. Assessment of cardiovascular effects of diabetic autonomic neuropathy and prognostic implications. Ann Intern Med. 1980;92:308-311.
15. Ewing D, Campbell I, Clarke B. The natural history of diabetic autonomic neuropathy. Q J Med. 1980;49:95-108.
16. Marchant B, Umachandran V, Stevenson R, Kopelman PG, Timmis AD. Silent myocardial ischemia: role of subclinical neuropathy in patients with and without diabetes. J Am Coll Cardiol. 1993;22:1433-1437.
17. Di Carli MF, Hachamovitch R. Should we screen for occult coronary artery disease among asymptomatic patients with diabetes? J Am Coll Cardiol. 2005;45:50 –53.
18. Marwick, TH, Sada, M Detrano R. Screening of CAD, Cardiac Stress testing and imaging: Seventh edition, Churchill Living Stone, 2005: pp126.
19. AK Agarwal, Sweta Singla, S Singla, R Singla, A Lal, H Wardhan, Rajbala Yadav Prevalence of Coronary Risk Factors in Type 2 Diabetics without Manifestations of Overt Coronary Heart Disease. J Assoc Physicians Ind 2009; 47;
20. George D. Harris, MD, MS, and Russell D. White, MD Exercise Stress Testing in Patients With Type 2 Diabetes: When are asymptomatic Patients Screened ? Clinical Diabetes 2007;25:126.

21. Devi Dayal and M. Jayashree ; Vitamin D levels in newly detected Type 2 diabetes; Indian J Endocrinol Metab 2015;19(2).
22. Rose G. McCartney P Reid DD. Self administration of a questionnaire on chest pain and intermittent claudication. Br. J Prev Soc Med 1977; 31: 42-48.
23. Hok-Hay SOei MD et al., The association of Rose questionnaire angina pectoris and coronary calcification in a general population: The Rotterdam Coronary Calcification Study. Annals of Epidemiology 2004;14:431-436.
24. Amanda Nicholson et al., Rose Questionnaire Angina in younger men and women: Gender differences in relationship to cardiovascular risk factors and other reported symptoms. J Clin Epidemiol, 1999;2:337 – 346.
25. Graham Douglas, Fiona, Colin Rbertson, Macleod's clinical examination, 12th edt; p 60.
26. Heng D et al. Modification of the NCEP ATP III definitions of the metabolic syndrome for use in Asians identifies individuals at risk of ischemic heart disease. Atherosclerosis. 2006;186:367-73.
27. J. Mokta et al. prevalence of cardiovascularrisk factors among diabetic population and awareness of diabetes among diabetic patients: a population based Himalayan study, journal of the association of physicians of india, 2017;65:48-52.
28. Premalatha G, Anirudhan MK, Mohan V,Sastry NG. Treadmill (Cardiac Stress) Test in the Diagnosis of Ischaemic Heart Disease in NIDDM Patients: Usefulness and Safety. Int J Diab Dev Countries 1995; 15:3-6.
29. H. E. Bays,1 R. H. Chapman,2 S. Grandy3 for the SHIELD Investigators' Group; The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: comparison of data from two national surveys; Int J Clin Pract 2007;61, 5, 737–747.
30. Meenaxi Sharda, Anil Kumar Soni, Shivraj Meena, Harish Nigam, Anuraj Singh. A Prospective Study on Utility of Exercise Treadmill Test in Type 2 Diabetes Mellitus Patients, Journal of The Association of Physicians of India 2016;64.
31. Guang-Yu Chen et al; Prevalence of and Risk Factors for Type 2 Diabetes Mellitus in Hyperlipidemia in China Med Sci Monit, 2015;21:2476-2484.
32. Amit Kumar Dixit, et al; The prevalence of dyslipidemia in patients with diabetes mellitus of ayurveda Hospital J Diabetes Metab Disord 2014;13.
33. Walia M, Agarwal AK, Shah P, et al. Prevalence of coronary risk factors in non-insulin dependent (type-2) diabetics. J Assoc Physicians Ind 1999;47:1051-5.
34. Mohan V, Premlatha G, Sastry NG. Ischaemic Heart Disease in south Indian NIDDM patients – A clinic based study on 6597 patients. Int J Diab Dev Countries 1995;15:64-7.
35. Wackers, FJ., Young, LH., Inzzuchi, SE., Chuyn, DA., Davey, JA., Barrett EJ., Taillefer, R., Wittlin, SD., Heller, GV., Filipchuck, N., Engel, S., Ratner, RE., and Iskandrian, AE. For The Detection of Ischemia in Asymptomatic Diabetics Investigators (2004). Detection of silent myocardial ischemia in asymptomatic diabetic subjects; the DIAD study. Diabetes Care 2004;27:1954-1961.
36. Boras J., Briklijacic N., ljubicc A. Silent ischemia and diabetes mellitus. Diabetologia Croatica 2010;39-2:57-65.
37. Jayshankar, Rajashree A.N, Ajit kumar study of prevalence of asymptomatic coronary artery disease in patients with diabetes mellitus by treadmill test. Int. J of clinical cases and investigation 2012;4:18.
38. AK Agarwal, Sweta Singla, S Singla, R Singla, A Lal, H Wardhan, Rajbala Yadav Prevalence of Coronary Risk Factors in Type 2 Diabetics without Manifestations of Overt Coronary Heart Disease. J Assoc Physicians Ind 2009; 47;
39. Gupta SB, Pandit RB. Silent myocardial ischemia and cardiac autonomic neuropathy in diabetes. Indian Heart J 1993; 44: 227-9.
40. Sukhija R, Dhanwal D, Gambhir DS, et al. Silent myocardial ischaemia in patients with type-2 diabetes mellitus and its relation with autonomic dysfunction. Ind Heart J 2000;52:540-6.
41. Achari V, thakur AK. Treadmill Testing in Asymptomatic Type 2 Diabetes. JAPI 2002; 50; 52.
42. Motoji N. Silent myocardial ischemia in patients with NIDDM as judged by treadmill exercise testing and coronary angiography. Am Heart J 1991; 123:
43. Koistinen M, Huikuir J, Pirttiaho H, Linnaluoto MK, Takkunen JT, et al. Evaluation of exercise electrocardiography and thallium tomographic imaging in detecting asymptomatic coronary artery disease in diabetic patients. Br Heart J. 1990;63:7–11.
44. Blandine JD, Bernard S, Habib G, Bory M, Vague P, Lassman-Vague V, et al. Silent myocardial ischemia in patients with diabetes: who to screen. Diabetes Care. 1999;22:1396 –1400.
45. Lee DP, Fearon WF, Froelicher VF, et al. Clinical utility of the exercise ECG in patients with diabetes and chest pain. Chest. 2001;119:1576 –1581.
46. Bacci S, Villela M, Villela A, Langialonga T, Grilli M, Rauseo A, et al. Screening for silent myocardial ischaemia in type 2 diabetic patients with additional atherogenic risk factors: applicability and accuracy of the exercise stress test. Eur J Endocrinol. 2002;147:649–654.
47. Mee Kyoung Kim, Ki Hyun Baek, et al. Exercise Treadmill Test in Detecting Asymptomatic Coronary Artery Disease in Type 2 Diabetes Mellitus. Diabetes Metab J 2011;35:34-40.
48. Faglia E, Favales F, Calia P, Paleari F, Segalini G, Gamba PL, et al. Cardiac events in 735 type 2 diabetic patients who underwent screening for unknown asymptomatic
49. Rubler S, Gerber D, Reitano J, Chokshi V, Fisher VJ, et al. Predictive value of clinical and exercise variables for detection of coronary artery disease in men with diabetes mellitus. Am J Cardiol. 1987;59:1310 –1313.
50. Peter F. Cohn, Kim M. Fox, Caroline Daly, Silent Myocardial Ischemia, circulation. 2003;108:1263-1277.
51. Falcone C, Nespoli L, Geroldi D, Gazzaruso C, Buzzi MP, Auguadro C, Tavazzi L, Schwartz PJ. Silent myocardial ischemia in diabetic and nondiabetic patients with coronary artery disease. Int J Card. 2003;90: 219–227.

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