# Correlation between HbA1c and transient stress induced left ventricular cavity dilatation during myocardial perfusion SPECT studies in diabetic and non-diabetic Egyptian cohort

Abd EL RahmanAbd EL Gawad Sharaf[1], Mohammad Abo Mandour Mousa[1] and Osama Fouad Abd El Monem[2]

[1]Cardiology Department, Faculty of Medicine, Al Azhar University, Egypt.
[2]Resident of Cardiology Helwan University Hospital, Egypt.
mohamed.fouad50@outlook.com

**Abstract:** Diabetes is an important factor in the development of cardiovascular disease. Myocardial ischemia can be a consequence of small vessel disease in diabetic subjects. The exercise myocardial SPECT is a non-invasive examination sufficiently specific for the diagnosis of ischemic heart disease. Transient ischemic dilation is characterized by an expansion of the left ventricle cavity on a post-exercise myocardial SPECT in comparison with rest images and considered a marker of serious coronary atherosclerosis and of a bad prognosis. The increased values of TID correlated with increased HbA1c values in type 2 diabetic subjects with proven myocardial ischemia. Diabetes and its long term inadequate control can be one of the factors which affect the transient ischemic dilation index.

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**Key words:** cardiovascular disease, myocardial perfusion, non-diabetic Egyptian cohort and atherosclerosis.

## 1. Introduction

Diabetes mellitus is an important independent risk factor for cardiovascular disease. Around 30-50% of patients with documented coronary artery disease (CAD) are diabetic. Also, cardiovascular disease is the main cause of death (60-80%) among diabetic patients. **(Fung et al, 2004).**

Disturbed coronary vasoreactivity and occurrence of non-atherosclerotic vascular abnormalities are also key pathologic findings predisposing to higher cardiovascular morbidity and mortality among diabetic patients**;** mainly secondary to impaired subendocardial perfusion, which is one of the strongest pathologic mechanisms described to explain the phenomenon of stress induced left ventricular cavity dilatation. **(Fung et al, 2004).**

Myocardial perfusion single photon emission computed tomography (SPECT) study is an important diagnostic and prognostic test for evaluation of CAD. The annual event rate is in the range of 0.2 - 0.8% per year among patients with negative (–ve) SPECT study. In contrary, patients with positive (+ve) SPECT study have a higher coronary event rate (in the range of 2-8% per year) in relation to severity and extent of ischemia.

However, patients with –veSPECT study who have certain high risk non-perfusion abnormalities (namely, stress induced LV cavity dilatation) are still having higher cardiac event rate compared to those with normal studies**.(Bangalore et al, 2006)**.

A finding of transient ischemic dilation (TID) of the left ventricle during myocardial SPECT studies is a marker of serious coronary atherosclerosis and of a bad prognosis.

TID mechanism remains controversial and few factors may be involved. TID was concluded to be related to subendocardial hypoperfusion. TID represents pseudo-dilationof the left ventricle due to diffuse subendocardial ischemia. **(Elhendy et al, 2005)**.

TID correlates with severity of ischemia among patients with multivessel disease. However, among patients with –ve SPECT studies the correlation is vague and should only cautiously considered as a marker of significant CAD. **(Mandour Ali et al, 2011)**

In our search for the possible factors related to development of TID phenomenon, we thought to investigate the correlation between HbA1c and TID among diabetic and non-diabetic Egyptian cohort referred for a clinically indicated myocardial SPECT study.

**Aim of the work**

To evaluate the correlation between HbA1c and transient stress induced left ventricular dilatation among diabetic and non-diabetic patients during myocardial perfusion SPECT studies.

## 2. Patients and Methods

**Study Cohort**:

128 Patients (diabetic and non-diabetic) referred for a clinically indicated myocardial SPECT study were recruited in a consecutive fashion to participate in this study. Nuclear studies were done at El-

Houssien and Sayed Galal University hospitals nuclear cardiac laboratories. Standard stress, imaging and interpretation protocols will be applied in all patients.

**Inclusion criteria:**

- Ages between 30 and 70 years old.
- Diabetic and non-diabetic patients.
- Male and female gender.
- Referred for a clinically indicated myocardial perfusion SPECT study.

**Exclusion criteria:**

- History of prior MI, PCI and/or CABG.
- Heart muscle disease.
- LBBB or IVCD.
- Significant valvular heart disease.
- Atrial fibrillation or frequent atrial and/or ventricular ectopic beats interfering with gated SPECT imaging.
- Acute or chronic heart failure.

**Procedures:**

- The following will be done to all patients:
- Full history taking.
- Clinical examination.
- Resting ECG.
- HbA1c and basic blood chemistry including kidney function test.
- Conventional transthoracic Echo-Doppler study.
- Stress and rest myocardial perfusion SPECT study.

**The study protocol:**

**1-Stress protocols:**

**-Exercise stress testing:**

All patients were exercised according to the standard Bruce protocol. All tests were symptom limited unless prematurely terminated according to the updated guidelines of stress testing.

**-Pharmacological stress test:**

Dipyridamole was infused according to the standard regimen (0.56 mg/kg) over 4 min.

**The SPECT imaging protocol:**

**-Technitium 99:**

**2- day protocol: the routine protocol used in both laboratories.**

Allow larger doses of dye to be administrated minimal interference between images, 15-30 mci is injected for stress and rest images increase count density and increase image quality consumption of fatty meals increase biliary extraction of technetium and improves image quality.

## 3. Results

Demographic characteristics of the study population:

128 patients were recruited into the current study patients were recruited from Al-Azhar university hospitals, Cardiac nuclear laboratories (EL-Houssein & Bab Al-sharia Hospitals) as well as from Alfa scan cardiac nuclear laboratory.

In our study, 128 patients with demographic criteria illustrated in table (1 and 2) as following:

Mean age of the patients was around 55.5 ± 8.92 years old with range from 35 to 70 years old.

The study showed 72 (56.2%) patients were diabetic, 81 (63.3%) patients were hypertensive, 108 (84.4%) patients were male, 104 (81.2%) patients were dyslipidemic and 59 (46.1%) patients were smoker.

The mean HbA1c of the study population was 6.48 ± 1.55 with range from 4 to 11.

ST-T wave changes were showed in 83 (65.4%) patients in their resting ECG.

Further ST segment depression was showed in 79 (61.7%) patients in their exercise ECG tests with mean duration of exercise 6.22 ± 2.00 min. with range from 2.5 to 15.09 min.

All patients underwent myocardial perfusion SPECT with data analysis as following:

The mean TID ratio was 1.18± 0.17 with range from 1 to 1.79 (table 1).

Normal study in 49 (38 %) patients showing no ischemia (Grade 0) while 12 (9%) patients showed mild ischemia (Grade 1), 24 (18%) patients showed moderate ischemia (Grade 2) and 34 (33%) patients showed severe ischemia (Grade 3) (table 2).

**Table (1) Demographic characteristics of the study population.**

| **Demographic criteria** | | **Total no.128** |
|---|---|---|
| **Age** | Mean ± SD | 55.52 ± 8.92 |
| | Range | 35 – 70 |
| **Male gender** | | 108 (84.4%) |
| **Hypertension** | | 81 (63.3%) |
| **Dyslipidemia** | | 104 (81.2%) |
| **Smoking** | | 59 (46.1%) |
| **DM** | | 72 (56.2%) |
| **HbA1c** | Mean ± SD | 6.48 ± 1.55 |
| | Range | 4.1 – 11 |
| **Resting ECG** | | 83 (65.4%) |
| **Exercise ECG** | | 79 (61.7%) |
| **Duration of exercise** | Mean ± SD<br>Range | 6.77 ± 2.00<br>2.5 – 15.09 |
| **TID** | Mean ± SD<br>Range | 1.18 ± 0.17<br>1 – 1.79 |

**Table (2) SPECT scan end result analysis of the study.**

| **SPECT scan result** | **Grading** | **No.** | **%** |
|---|---|---|---|
| **Ischemia** | 0 | 49 | 38 % |
| | 1 | 12 | 9 % |
| | 2 | 24 | 18 % |
| | 3 | 43 | 33 % |

There are 2 groups in the study population as showed in tables (3,4 and 5) classified according to patient history of anti-diabetic drug uptake into 56 patients non diabetic (group I ) and 72 patients diabetic (group II ) and according to different demographic criteria showing no statistically significance regarding the following data**:**

**1- Age**: Mean age was 54 ± 9.23 years old with range (38 – 70) years old in group (I), while mean age was 56 ± 8.69 years old with range (35 – 70) years old in group (II) with P-value = 0.368.

**2- Sex:** In group (I), 51(91.1%) patients were male, while 57 (79.2%) patients were male in group (II) with P-value = 0.066.

**3- Smoking**: In group (I), 30 (53.6%) patients were smokers, while 29 (40.3%) patients were smoker in group (II), with P-value = 0.134.

**4-Resting ECG**: In group (I), 38 (69.1%) patients showed ST-T wave changes in resting ECG while 45 (62.5%) patients showed ST-T wave changes in resting ECG in group (II) with P-value = 0.439.

**5-Exercise ECG test**: In group (I), 37 (66.1%) patients showed further ST segment depression in exercise ECG test, while 42 (58.3%) patients in group (II) showed further ST segment depression in the test P-value = 0.372.

On the other hand, other criteria showed statistically significance correlation regarding the following:

**1-Hypertension:** In group (I), 29 (51.8%) patients were hypertensive, while 52 (72.2%) patients were hypertensive in group (II) with P-value =5.662, figure (4).

**2-Dyslipidemia**: In group (I), 38 (67.9%) patients were dyslipidemic, while 66 (91.7%) patients in group (II) were dyslipidemic with, P-value =0.001, figure (3).

**3-HbA1c**: In group (I), the mean HbA1c was 5 ± 0.54 with range (4.1-6.1), while in group (II) the mean HbA1c was 7.6 ± 1.06 with range (5.9-11) with P-value=0.000, figure (5).

**4-Duration of exercise**: In group (I), the mean duration of exercise was 7.4 ± 2.37 min. with range (3-15) min., while in group (II) the mean duration of exercise was 6 ± 1.50 min. with range (2.5-9) min P-value=0.001, figure (5).

**5-TID**: In group (I), the mean TID was 1.12 ± 0.14 with range (1-1.79), while in group (II) the mean TID was 1.22 ± 0.18 with range (1.01 – 1.79) with P-value=0.001, figure (1).

**6-Ischemia**: In SPECT study, In group (I) 15 (26.8%) patients were normal showing no ischemia (grade 0), 5 (8.9%) patients showed mild ischemia (grade 1), 10 (17.9%) patients showed moderate ischemia (grade 2) and 26 (46.4%) patients showed severe ischemia (grade 3), while in group (II) 34 (47.2%) patients were normal showing no ischemia (grade 0), 7 (9,7%) patients showed mild ischemia (grade1), 14 (19.4%) patients showed moderate ischemia (grade 2), 17 (23.6%) patients showed severe ischemia (grade 3), P-value =0.039, figure (2).

**Table (3) Correlation between diabetic groups and other demographic criteria.**

| | | Group I (non diabetics) | Group II (diabetics) | Independent t-test | |
|---|---|---|---|---|---|
| | | No = 56 | No = 72 | t/$X^2$* | P-value |
| Age | Mean ± SD | 54.71 ± 9.23 | 56.15 ± 8.69 | 0.904 | 0.368 |
| | Range | 38 – 70 | 35 – 70 | | |
| Male gender | | 51 (91.1%) | 57 (79.2%) | 3.386 | 0.066* |
| Hypertension | | 29 (51.8%) | 52 (72.2%) | 5.662 | 0.017* |
| Dyslipidemia | | 38 (67.9%) | 66 (91.7%) | 11.722 | 0.001* |
| Smoking | | 30 (53.6%) | 29 (40.3%) | 2.240 | 0.134* |

**Table (4) Correlation between diabetic groups and SPECT scan end results.**

| | Grading | Group I(non diabetics) | | Group II(diabetics) | | Chi-square test | |
|---|---|---|---|---|---|---|---|
| | | No = 56 | | No = 72 | | $X^2$ | P-value |
| Ischemia | 0 | 15 | 26.8% | 34 | 47.2% | 8.382 | 0.039 |
| | 1 | 5 | 8.9% | 7 | 9.7% | | |
| | 2 | 10 | 17.9% | 14 | 19.4% | | |
| | 3 | 26 | 46.4% | 17 | 23.6% | | |

**Table (5) Correlation between diabetic groups and TID, HbA1c and exercise test.**

| | | Group I (non diabetics) | Group II (diabetics) | Independent t-test | |
|---|---|---|---|---|---|
| | | No = 56 | No = 72 | T | P-value |
| **HbA1c** | Mean ± SD<br>Range | 5.03 ± 0.54<br>4.1 – 6.1 | 7.60 ± 1.06<br>5.9 – 11 | 16.586 | 0.000 |
| **Resting ECG** | | 38 (69.1%) | 45 (62.5%) | 0.598 | 0.439 |
| **Exercise ECG** | | 37 (66.1%) | 42 (58.3%) | 0.798 | 0.372 |
| **Duration of exercise** | Mean ± SD<br>Range | 7.42 ± 2.37<br>3 – 15.09 | 6.27 ± 1.50<br>2.5 – 9.21 | -3.365 | 0.001 |
| **TID** | Mean ± SD<br>Range | 1.12 ± 0.14<br>1.0 – 1.79 | 1.22 ± 0.18<br>1.01 – 1.79 | 3.423 | 0.001 |

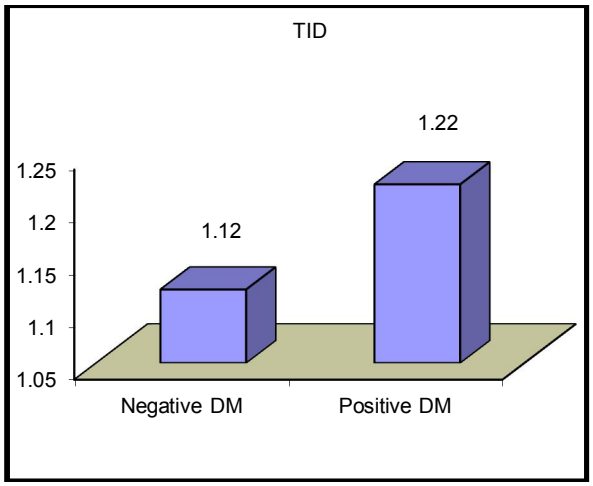


**Figure (1) Signficance of diabetic groups with TID.**

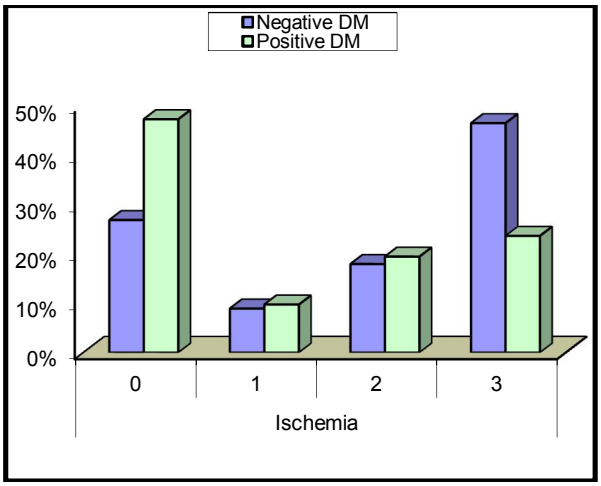


**Figure (2) Signficance of diabetic group with ischemia.**

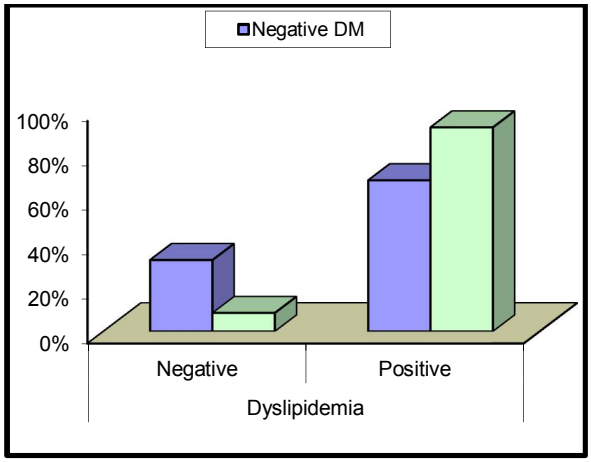


**Figure (3) Signficance of diabetic group with dyslipidemia.**

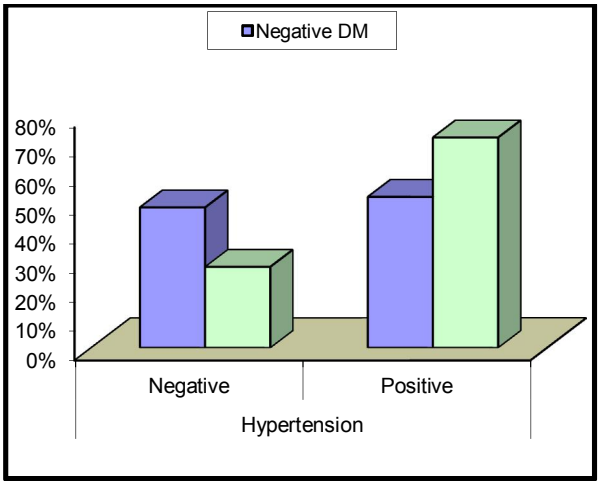


**Figure (4) Signficance of diabetic group with hypertension.**

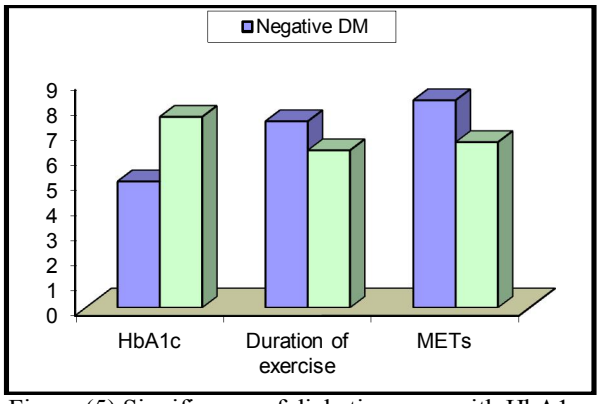

Figure (5) Significance of diabetic group with HbA1c

According to the level of HbA1c in the study population 79 patients which HbA1c level below 7 in diabetics and below 6 in non diabetics are classified as normal or controlled HbA1c group (group I) while 49 patients which HbA1c level above 7 in diabetics and above 6 in non diabetics are classified as high HbA1c group (group II) and so in correlation with different characteristics in the study cohort as showed in tables (6,7and 8) there was no statistically significance regarding the following data:

**1-Age**: Patients in group (I) showed mean age 56 ± 8.37 years old with range (38 – 70) years old, while patients in group (II) showed mean age 54 ± 9.65 years old with range (35 – 68) years old, with P-value=0.134.

**2-Sex**: In group (I), 66 (83.5%) patients were male, while 42 (85.7%) patients were male in group (II) with P-value=0.742.

**3-Hypertension**: In group (I), 49 (62.0%) patients were hypertensive, while 32 (65.3%) patients were hypertensive in group (II) with P-value= 0.708.

**4-Dyslipidemia**: In group (I), 63 (79.7%) patients were dyslipidemic, while 41 (83.7%) patients were dyslipidemic in group (II) with P-value= 0.580.

**5-Resting ECG**: In group (I), 53 (67.9%) patients showed ST-T wave changes in resting ECG, while 30 (61.2%) patients showed ST-T wave changes in resting ECG in group (II), with P-value= 0.438.

**6-Exercise ECG test**: In group (I), 52 (65.8%) patients showed further ST segment depression in exercise ECG test, while 27 (55.1%) patients in group (II) showed further ST segment depression in exercise ECG test, with P-value= 0.225.

**7-Duration of exercise**: Patients in group (I) showed mean duration of exercise 6.98 ± 2.16 min. with range (1 – 27) min., while patients in group (II) showed mean duration of exercise 6.45± 1.70 min. with range (2.5 – 9.21) min. with P-value=0.147.

**8-Ischemia**: In SPECT study, in group (I) 27 (34.2%) patients were normal showing no ischemia (grade 0), 5 (6.3%) patients showed mild ischemia (grade 1), 14 (17.7%) patients showed moderate ischemia (grade 2) and 33 (41.8%) patients showed severe ischemia (grade 3), while in group (II) 22 (44.9%) patients were normal showing no ischemia (grade 0), 7 (14.3%) patients showed mild ischemia (grade 1), 10 (20.4%) patients showed moderate ischemia (grade 2) and 10 (20.4%) patients showed severe ischemia (grade 3) with P-value = 0.067.

On the other hand, other demographic criteria showed statistically

98significant correlation regarding the following criteria:

**1-Smoking**: In group (I), 42 (53.2%) patients were smokers, while 17 (34.7%) patients were smoker in group (II) with P-value=0.042, figure (8).

**2-DM**: In group (I), 27 (34.2%) patients were diabetics, while 45 (91.8%) patients were diabetic in group (II) with P-value=0.000, figure (6).

**3-TID**: Patients in group (I), the mean level of TID was 1.14 ± 0.14 with range (1-1.70), while patients in group (II) the mean level of TID was 1.42 ± 0.20 with range (1-1.79) with P-value=0.001, figure (7).

**Table (6 ) Correlation between HbA1c groups and other demographic criteria.**

| | | (Normal HbA1c ) Group I | (High HbA1c) Group II | Independent t-test | |
|---|---|---|---|---|---|
| | | No = 79 | No = 49 | t/$X^2$* | P-value |
| **Age** | Mean ± SD<br>Range | 56.46 ± 8.37<br>38 – 70 | 54.02 ± 9.65<br>35 – 68 | -1.508 | 0.134 |
| **Male gender** | | 66 (83.5%) | 42 (85.7%) | 0.108 | 0.742 |
| **Hypertension** | | 49 (62.0%) | 32 (65.3%) | 0.140 | 0.708 |
| **Dyslipidemia** | | 63 (79.7%) | 41 (83.7%) | 0.306 | 0.580 |
| **Smoking** | | 42 (53.2%) | 17 (34.7%) | 4.152 | 0.042 |
| **DM** | | 27 (34.2%) | 45 (91.8%) | 40.856 | 0.000 |

**Table (7) Correlation between HbA1c groups, TID and exercise test results.**

| | | Normal HbA1c Group I | (High HbA1c) Group II | Chi-square test | |
|---|---|---|---|---|---|
| | | No = 79 | No = 49 | $X^2$/t* | P-value |
| Resting ECG | | 53 (67.9%) | 30 (61.2%) | 0.601 | 0.438 |
| Exercise ECG | | 52 (65.8%) | 27 (55.1%) | 1.471 | 0.225 |
| Duration of exercise | Mean ± SD<br>Range | 6.98 ± 2.16<br>3 – 15.09 | 6.45 ± 1.70<br>2.5 – 9.21 | -1.458 | 0.147 |
| TID | Mean ± SD<br>Range | 1.14 ± 0.14<br>1.0 – 1.79 | 1.24 ± 0.20<br>1.0 – 1.79 | 3.340 | 0.001 |

**Table (8) Correlation between HbA1c groups and SPECT end results.**

| | Grading | (Normal HbA1c) Group I | | (High HbA1c) Group II | | Chi-square test | |
|---|---|---|---|---|---|---|---|
| | | No = 79 | | No = 49 | | $X^2$ | P-value |
| Ischemia | 0 | 27 | 34.2% | 22 | 44.9% | 7.175 | 0.067 |
| | 1 | 5 | 6.3% | 7 | 14.3% | | |
| | 2 | 14 | 17.7% | 10 | 20.4% | | |
| | 3 | 33 | 41.8% | 10 | 20.4% | | |

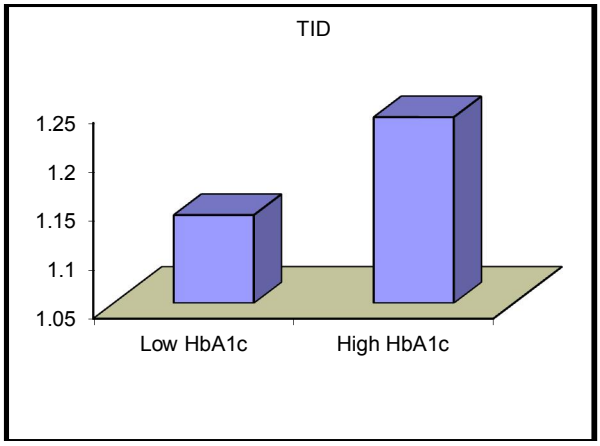


**Figure (7) Signficance of HbA1c groups and TID**

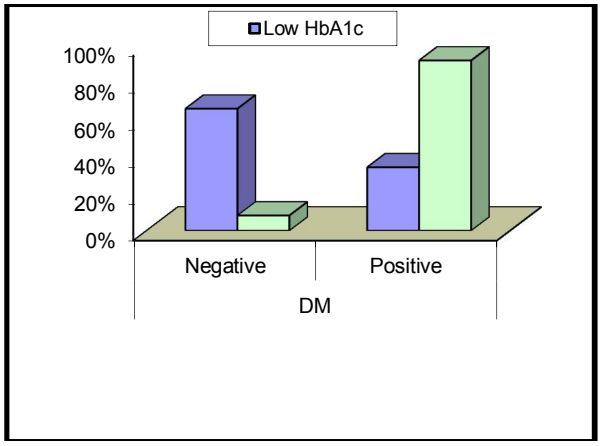


**Figure (6) Signficance of HbA1c group with DM.**

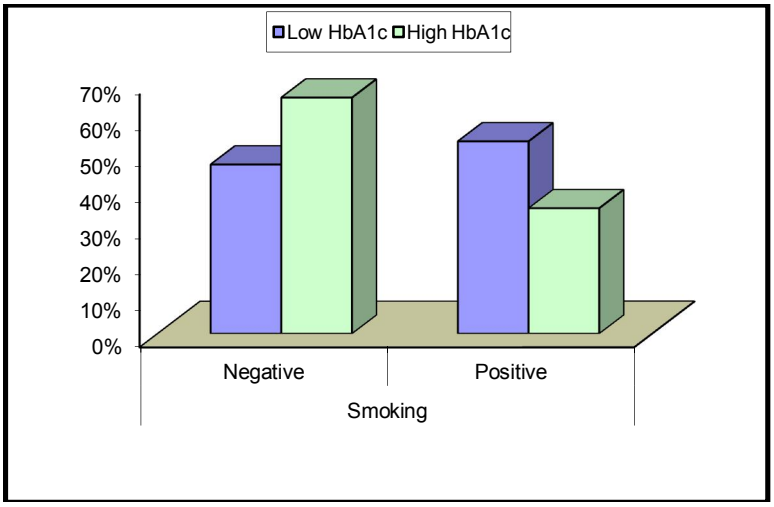


**Figure (8) Signficance of HbA1c groups with smoking.**

According to various values in different TID definitions three groups of the study population as showed in tables (9 and 10) were classified as the following: group (I) with TID value from 1.16 to1.19, group (II) with TID value from 1.2 to 1.22, group (III) with TID value >1.22 and showing no statistically significance correlation regarding the following criteria:

**1-Age**: Patients in group (I ) showed mean age 54 ± 8.25 years old with range (35 – 70 ) years old, while patients in group (II) the mean age was 57 ± 9.30 years old with range (45 – 70) years old and patients in group (III) showed mean age 56 ± 10.30 years old with range (37– 70) years old with P-value= 0.376.

**2-Hypertension**: It was showed that 53 (63.1%) patients in group (I), 6 (66.7%) patients in group (II) and 22 (62.9%) patients in group (III) were hypertensive with P-value=0.976.

**3-Smoking**: It was showed that 35 (41.7%) patients in group (I), 6 (66.7%) patients in group (II), 18 (51.4%) patients in group (III) were smoker with P-value=0.273.

**4-Exercise ECG test**: There were 50 (59.5%) patients in group (I), 5 (55.6%) patients in group (II), 24 (68.6%) patients in group (III) showed further ST segment depression in exercise ECG test, with P-value=0.603.

**5-Duration of exercise**: Patients in group (I) showed mean duration of exercise 6.9 ± 2.12 min. with range (3 – 15) min., while patients in group (II) showed mean duration of exercise 6 ± 2.12 min. with range (3 – 10) min. and patients in group (III) showed mean duration of exercise 6.5 ± 1.70 min. with range (2.5 – 9.5) with P-value= 0.558.

**6-Ischemia**: In SPECT study, 37 (44.0%) patients in group (I), 3 (33.3%) patients in group (II) and 9 (25.7%) patients in group (III) were normal showing no ischemia (grade 0), while 11 (13.1%) patients in group (I), 1 (11.1%) patients in group (II) and no patient in group (III) showed mild ischemia (grade1), 13 (15.5%) patients in group(I), 1 (11.1%) patients in group (II) and 10 (28.6%) patients in group (III) showed moderate ischemia (grade II) and 23 (27.4%) patients in group (I), 4 (44.4%) patients in group (II) and 16 (45.7%) patients in group (III) showed severe ischemia (grade III) with P-value= 0.059.

While other demographic criteria showed statistically significant correlation as following:

**1- Sex**: Male patients were 76 (90.5%) patients in group (I), 6 (66.7%) patients in group (II) and 26 (74.3%) patients in group (III), with. P-value=0.027. figure (9).

**2-Dyslipidemia**: The study showed 63 (75%) patients in group (I), 8 (88.8%) patients in group (II) and 33 (94.3%) patients in group (III) were dyslipidemic with P-value=0.041, figure (10).

**3-DM**: The study showed 42 (50%) patients in group (I), 8 (88.8%) patients in group (II), 22 (62.9%) patients in group (III) were diabetic with P-value=0.054. figure (13).

**4-HbA1c**: Patients in group (I) showed mean HbA1c 6.3 ± 1.52 with range (4.1-9.3) and 30 (35.71%) patients showed high HbA1c, while patients in group (II) showed mean HbA1c 6.6 ± 1.61 with range (4.3-9.2) and 3 (33.3%) patients showed high HbA1c and patients in group (III) showed mean HbA1c 7 ± 1.53 with range (5.7-11) and 16 (85.71%) patients showed high HbA1c with P-value =0.043.0.011 respectively, figure (11).

**5-RestingECG**: There were 48 (57.8%) patients in group (I), 5 (55.6%) patients in group (II) and 30 (85.7%) patients in group (III) showed ST-T wave changes in resting ECG with P-value=0.012. figure (12).

**Table(9) Correlation between TID groups and other demographic criteria of the study population.**

| | | TID 1.16 - 1.19 (Group I) | TID 1.20 - 1.22 ( Group II) | TID > 1.22 (Group III) | One Way ANOVA | |
|---|---|---|---|---|---|---|
| | | No.= 84 | No.= 9 | No.= 35 | F/X² | P-Value |
| Age | Mean ± SD<br>Range | 54.73 ± 8.25<br>35 – 70 | 57.44 ± 9.30<br>45 – 70 | 56.94 ± 10.30<br>37– 70 | 0.986 | 0.376 |
| Sex | | 76 (90.5%) | 6 (66.7%) | 26 (74.3%) | 7.215 | 0.027 |
| Hypertension | | 53 (63.1%) | 6 (66.7%) | 22 (62.9%) | 0.048 | 0.976 |
| Dyslipidemia | | 63 (75.0%) | 8 (88.9%) | 33 (94.3%) | 6.403 | 0.041 |
| Smoking | | 35 (41.7%) | 6 (66.7%) | 18 (51.4%) | 2.597 | 0.273 |
| DM | | 42 (50.0%) | 8 (88.9%) | 22 (62.9%) | 5.850 | 0.054 |
| HbA1c | Mean ± SD<br>Range | 6.34 ± 1.52<br>4.1 – 9.3 | 6.63 ± 1.61<br>4.3 – 9.2 | 7.12 ± 1.53<br>5.7– 11 | 3.223 | 0.043 |
| | Normal HbA1c<br>High HbA1c | 54 (64.29%)<br>30 (35.71%) | 6 (66.7%)<br>3 (33.3%) | 19 (14.29%)<br>16 (85.71%) | 8.864 | 0.011 |
| Resting ECG | | 48 (57.8%) | 5 (55.6%) | 30 (85.7%) | 8.864 | 0.012 |
| Exercise ECG | | 50 (59.5%) | 5 (55.6%) | 24 (68.6%) | 1.012 | 0.603 |
| Duration of exercise | Mean ± SD<br>Range | 6.91± 2.12<br>3 – 15.09 | 6.32 ± 2.12<br>3.45 – 10.33 | 6.57± 1.70<br>2.5 – 9.58 | 0.587 | 0.558 |

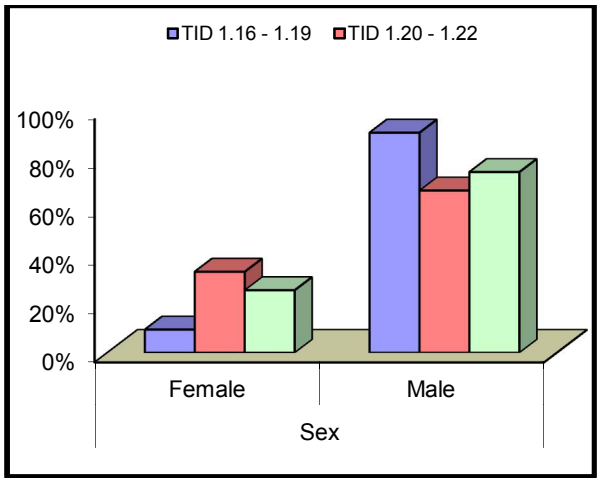


**Figure (9) Signficance of TID groups with sex.**

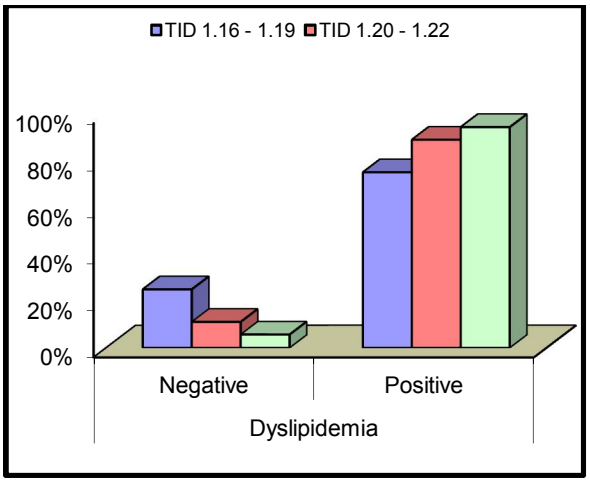


**Figure (10) Signficance of TID groups with dyslipidemia.**

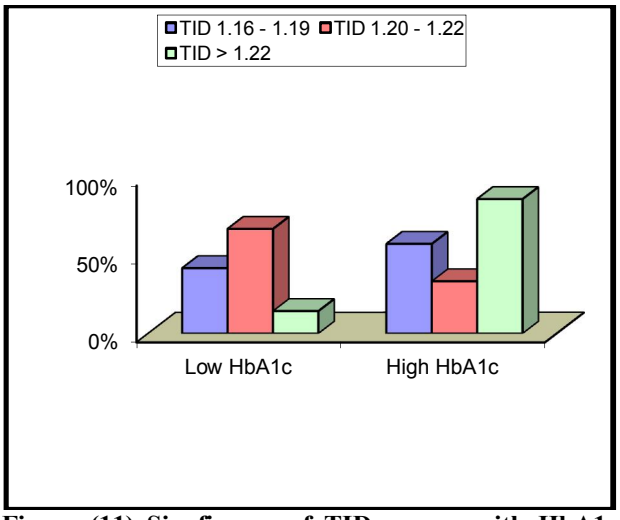


**Figure (11) Signficance of TID groups with HbA1c groups.**

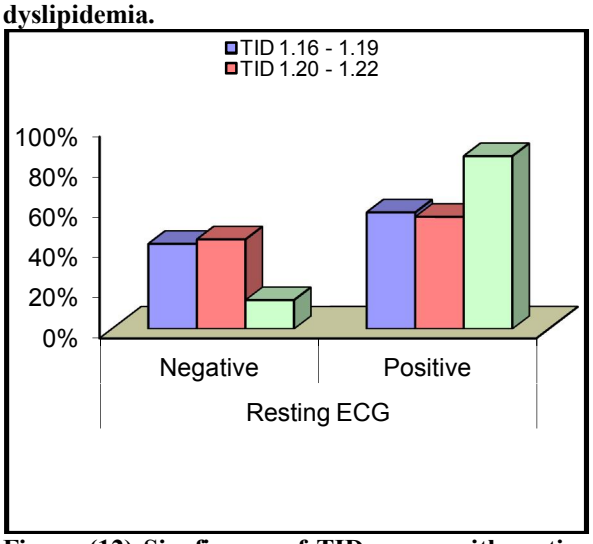


**Figure (12) Signficance of TID group with resting ECG.**

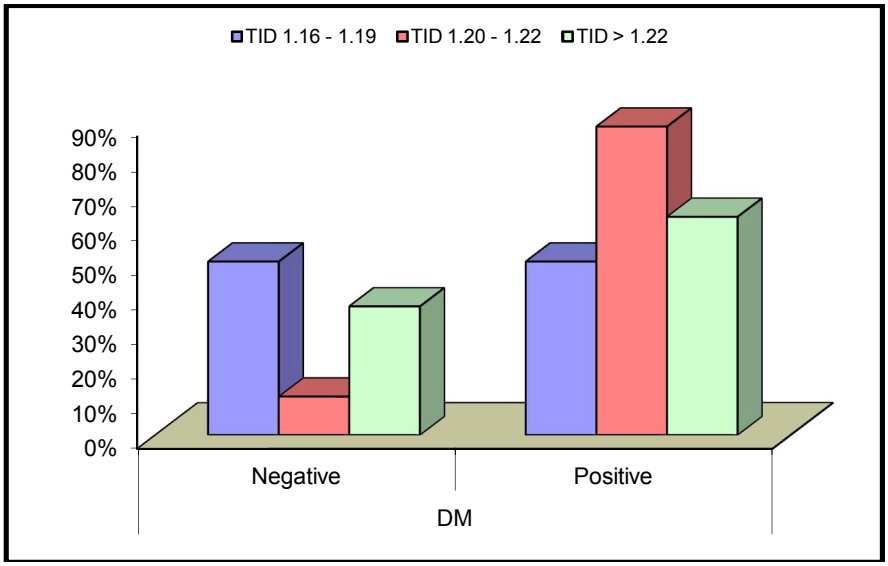


**Figure (13) Signficance of TID group with diabetic groups.**

**Table (10) Correlation between TID groups and cardiac scan end results.**

| | Grading | TID 1.16 - 1.19 (Group I) | | TID 1.20 - 1.22 (Group II) | | TID > 1.22 (Group III) | | Chi Square Test | |
|---|---|---|---|---|---|---|---|---|---|
| | | No | % | No | % | No | % | $X^2$ | P-Value |
| Ischemia | 0 | 37 | 44.0% | 3 | 33.3% | 9 | 25.7% | 12.153 | 0.059 |
| | 1 | 11 | 13.1% | 1 | 11.1% | 0 | 0.0% | | |
| | 2 | 13 | 15.5% | 1 | 11.1% | 10 | 28.6% | | |
| | 3 | 23 | 27.4% | 4 | 44.4% | 16 | 45.7% | | |

In the study population regarding the most important demographic criteria which are HbA1c and TID and in correlation with each other showing the relationship and its statistically significance.

We studied the impact of rising HbA1c level on stress and perfusion data like TID ratio as in table (11) showing strong direct correlation between the increase of HbA1c and the increase of TID ratio with P-value=0.00, figure (14).

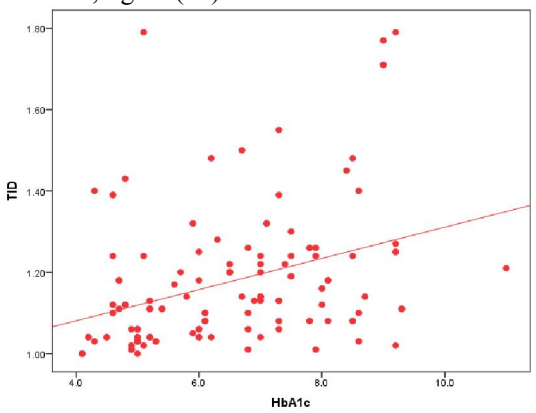


**Figure (14) Correlation between TID and HbA1c.**

**Table (14) Correlation between TID and HbA1c.**

| | HbA1c | |
|---|---|---|
| | R | P-value |
| TID | 0.390** | 0.000 |

In table (15) different cut off points of HbA1c values showed various values of sensitivity and specificity as showed and prediction of TID level, figure (15).

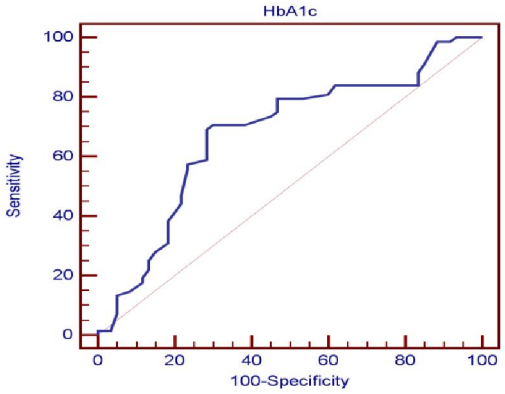


**Figure (15) ROC curve for HbA1c in prediction of TID**

**Table (15) Cut off points of HbA1c levels.**

| Cut off point | AUC | Sensitivity | Specificity | +PV | -PV |
|---|---|---|---|---|---|
| > 6 | 66.13 | 70.59 | 61.67 | 67.6 | 64.9 |
| >6.2 | 67.5 | 69.12 | 71.67 | 73.4 | 67.2 |
| > 7 | 62.70 | 47.06 | 78.33 | 71.1 | 56.6 |
| > 7.5 | 56.275 | 30.88 | 81.67 | 65.6 | 51.0 |

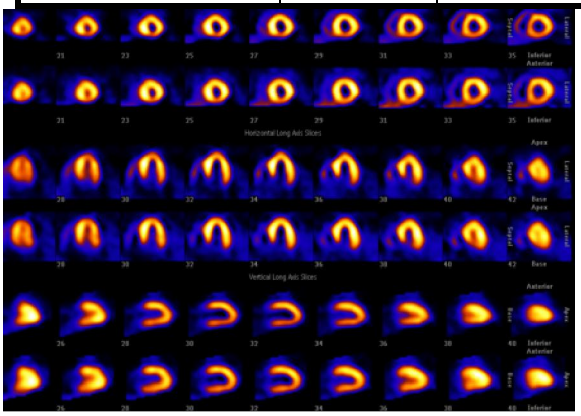

**Figure (16) Myocardial perfusion scan showing normal uptake on stress and rest images.**

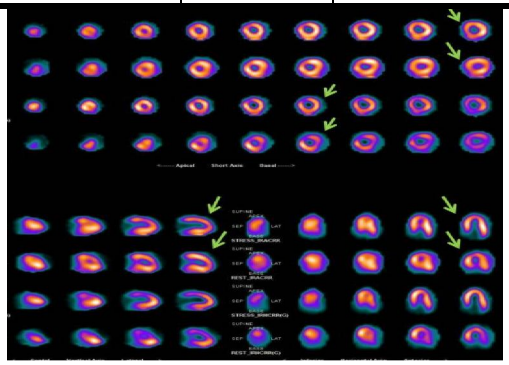

**Figure (17) There is a small, fixed apicoseptal perfusion defect showing transient ischemic dilatation with stress. The green arrows point to representative pairs of stress/rest images (stress on top, rest on bottom), demonstrating an increase in the size of the left ventricle with stress.**

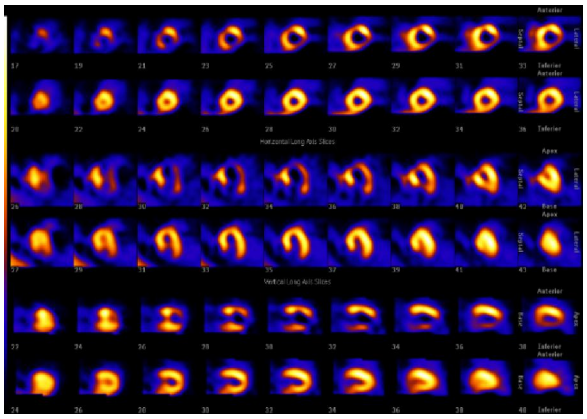

**Figure (18) SPECT study showed antero-lateral wall ischemia.**

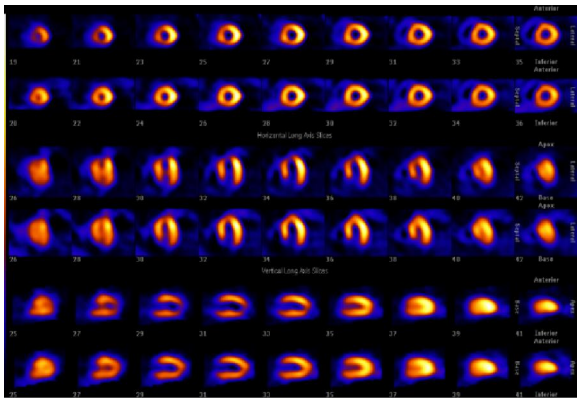

**Figure (19) SPECT study showed apico-lateral wall ischemia.**

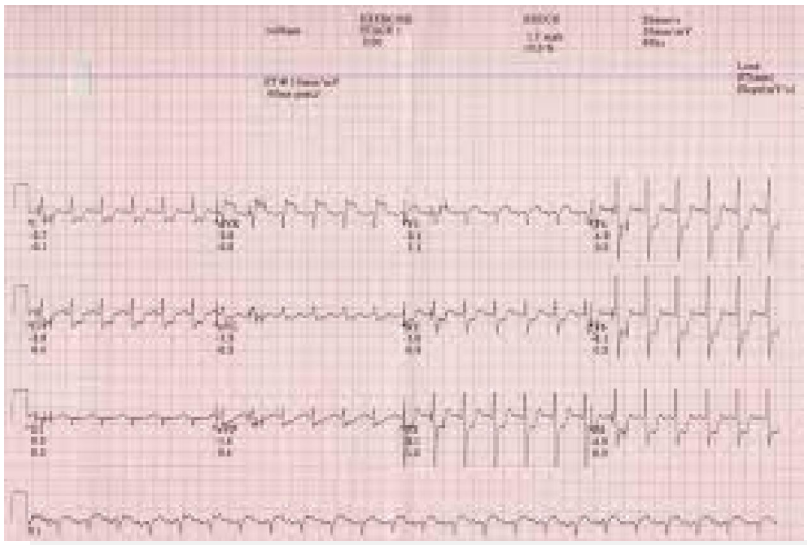

**Figure (20) Exercise ECG stress test shows ST-segment depression on anterolateral leads**

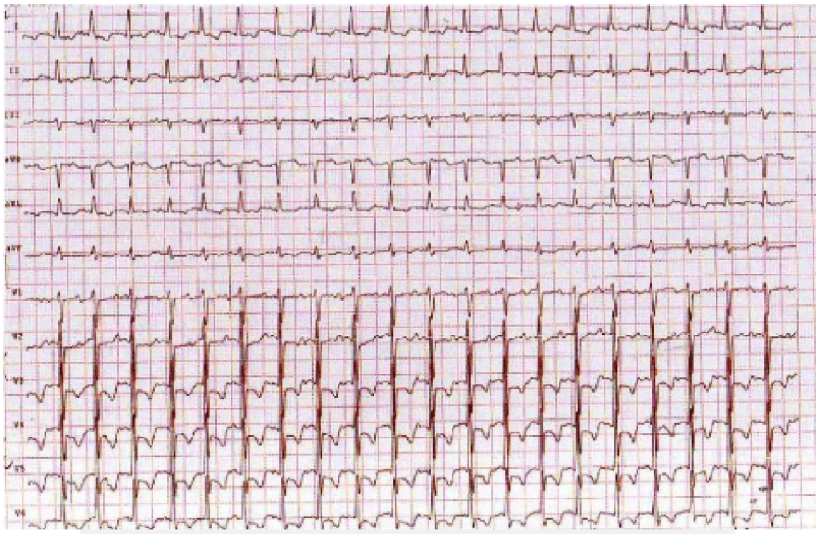

**Figure (21) Strongly positive Treadmill exercise ECG test**

**4. Discussion:**

Diabetes is an important factor in the development of cardiovascular disease. It is stated that 80% of diabetic subjects die of CVD and 75% directly from atherosclerosis. Contrary to non-diabetic subjects their findings are more extensive. Further they have a lower left ventricular ejection fraction, more cardiac events and more frequent silent ischemia. Myocardial ischemia can be a consequence of small vessel disease in diabetic subjects. In addition to this it was proven that in diabetic subjects there were changes of coronary vasoreactivity and incidence of non-atherosclerotic vascular abnormalities. The exercise myocardial SPECT is a non-invasive examination sufficiently specific for the diagnosis of ischemic heart disease.

A finding of transient ischemic dilation of the left ventricle (TID > 1.22) during perfusion of the myocardium, diagnosed either by a pharmacological or exercise stress test is a marker of serious coronary atherosclerosis and of a bad prognosis. However, some studies have proved more coronary events with transient ischemic dilation and negative perfusion myocardial SPECT than in the group without transient ischemic dilation. It is known that some diseases especially diabetes mellitus, can influence subendocardial perfusion. Our work was concerned with the relationship between glycosylated hemoglobin and the value of the transient ischemic dilation index in diabetic and non diabetic subjects with proven myocardial ischemia according to the exercise myocardial SPECT.

Transient ischemic dilation is characterized by an expansion of the left ventricle cavity on a post-exercise myocardial SPECT in comparison with rest images. In the study of Abidov et al. subjects were investigated for adenosine stress myocardial perfusion SPECT and then also angiographically. Abnormal values of TID correlated with a serious angiographic finding of 90% stenosis in the proximal left anterior descending artery or in 2or more coronary arteries.

In a published work the same authors Abidov et al. proved in a group with transient ischemic dilation and normal perfusion myocardial SPECT2.4% of cardiac events, while in a group without transient ischemic dilation the incidence was only 1% per year.

Emmett et al. concerned themselves with etiologic transient ischemic dilation. Nineteen (18%) of 103 subjects had transient ischemic dilation, 19 (18%) had left ventricular hypertrophy, and 23 (22%) had diabetes. A high percentage had severe coronary artery disease (45%), where as 55% had less severe coronary artery disease(29%) or non-significant coronary artery disease (25%). Severe coronary artery disease, diabetes, left ventricular hypertrophy and the ischemia scores were independent predictors of transient ischemic dilation by multivariate logistic regression. In subjects with severe coronary artery disease, the effect of left ventricular hypertrophy on the incidence of transient ischemic dilation was additive and also in diabetic subjects the incidence of transient ischemic dilation increased to 54%, while in non-diabetic subjects the incidence was 21%.

The authors conclude that the incidence of transient ischemic dilation is associated with the presence of severe coronary artery disease. However the association is modified by the presence of left ventricular hypertrophy and by diabetes. In these work all subjects had diabetes mellitus type 2. The markers of cardiovascular disease microalbuminuria, hyperlipoproteinemia and hypertension present. During exercise gated myocardial SPECT the mean value of SSS moved within 10.55 6.52. In 53% of the subjects demonstrated the value of stress total severity score above 100. Only 2 subjects had TID values above the normal, i.e. 1.22. During statistical evaluation using Pearson's correlation at the level of significance P< 0.05 we proved a statistically significant correlation between the value of TID and HbA1c (p = 0.035).

It has been stated already in the work of Emmett et al. that the TID mechanism remains controversial and that quite a few factors may be involved. In the work of Takeishi et al, Sugihara et al. and others transient ischemic dilatation was concluded to be related subendocardial hypoperfusion. Diabetes is a disease in which inadequate compensation leads primarily to microvascular damage. Levels of CRP above 3 mg/*l* bore witness to the high risk of developing cardiovascular disease despite the fact that they correlated with levels of TID only in the subgroup above the regression line. The absence of a correlation between TID and adhesion molecule levels may be caused by the participation of advanced glycation end products in the etiology of microangiopathy as a consequence of inadequate compensation of diabetes, more than low active inflammation which leads to the development of atherosclerotic lesions. Correlation of certain left ventricle parameters with atherosclerosis inflammation markers (CRP, E-selectin) and also with triglyceride levels documents the presence of an active atherosclerotic process, which is considered to be low-grade inflammation.

TID represents pseudo-dilatation of the left ventricle due to diffuse subendocardial ischemia. Diabetic cardiomyopathy and diabetic autonomous neuropathy are present in diabetic patients as opposed to non-diabetic patients. Diabetic cardiomyopathy expresses a complex of changes evoked in the myocardium by the metabolic pathways. Hyperglycemia leads to glycation of myocardial

proteins. Studies confirm cardiac myocyte hypertrophy, interstitial fibrosis and apoptosis. Dysfunction of myocardial contractility develops from the aspect of hemodynamics. Cardiac autonomic neuropathy leads to impairment of parasympathetic innervations, domination of sympathetic innervation, development of coronary vasoconstriction and ischemia.

Results of the UKPDS study show that better compensation of diabetes type 2 leads to a distinct reduction of the risk of microangiopathy, yet the risk of coronary events is reduced only by 16%, which is at the borderline of significance. This study confirms the fact that the total risk of macrovascular complications is less affected by diabetes control than the risk of microvascular changes.

The results from coronary angiography testing also confirmed propensity towards small vessel disease, which also influences transient ischemic disease of the left ventricle. A number of observations have already shown that patients with poor diabetes control have a higher mortality rate. Myocardial disease in diabetes is complex in nature and for this reason improved diabetes control is in any case, a desirable target.

In our study, 128 patients with demographic criteria as following: 72 diabetics,47 hypertensive.108 male, 104 dyslipidemic and 59 smoker. The mean HbA1c was 6.48± 1.55 range from 4 to 11. All patients underwent resting ECG showing 83 patients with ST-T wave changes. Exercise ECG tests showed 79 patients with further ST segment depression with mean duration of exercise 6.22± 2.00 range from 2.5 to 15.09. All subjects underwent myocardial perfusion SPECT with data analysis as following:

The mean TID ratio was 1.18± 0.17 with range from 1 to 1.79. Normal study in 49 (38 %) patients showing no ischemia (Grade 0) while 12 (9%) patients showed mild ischemia (Grade 1), 24 (18%) patients showed moderate ischemia (Grade 2) and 34 (33%) patients showed severe ischemia (Grade 3).

There are 2 groups in the study population classified according to patient history of anti-diabetic drug uptake into 56 patients non diabetic (group I ) and 72 patients diabetic (group II ) and according to different demographic criteria findings showed no statistically significance regarding age, sex, smoking, resting ECG, exercise ECG, On the other hand, other criteria showed statistically significance correlation regarding the following:

**1-Hypertension**: In group (I), 29 (51.8%) patients were hypertensive, while 52 (72.2%) patients were hypertensive in group (II) with P-value =5.662.

**2-Dyslipidemia**: In group (I), 38 (67.9%) patients were dyslipidemic, while 66 (91.7%) patients in group (II) were dyslipidemic with, P-value =0.001.

**3-HbA1c**:: In group (I), the mean HbA1c was 5 ± 0.54 with range (4.1-6.1), while in group (II) the mean HbA1c was 7.6 ± 1.06 with range (5.9-11) with P-value=0.000**.**

**4-Duration of exercise**:: In group (I), the mean duration of exercise was 7.4 ± 2.37 min. with range (3-15) min., while in group (II) the mean duration of exercise was 6 ± 1.50 min. with range (2.5-9) min. with P-value=0.001.

**7-TID**: In group (I), the mean TID was 1.12 ± 0.14 with range (1-1.79), while in group (II) the mean TID was 1.22 ± 0.18 with range (1.01 – 1.79) with P-value=0.001.

**8-Ischemia**:: In SPECT study, In group (I) 15 (26.8%) patients were normal showing no ischemia (grade 0), 5 (8.9%) patients showed mild ischemia (grade 1), 10 (17.9%) patients showed moderate ischemia (grade 2) and 26 (46.4%) patients showed severe ischemia (grade 3), while in group (II) 34 (47.2%) patients were normal showing no ischemia (grade 0), 7 (9,7%) patients showed mild ischemia (grade1), 14 (19.4%) patients showed moderate ischemia (grade 2), 17 (23.6%) patients showed severe ischemia (grade 3), P-value =0.039.

According to the level of HbA1c in the study population patients which HbA1c level above 7 in diabetics and above 6 in non diabetics are classified as High HbA1c group (group II) while patients which HbA1c level below 7 in diabetics and below 6 in non diabetics are classified as normal HbA1c group (group I) and so in correlation with different characteristics in the study cohort there was no statistically significance regarding age, sex, HTN, dyslipidemia, resting ECG, exercise ECG, duration of exercise and ischemia finding of cardiac scan study. On the other hand, other demographic criteria were showed statistically significant correlation as following:

**1-Smoking**: In group (I), 42 (53.2%) patients were smokers, while 17 (34.7%) patients were smoker in group (II) with P-value=0.042.

**2-DM**: In group (I), 27 (34.2%) patients were diabetics, while 45 (91.8%) patients were diabetic in group (II) with P-value=0.000,

**3-TID**: Patients in group (I), the mean level of TID was 1.14 ± 0.14 with range (1-1.70), while patients in group (II) the mean level of TID was 1.42 ± 0.20 with range (1-1.79) with P-v Page 92

According to various valu nt TID definitions three groups of the study population classified as following group I with TID value from1.16 to1.19 group II with TID value from 1.2 to 1.22 group III with TID value >1.22 and showing no statistically significance correlation regarding age, sex, HTN, smoking, exercise ECG, duration of exercise, ischemia while other demographic criteria showed statistically significant correlation as following:

**1- Sex**: Male patients were 76 (90.5%) patients in group (I), 6 (66.7%) patients in group (II) and 26 (74.3%) patients in group (III), with. P-value=0.027.

**1-Dyslipidemia**: The study showed 63 (75%) patients in group (I), 8 (88.8%) patients in group (II) and 33 (94.3%) patients in group (III) were dyslipidemic with P-value=0.041.

**2-DM**: The study showed 42 (50%) patients in group (I), 8 (88.8%) patients in group (II), 22 (62.9%) patients in group (III) were diabetic with P-value=0.054.

**3-HbA1c**: Patients in group (I) showed mean HbA1c 6.3 ± 1.52 with range (4.1-9.3) and 30 (35.71%) patients showed high HbA1c, while patients in group (II) showed mean HbA1c 6.6 ± 1.61 with range (4.3-9.2) and 3 (33.3%) patients showed high HbA1c and patients in group (III) showed mean HbA1c 7 ± 1.53 with range (5.7-11) and 16 (85.71%) patients showed high HbA1c with P-value =0.043.0.011 respectively.

**4-Resting ECG**: were 48 (57.8%) patients in group (I), 5 (55.6%) patients in group (II) and 30 (85.7%) patients in group (III) showed ST-T wave changes in resting ECG with P-value=0.012.

In the study population regarding the most important demographic criteria which are HbA1c and TID and in correlation with each other showing the relationship and its statistically significance We studied the impact of rising HbA1c level on stress and perfusion data like TID ratio showing strong direct correlation between the increase of HbA1c and the increase of TID ratio with P-value=0.00.

## Conclusion

Diabetes is an important factor in the development of cardiovascular disease. It is stated that 80% of diabetic subjects die of CVD and 75% directly from atherosclerosis. Contrary to non-diabetic subjects their findings are more extensive. Further they have a lower left ventricular ejection fraction, more cardiac events and more frequent silent ischemia.

Myocardial ischemia canbe a consequence of small vessel disease in diabetic subjects. In addition to this it was proven that in diabetic subjects there were changes of coronary vasoreactivity and incidence of non-atherosclerotic vascular abnormalities. The exercise myocardial SPECT is a non-invasive examination sufficiently specific for the diagnosis of ischemic heart disease. A finding of transient is chemicdilation of the left ventricle (TID > 1.22) during perfusion of the myocardium, diagnosed either by a pharmacologicalor exercise stress test is a marker of serious coronary atherosclerosis and of a bad prognosis. However, some studies have proved more coronary events with transient ischemic dilation and negative perfusion myocardial SPECT than in the group without transientischemic dilation. It is known that some diseases especially diabetes mellitus, can influence subendocardial perfusion. Our work was concerned with the relationship between glycosylated hemoglobin and the value of the transientischemic dilation index in diabetic and non diabetic subjects with proven myocardial ischemia according to the exercise myocardial SPECT. Transient ischemic dilation is characterized by an expansion of the left ventricle cavity on a post-exercise myocardial SPECT in comparison with rest images. TID represents pseudo-dilatation of the left ventricle due to diffuse subendocardialischemia.

According to the results, it is possible to consider the cumulative effect of long term inadequate diabetes control on the post-exercise dilation of the left ventricle, as determined by the transient ischemic dilation index.

In conclusion, the increased values of TID correlated with increased HbA1c values in type 2 diabetic subjects with proven myocardial ischemia. Diabetes and its long term inadequate control can be one of the factors which affect the transient ischemic dilation index.

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