Symbiosis

www.symbiosisonlinepublishing.com
ISSN Online: 2374-6890

Research Article | Journal of Endocrinology and Diabetes | Open Access

Silent Myocardial Ischemia in Type 2 Diabetic Patients Asymptomatic For Coronary Artery Disease

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Received: September 1,2020; Accepted: December 14,2020; Published: December 17,2020

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Abstract

Background

Coronary Artery Disease (CAD) is a common cause of premature morbidity and mortality in diabetics and is often asymptomatic because of silent myocardial ischemia (SMI). Early detection of SMI may prevent catastrophic cardiac events.

Objective

To study the prevalence of SMI in patients of type 2 diabetes mellitus (Type 2 DM), asymptomatic for CAD and to assess the role of conventional CAD risk factors in diabetic patients asymptomatic for CAD in the development of SMI.

Methodology

102 cases of Type 2 DM without any clinical and electrocardiographic evidence of CAD, who attended a tertiary care hospital in North Delhi, over a period of one year, were studied for the present cross-sectional study. Detailed history, general physical examination, BMI, systemic examination and investigations like glycosylated hemoglobin (HbA1c), lipid profile, resting 12-leads electrocardiography (ECG) and treadmill test (TMT) were carried out.

Results

Out of 102 patients, TMT was found positive in 23 patients. It was positive in 12% among diabetic patients with duration of diabetes ≤5 years, 14.8% in patients with duration 6-10 years, 37.5% in patients with duration 10-15 years and 77.7% in patients with duration 16-20 years, respectively with $p<0.001$.

Conclusion

The prevalence of SMI in asymptomatic Type 2 DM without history of CAD is 22.54%. Duration of diabetes, presence of autonomic neuropathy (AN), dyslipidemia and HbA1c level are strong clinical predictors of SMI in asymptomatic Type 2 DM.

Keywords: Silent myocardial ischemia; Type 2 Diabetes mellitus; Coronary artery Disease; Treadmill test Asymptomatic; Autonomic Neuropathy.

Introduction

Diabetes mellitus (DM) is a leading cause of cardiovascular mortality [1] Coronary artery disease (CAD) is the leading cause of death in patients with type 2 diabetes mellitus (Type 2 DM) and is often asymptomatic because of silent myocardial ischemia (SMI). The prevalence of CAD in our country has increased, making it a major cause of morbidity and mortality [2]. CAD is multi-factorial in etiology and has several important risk factors, out of which DM is one of the important modifiable risk factor.

According to the International Diabetes Federation, India has over 61.3 million diabetic patients which had increased from 50.8 million last year. By 2030, India's diabetes burden is expected to cross the 101.2 million mark against the earlier estimated 87 million [3].

Data from Framingham heart study demonstrates the increased and poor prognosis of cardiovascular disease (CVD) in DM. Mortality related to CVD is doubled in diabetic men and quadrupled in diabetic women over that in their non-diabetic counter parts [4]. Routine screening of patients with Type 2 DM for asymptomatic CAD with ECG remains controversial, as majority of them present with normal ECG [5]. Previous studies show that treadmill test is a useful, specific and cost-effective non- invasive tool for detection of SMI in diabetic patients asymptomatic for CAD [6].

Methods

Study design

The present cross-sectional and observational study was conducted in a tertiary care hospital in northern India over one year.

Study subjects

Patients of asymptomatic type 2 DM without clinical evidence of CAD attending cardiology and medicine OPD were taken for the study. Using the formula for descriptive study ($Z^2 \times p \times q)/d^2$), the prevalence of SMI in asymptomatic patient of type 2 DM was expected to be 30%. With a precision error of estimation (d) = 0.06 (20% of p) and alpha error = 0.05, a sample size of 225 was estimated. All the patients who attended the cardiology and medicine OPD and fulfilled the inclusion-exclusion criteria during the period of one year of study were enrolled. The study had been approved from Institutional Ethical Committee.

Inclusion and exclusion criteria

We included all the patients of Type 2 DM of any duration diagnosed according to ADA criteria without any clinical evidence or history of CAD and ageing between 30 to 60 years. Patients having absolute contraindication to TMT e.g. acute myocardial infarction, unstable angina, uncontrolled cardiac arrhythmias, active endocarditis, severe aortic stenosis, heart failure, acute pulmonary embolism or pulmonary infarction, acute myocarditis or pericarditis, physical disability that would preclude safe and adequate testing and patients not given written consent, were excluded. Others with relative contraindications to TMT were also excluded e.g. left main coronary stenosis, valvular heart disease, electrolyte abnormalities, pulmonary hypertension, tachy- or brady-arrhythmias, hypertrophic cardiomyopathy, higher degree A-V block, any thrombotic disorder, uncontrolled hypertension (BP>200/110 mm Hg), Ventricular aneurysm, LVEF <30% on Echo, etc.

Data collection

All the patients attending the cardiology and medicine OPD were screened for eligibility. DM is defined as a metabolic disorder characterized by hyperglycemia resulting from defect in insulin secretion, insulin action or both. As per ADA criteria, DM was diagnosed on basis of symptoms plus blood sugar levels as described in Table 1.

Table 1: Diagnostic criteria for Diabetes Mellitus
Symptoms of diabetes plus
random blood sugar (RBS) ≥200 mg/dl (11.1 mmol/l)[A] or Fasting blood sugar (FBS) ≥126 mg/dl (7.0 mmol/l)[B] or 2-hour blood sugar (PPBS) ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test[C]
A-Random is defined as without regard to time since the last meal. B-Fasting is defined as no caloric intake for at least 8h. C-The test should be performed using a glucose load containing the equivalent of 75 gm of anhydrous glucose dissolved in water.
(Source adapted from American Diabetes Association, 2011).

As per NCEP ATP III 2001 guidelines,[7] dyslipidemia has been defined a disorder of lipoprotein metabolism, which may be manifested by elevation of the total cholesterol, the "bad" low density lipoprotein (LDL) cholesterol and the triglyceride (TGs) concentrations and a decrease in the "good" high-density lipoprotein (HDL) cholesterol concentration in the blood. Dyslipidemia in the study is stated when fasting total cholesterol was found ≥240 mg/dl for both sexes; LDL cholesterol ≥190 mg/dl for both sexes; TGs level ≥150 mg/dl for both sexes and HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women.

Descriptive data of all the eligible and consented patients was collected and proper history was recorded on predesigned and pretested proforma with emphasis on duration of DM. They underwent thorough general physical examination and systemic examination. Blood pressure was measured on the right arm after a 20-minute rest in the sitting position using a digital sphygmomanometer by the auscultatory method in accordance with the American Heart Association protocol.[8] Waist circumference was measured on bare skin during mid-inspiration at the narrowest indentation between the tenth rib and the iliac crest using a plastic anthropometric tape. Body mass index (BMI) was calculated according to Quetelet's formula. Their blood sugar levels, lipid profile and glycosylated hemoglobin (HbA1c) were performed. All of them underwent 12-lead electrocardiography (ECG) and two-dimensional echocardiography (2D-ECHO) before TMT. TMT was done in patients with ejection fraction more than 35%. Autonomic neuropathy (AN) was diagnosed if either one or both responses to Valsalva maneuver and sustained hand grip were abnormal or if both were border line.

Valsalva maneuver

The patients were asked to blow into a tube connected to a mercury manometer and hold a pressure of 40 mmHg for 15 seconds, while the heart rate was recorded continuously from an ECG. The valsalva ratio was then calculated from the ratio of the

longest R-R interval after the maneuver (reflecting the rebound bradycardia) to the shortest R-R interval during the maneuver (reflecting the tachycardia during strain). A valsalva ratio of ≥1.21 was considered as normal, from 1.11 to 1.20 as borderline and≤1.10 as abnormal.

Sustained handgrip test

Maximum voluntary contraction (MVC) was first determined using a handgrip manometer and handgrip was then maintained steadily at 30% MVC for as long as possible up to a maximum of five minutes. During sustained handgrip, patient's blood pressure was measured with a sphygmomanometer on the non-exercising arm. The response to sustained handgrip was measured as the difference in diastolic blood pressure (DBP) between the resting and during the handgrip. A rise in DBP of ≥16 mmHg was considered normal, 11 to 15 mmHg borderline and ≤10 mmHg as abnormal.

Technique of treadmill test

The patient was instructed to avoid eating or drinking caffeinated beverages three hours prior to testing and to wear comfortable shoes and loose-fitting clothes. A written informed consent was taken. A standard 12-lead ECG was obtained, blood pressure was recorded in both supine & sitting positions and the patient was explained how to perform the test. Standard multistage maximal exercise test was done on a motorized treadmill according to Bruce protocol. The heart rate, blood pressure and ECG were recorded at the end of each stage of exercise, immediately before and after stopping the exercise and for each minute for at least 5 to 10 minutes in the recovery phase. Exercise test was terminated in all patients following the achievement of target heart rate or an abnormal ischemic response. This was defined as development of 0.10 mV (1 mm) of J point depression measured from the PQ junction, with a relatively flat ST segment slope (<l mV/sec), depressed ≥0.10 mV after the J point in three consecutive beats with a stable baseline. Exercise test was also terminated in patients who developed dyspnea, fatigue or chest pain.

Statistical Methods

Descriptive statistics were analyzed with SPSS version 17.0 software. Continuous variables were presented as mean ± SD or median when the data was skewed. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups was compared using Chi-squared test or Fisher's exact test as appropriate. Non-normal distribution continuous variables were compared using Mann Whitney U test. For all statistical tests, a p-value of less than 0.05 was taken as an indicator for significant difference. Univariate logistic regression analysis was done for comparing various variables for correlation. Only few variables showed statistical significance.

Results

We encountered a total number of 102 patients with asymptomatic Type 2 DM without clinical and electrocardiographic evidence of ischemic heart disease and the following results were found. The mean age was 48.75 ± 7.46 years with range of 34-60 years. Most of the patients belonged to the age group 40-60 years. The ratio of female to male was 1:1.5. 24 patients (23.5%) in the study were in the age group 30-39 years of which 15 were males and 9 were females. 35 patients (34.3%) were in the age group of 40-49 years of which 23 were males and 12 were females. 43 patients (42.15%) were in the age group of 50-59 years of which 24 were males and 19 were females.In the study population, 50 patients (49%) were having diabetes for duration ≤5 years, followed by 27 patients (26.4%) with the duration of 6-10 years, 16 patients (15.7%) between 11-15 years and only 9 patients (8.8%) between 16-20 years. Statistically, no significant correlation was seen between the sexes as far as their mean age, BMI, blood pressure, HbA1C, lipid profile and blood sugar levels were concerned (Table 2).

The average HbA1c was 7.70%, 8.89%, 9.97%, 10.52% for the patients with duration of diabetes≤5 years, 6-10 years, 11-15 years and 16-20 years, respectively. Statistically, no significant correlation was seen in average cholesterol, triglycerides, LDL and HDL with respect to the duration of diabetes (p≥0.05).

Among102 patients, TMT was positive in 23 and negative in 79 patients. TMT was positive in 26% of patients with duration of diabetes ≤5 years, 17% of patient with 6-10 years, 26% of patients with 10-15 years and 30% ofpatient with duration 16-20 years, respectively with p<0.001.There was a significant correlation between TMT negative and TMT positivepatients with reference to the average duration of diabetes (p<0.001), HbA1c (p<0.001) and triglycerides (TG) level (p=0.001) (Table 3).

12/79 (15.2%) with AN and 67/79 (84.8%) without AN had TMT negative, while 11/23 (47.8%) diabetics with Anand 12/23 (52.2%) diabetics without AN had TMT positive. Statistically, a significant correlation was observed between TMT negative and TMT positive diabetics as far as presence of signs of A was concerned (p=0.001) (Table 4).

Discussion

Coronary atherosclerosis is one of the most common and chronic complications of diabetes mellitus. A recently observed and focused aspect of CAD is its silent and asymptomatic presentation. The present study was aimed at the asymptomatic presentation of CAD in the form of SMI in patients with Type 2 DM. It consisted of two aspects; firstly, the prevalence of SMI in patients with Type 2 DM asymptomatic for CAD and secondly, assessing the clinical predictors of SMI in these patients.

The study consisted of 102 patients of asymptomatic Type 2 DM without any clinical and electrocardiographic evidence of CAD who were then evaluated for the prevalence of SMI by using treadmill test (TMT). The mean age was 48.75 ± 7.46 years with

Table 2: Comparison of characteristics between males and females

	Males (n=62)	Females (n=40)	p value
	Mean ± SD	Mean ± SD	
Age (years)	48.44 ± 7.49	49.25 ± 7.49	0.593
BMI (Kg/m2)	24.54 ± 3.90	24.34 ± 3.80	0.804
SBP (mmHg)	128.19 ± 4.20	128.30 ± 4.29	0.902
DBP (mmHg)	75.87 ± 4.99	74.60 ± 5.40	0.227
HbA1c (%)	8.60 ± 1.45	8.67 ± 1.41	0.815
Cholesterol(mg/dl)	179.06 ± 28.89	178.73 ± 29.22	0.954
TG(mg/dl)	128.35 ± 31.66	130.45 ± 32.53	0.747
LDL(mg/dl)	119.00 ± 31.04	119.48 ± 24.15	0.935
HDL(mg/dl)	35.84 ± 3.31	35.80 ± 3.56	0.955
FBS(mg/dl)	175.58 ± 37.71	185.23 ± 37.88	0.211
PPBS(mg/dl)	215.73 ± 67.00	241.13 ± 68.31	0.067

Table 3: Comparison of characteristics in diabetic patients with TMT negative & TMT positive.

	TMT negative (n=79)	TMT positive (n=23)	
	Mean ± SD	Mean ± SD	p value
Age (years)	48.53 ± 8.12	49.52 ± 4.56	0.578
Duration of DM (years)	5 (4 - 9)	12 (5 - 16)	<0.001
BMI (Kg/m2)	24.41 ± 3.62	24.64 ± 4.64	0.805
SBP (mmHg)	127.97 ± 4.28	129.13 ± 3.95	0.249
DBP(mmHg)	74.91 ± 4.63	75.22 ± 6.87	0.805
HbA1c (%)	8.26 ± 1.23	9.87 ± 1.38	<0.001
Cholesterol(mg/dl)	180.06 ± 30.39	175.04 ± 23.08	0.466
TG(mg/dl)	123.59 ± 30.06	148.35 ± 30.98	0.001
LDL(mg/dl)	120.09 ± 25.51	116.09 ±37.21	0.555
HDL(mg/dl)	35.95 ± 3.36	35.39 ± 3.54	0.49
FBS(mg/dl)	178.51 ± 35.71	182.30 ± 45.35	0.674
PPBS(mg/dl)	228.38 ± 72.75	216.43 ± 55.51	0.375

Table 4: Correlation between Diabetic Autonomic Neuropathy &SMI.

AN Sign	TMT negative		TMT positive		p-value
	Frequency	%	Frequency	%	
With	12	15.20%	11	47.80%	
Without	67	84.80%	12	52.20%	0.001
Total	79	100.00%	23	100.00%	

range being 34-60 years.62 were males and 40 were females with female to male ratio of 1:1.5. 50 patients were having diabetes of duration ≤5 years followed by 27 patients with the duration of 6-10 years, 16 patients with duration of 11-15 years and 9 patients with duration of 16-20 years. Among 102 patients, TMT was positive in 23 and negative in 79 patients. Out of 23 TMT positive patients, 13 were males and 10 were females. The prevalence of SMI in asymptomatic Type 2 DM was found to be 22.54% (23/102).

Another similar study by Scheidt-Nave et al.[9] showed higher prevalence of SMI in diabetics as compared to non-diabetics. In the study, 31% diabetics without prior evidence of CAD had TMT positive and SMI was 2.2 times more in diabetics as compared with non-diabetics. Gupta et al. [10] in India found that 38.3% of diabetics without prior CAD had SMI on TMT. Another study by Ahluwalia et al. [11] from India reported 50% as the incidence of SMI in diabetics on exercise electrocardiogram and 35% on ambulatory monitoring. A study by Misadgroup [12] found that

12.1% of diabetic patients without CAD had SMI on exercise electrocardiogram testing. Sukhija et al. [13] found that SMI was seen in 14 (46.7%) out of 30 diabetics by using TMT. Wackers et al. [14] found that a total of 113 patients (22%) out of 522 had SMI using stress testing in asymptomatic patients with Type 2 DM. One more study by Sargin et al. [15] found that 62 patients (12.4%) out of 500 had SMI in patients with Type 2 DM by using exercise electrocardiogram. So, the present study is an agreement with the fact that diabetics have a higher prevalence of SMI.

Duration of Type 2 DM and SMI

In 102 of our patients, TMT was positive in 23 patients (22.54%) and negative in 79 patients (77.45%). TMT was positive in 6/50 (12%) diabetic patients with duration ≤5 years, 4/27 (14.8%) patients with duration between 6-10 years, 6/16 (37.5%) patients with duration between 11-15 years and 7/9 (77.7%) patients with duration between 16-20 years. It was observed that the presence SMI is directly related to the duration of diabetes. Longer the duration of diabetes in patients, higher are the chances of having SMI. Our results were comparable with previous study by Ahluwalia V et al. [16] which concluded that 70% patients (7/10) with diabetes of duration more than 5 years had associated SMI while only 30% patients (3/10) with diabetes of duration less than 5 years had associated SMI. Sargin et al. [15] studied 500 patients with Type 2 DM with normal resting ECG and found that 62/500 (12.4%) patients had asymptomatic CAD on exercise TMT. The abnormalities of exercise test were associated with longer duration of diabetes ($p<0.005$). There is paucity of data to correlate the prevalence of SMI with duration of diabetes.

SMI and AN

In our study, 47.8% (11/23) of diabetic patients with AN had SMI while only 15.2% (12/79) of diabetics without AN had SMI. Thus, it was observed that diabetics with AN had higher incidence of associated SMI than those without it. In the study by Quek DK et al. [17] the incidence of asymptomatic CAD with evidence of AN (76.9%) was found to be 37.5%. Another study by Gupta et al. in India10 found that 38.3% diabetic patients had SMI with a greater prevalence in those with AN (59%) than those without it (20%). Another study by Jalal et al. [18] from India found that incidence of SMI was significantly higher in 12/30 (40%) patients with AN as compared to those 3/30 (10%) patients without AN ($p<0.001$).

Dyslipidemia and SMI

In our study, we found that the average total cholesterol in TMT positive and negative patients was 175.04 mg% and 180.06 mg%, respectively. Average triglyceride in TMT positive and negative patients was 123.59 mg% and 148.35 mg%, respectively. Average LDL was 120.09 mg% in TMT positive patients and 116.09 mg% in TMT negative patients. Average HDL was 35.95 mg% in TMT positive patients and 35.39 mg% in TMT negative patients. Statistically, a significant value of $p=0.001$ was found in triglycerides levels between both the groups. It was concluded from the results that diabetics with dyslipidemia are at higher risk for developing CAD. The similar results were observed by Gupta et al. [19] who found that dyslipidemia was very common in type 2 diabetics and the most common abnormality seen was increased serum triglycerides levels (73.3%). Hence, it was concluded that CAD had a stronger correlation with high levels of triglycerides. De Luca et al. [20] also found that CAD had strong correlation with high levels of triglycerides and low HDL. Achari et al. [21] found that triglycerides levels were elevated in 28 treadmill positive patients compared to 15 treadmill negative patients ($p<0.01$). Hence, it is concluded that dyslipidemia is very common in Type 2 DM and has great influence on CAD.

HbA1c and SMI

In our study, it was found that the average HbA1c in TMT positive and negative patients was 9.87% and 8.26%, respectively. Statistically, a significant value of $p<0.001$ was found in HbA1c levels between both the groups. De Luca et al. [20] found that among 54 patients who had diabetes, SMI was present in 27 patients (50%) who had HbA1c ≥ 7.6% ($p<0.005$). In another study by Gautam et al. [22] it was observed that there was significant increase in HbA1c levels in diabetics over the increasing number of coronary vessels involvement ($p<0.0001$). Hence, it is concluded that the increased levels of HbA1c indicates poor glycemic control and has a great influence on CAD.

Conclusion

We concluded in the study that the prevalence of SMI in Type 2 DM patients without history of CAD is 22.54%. Univariate logistic regression analysis applied which showed that only 4 variables were statistically significant for the results of TMT. Longer the duration of diabetes, greater the risk of SMI. Dyslipidemia (mainly raised TGs) is found to be more in diabetics and is directly related to higher prevalence of SMI in them. Diabetics with clinical signs of A had higher incidence of SMI. HbA1c levels are found to be more in diabetics with poor glycemic control and had greater influence on CAD. Hence, it is concluded from the study that duration of diabetes, triglycerides level, presence of AN and HbA1c level are strong clinical predictors for SMI in patients of Type 2 DM asymptomatic for CAD.

Conflicts of interest

The authors have none to declare.

References

1. API text book of medicine, 9th Edition. Association of physicians of India, Mumbai 2012.
2. Park K. Park's text book of preventive and social medicine. 20thEdition. Jabalpur: Banarasi Das Bhanot Publishers; 2009.
3. International Diabetes Federation (IDF). Diabetes atlas 4thEdition. 2009. 39.
4. Kahn RC, Weir CG, King LG, Jacobson MA, Moses CA, Smith. Joslin's Diabetes Mellitus 14th Edition. Philadelphia: Lippincott Williams & Wilkins Co; 2007.
5. American Diabetes Association. Standards of medical care in diabetes-2010. Diabetes Care. 2010;33(Supp 1):S11-S61.
6. Bhatia LC, Singal R, Jain P, Mishra N, Mehra V. Detection of silent myocardial ischaemia in asymptomatic diabetic patients during treadmill exercise testing. High Blood Pressure & Cardiovascular Prevention.2012; 19(3):137-142.doi: 10.1007/bf0326246.
7. Surana SP, Shah DB, Gala K, Susheja S, Hoskote SS, Gill N, et al. Prevalence of metabolic syndrome in an urban Indian diabetic population using the NCEP ATP III guidelines. J Assoc Physicians India.2008;56:865-868.
8. Pearson TA, Blair SN, Daniels SR, Eckel RH, Fair JM, Fortmann SP, et al. AHA guidelines for primary prevention of cardio vascular disease and stroke:2002update.Circulation.2002;106(3):388-391. doi:10.1161/01.CIR.0000020190.45892.75
9. Scheidt-Nave C, Barrett-Connor E, Wingard DL. Resting electrocardiographic abnormalities suggestive of asymptomatic ischemic heart disease associated with non-insulin-dependent diabetes mellitus in a defined population. Circulation.1990;81(3):899-906.doi: 10.1161/01.cir.81.3.899.
10. Gupta SB, Pandit RB. Silent myocardial ischaemia and cardiac autonomic neuropathy in diabetics. Indian Heart J. 1992;
44(4):227-229.
11. Ahluwalia G, Jain P, Chugh SK, Wasir HS, Kaul U. Silent myocardial ischemia in diabetics with normal autonomic function. Int J Cardiol.1995; 48(2):147-153.doi:10.1016/0167-5273(94)02233-9.
12. Misad Group. Prevalence of Unrecognized Silent Myocardial Ischemia and Its Association with Atherosclerotic Risk Fact ors in Noninsulin-Dependent Diabetes Mellitus. Am J Cardiol.1997;79(2):134-139.doi:10.1016/S0002-9149(96)00699-6.
13. Sukhija R, Chanwal D, Gambhir DS, Dewan R. Silent myocardial ischaemia in patients with type II diabetes mellitus and its relationship with autonomic dysfunction. Indian Heart J. 2000;52(5):540-546.
14. Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, et al. Detection of Silent Myocardial Ischemia in Asymptomatic Diabetic Subjects. Diabetes Care. 2004;27(8):1954-1961. doi:10.2337/diacare.27.8.1954.
15. Sargin H, Ozisik M, Ozisik NC, Seven O, Orbay E, Go zu H, et al. The prevalence of silent ischemia in Turkish patients with type 2 diabetes mellitus. Tohoku J Exp Med. 2005;205(4):351-355. doi:10.1620/tjem.205.351.
16. Ahluwalia V. Incidence of silent myocardial ischemic in non-insulin dependent diabetes mellitus; 1998.
17. Quek DK, Khor PG, Ong SB. Association of diabetic autonomic neuropathy with painless myocardial ischaemia induced by exercise. Singapore Med J. 1992;33(2):177-181.
18. Jalal S, Alai MS, Khan KA, Jan VM , Rather HA, Iqbal K, et al. Silent myocardial ischemia and cardiac autonomic neuropathy in diabetics. J Assoc Physicians India. 1999; 47(8):767-769.
19. Agrawal RP, Sharma P, Pal M, Kochar A, Kochar DK. Magnitude of dyslipidemia and its association with micro and macro vascular complications in type 2 diabetes: a hospital based study from Bikaner (Northwest India). Diabetes Res Clin Pract. 2006;73(2):211-214.doi:10.1016/j.diabres.2006.01.006.
20. De Luca AJ, Saulle LN, Aronow WS, Ravipati G, Weiss MB. Prevalence of silent myocardial ischemia in persons with diabetes mellitus or impaired glucose tolerance and association of hemoglobin A1c with prevalence of silent myocardial schemia. Am J Cardiol.2005;95(12):1472-1474.doi:10.1016/j.amjcard.2005.02.016.
21. Achari V, Thakur AK. Treadmill Testing in Asymptomatic Type 2 Diabetes. JAPI. 2002;50:52.
22. Gautham Ravipati, Wilbert S Aronow, Chul Ahn, Kumbar Sujata, Leonardo N Saulle, Melvin B Weiss. Association of hemoglobin A(1c) level with the severity of coronary artery disease in patients with diabetes mellitus. Am J Cardiol. 2006;97(7):968-969. doi: 10.1016/j.amjcard.2005.10.039.