The role of Exercise Electrocardiogram, 2-Dimensional Echocardiograph, and Biochemical analysis in the diagnosis of Coronary Heart Diseases in diabetic and non-diabetic individuals

Aboubakr KS[1], Rahuma ZOM[2], Ben Khalifa KM[2], Ben-Mahmud BM[1]

1. Department of Biological Science, School of Basic Science, Libyan Academy, Tripoli-Libya
2. Medical Faculty, University of Tripoli

Correspondence should be addressed to:

Dr Bahaedin M. Ben-Mahmud
Department of Life Science,
Basic Science School,
Libyan Academy, Tripoli-Libya
Telephone number: 00218 922788286
bahaedin.benmahmud@academy.edu.ly
b.benmahmud@outlook.com

ABSTRACT

Coronary heart disease (CHD) remains the leading cause of death in DM2. The purpose of this study is to determine the usefulness and effectiveness of exercise electrocardiography (Ex-ECG) and standard two-dimensional echocardiography (2DE) among type 2 diabetic (DM2) and non-diabetic (NDM) of both genders in the diagnosis of CHD accompanied with biochemical risk factors for CHD

A total of 102 age-matched DM2 and non-diabetic individuals in both genders were recruited in the current study. All cases were assessed for CHD diagnosis using the guidelines of the Bengali version of the Rose Angina Questionnaire. All groups were examined clinically by cardiologists and applying Ex-ECG and 2DE accompanied by biochemical parameters analysis of all participants in Ematiga's laboratory.

All diabetic and non-diabetic subjects are age-matched. The diabetic women were obese with a BMI of (>30 kg/m^2). The duration of diabetes in females was (10.2±1.02 yrs) and in males was (9.7±0.8 yrs). There was a positive relationship between the duration of diabetes and HbA1c level. Some evidence presented in this study revealed that the percentage of LVEF is negatively correlated with the duration of diabetes mellitus. In addition, there is statistical significance in ST-depression between both genders in (ND) and (D) groups. The relationship between ST-depression expressed as mV detected by Ex-ECG and duration of diabetes in females and males.

In conclusion, both Ex-ECG, and 2DE testing are non-invasive, easy to perform, and accessible in rural hospitals and clinics. It can be beneficial in diagnosing, risk stratifying or assessing patients with CHD provided appropriate patient selection is used to enhance its sensitivity and specificity, especially in presence of biochemical risk factors for coronary heart disease explained in this study helped identify or exclude the early diagnosis of CHD.

INTRODUCTION

The International Diabetes Federation (IDF) estimates that 537 million people have diabetes mellitus (DM), over 90% of whom have DM2. People with diabetes comprise 8.8% of the world's population, and IDF predicts that the number of cases of diabetes will rise to 783 million by 2045 [(1)]. DM2 is associated with an estimated two-fold increased risk of coronary heart disease (CHD). Therefore, there is a positive relationship between the duration of diabetes mellitus and the level of HbA_{1c}, which means that the severity of diabetic control will deteriorate by incremental diabetic duration, which is expected that the increased duration of DM2 would lead to an increase in the prevalence of CHD. In particular, the degree to which the decline in CHD mortality has been shortened by the increase in DM2 prevalence, or is likely to be curtailed in the future, is of main interest [(2-8)].

DM2 is a major cause of morbidity and mortality rates for its role in the microvascular and macrovascular complications affecting multiple organ systems [(9)]. The macrovascular lesion mainly affects large- or medium-calibre artery atherosclerosis which that is responsible for serious cardiovascular complications such as (heart attacks, strokes, and/or peripheral vascular diseases) that may require limb amputation. The severity of these complications is related to the duration and severity of hyperglycemias. The latter is also linked to other co-morbidities and disorders that aggravate the direct diabetic effect. These include hypertension, dyslipidemia, and generalized glycosylation of cells and membranes aggravating atherosclerosis [(10)]. The main pathological risk factor in macrovascular diseases is the role of diabetes in developing atherosclerosis within the medium and large vessels and the formation of atheroma and/or plaque [(11)]. Also, there is an increased leukocyte adherence to endothelial cells and hyperviscosity of blood in diabetes that contribute to macrovascular and microvascular complications [(12)].

Patients with DM2 also have hypertension, hyperlipidemia, obesity, endothelial cell dysfunction, and prothrombotic factors, called "metabolic syndrome". Not only the incidence of CHD is higher in DM2, but the mortality of diabetic patients after a cardiac event is also significantly increased as compared to non-diabetic people, including sudden death [(13,14)].

Plaque formation in CHD occurs due to the deposition of Low-Density Lipoprotein (LDL) within endothelial cells of coronary arteries. The narrowing of the coronary artery lumen with the insufficiency of blood supply to the heart leads to ischemia. Although, acute ischemic changes due to the rupture of the thrombus and the formation of emboli released cause an acute obstruction in blood flow (acute myocardial infarction) [(15)].

The prevalence of typical myocardial ischemia and silent MI, detected by Ex-ECG was increased in diabetic patients and people with pre-diabetes [(16-19)]. Diabetic patients without a history of MI were diagnosed by Ex-ECG in 18% of patients with diabetes, and only 7% of people without DM. Whereas Ex-ECG diagnosed silent ischemia in 33% of diabetics without a history of angina pectoris and only 15% of those without diabetes [(20)].

Our data revealed a statistical confirmation of diagnostic links of the role of stress electrocardiogram and echocardiogram previously observed in hospitals, which proves the importance of their use in the initial diagnosis except for a small percentage that requires surgical intervention. We also noted that there was statistical correspondence between levels of cardiac enzymes among DM2 compared to non-diabetic individuals, also the presence of impaired left ventricular ejection fraction with the duration of diabetes mellitus.

METHODS

Subjects: This study included 67 DM2 (40 females and 27 males) and 35 NDM (17 females and 18 males) recruited from the cardiac clinic at Emattiga's teaching hospital, presented in tables (1) and (2), respectively. Cardiologists and diabetologists clinically examined all the groups for vascular macroangiopathy (coronary heart disease peripheral vascular disease and stroke) and microangiopathy (neuropathy, retinopathy, and nephropathy). The related biochemical risk factors for CHD were assessed, and the strategy of medical and surgical treatments was obtained for each individual. The severity of coronary heart disease was determined according to the number of vessels affected, the depth and quality of download sloping of ST-depression detected by Ex-ECG, also the detection of left ventricular ejection fraction (LVEF) and myocardial wall movement determined by 2DE.

Collection of blood and analytical methods:

Whole blood was drawn and collected in an EDTA tube, fluorinated plasma tube, and plane tube for serum analysis. Analyses of fasting blood glucose, cardiac enzymes, and lipid profile were measured using Abbott Architect c4000 Chemistry Analyzer (Irving TX, USA) and HbA1c (Fully Automatic Mindray CL-960i, China). Blood sample for measurement of cardiac enzymes includes creatinine phosphokinase isoenzyme (CK-MB), troponin-T, aspartate aminotransferase (GOT), and lactic dehydrogenase (LDH). The biochemical risk factors for atherosclerosis determined include lipid profiles {total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL)}, fasting blood sugar (FBS), and HbA_{1c}.

Exercise electrocardiography (Ex-ECG)

All patients underwent symptom-limited according to Bruce and Bruce's modified protocol using Nihon Kohden Cardiofax V ECG 9320K testing with continuous 12-lead ECG monitoring. A 12-lead ECG was recorded before exercise and at the end of each exercise stage (every 2 minutes), at peak exercise, and during recovery. Patient symptoms, rest and peak heart rate, blood pressure, and any ECG changes were noted immediately. The test was discontinued for limiting symptoms (angina, dyspnoea, fatigue), abnormalities of rhythm or blood pressure, marked ST-segment deviation (> 0.2 mV in the presence of typical angina), or attainment of age-predicted maximal heart rate calculated as {(220 - age) X 0.85}. All the Ex-ECG records were interpreted by 2 cardiologists, and the positive criteria for CHD determined if there is more than or equal horizontal or down-sloping ST-depression or elevation in any lead for at least 60-80 milliseconds

[21]. Patients with left bundle branch block on standard ECG were excluded from this study. The indications and contraindications for Ex-ECG testing were explained in tables (1) and (2), respectively.

Table (1) Indications for Ex-ECG testing
1. Diagnosis of CHD
2. Assessment of CHD prognosis
3. Evaluation of therapeutic response
4. Assessment of preoperative cardiac risk for non-cardiac surgery
5. Evaluation of functional capacity

Table (2) Contra-indications to do Ex-ECG testing
1. Recent AMI (3-4 days)
2. Malignant hypertension > 220/130
3. Unstable angina
4. Severe symptomatic left ventricular dysfunction
5. Severe aortic stenosis and aortic dissection
6. Acute myocarditis and pericarditis
7. Acute aortic dissection
8. Pulmonary embolism or infarction
9. Advanced atrioventricular block
10. Hypertrophic obstructive cardiomyopathy

Two-Dimension Echocardiography (2DE)

Echocardiography is a non-invasive diagnostic technique performed with Hitachi Aloka echocardiography (ARIETTA 70) in this study. The 2DE can determine the location and extent of any wall tissue damage. Moreover, 2DE is an important tool in assessing wall motion abnormality in patients with suspected cardiac disease. It is a tool that helps in reaching an early diagnosis of myocardial infarction showing regional wall motion abnormality of the heart. Also, it is important in treatment and follow-up in patients with heart failure, by assessing LVEF [22,23].

2DE can detect abnormal heart wall movement and if combined with a quantitative left ventricular ejection fraction (LVEF) of less than 55% might be due to the lesion of microvascular and macrovascular changes in the heart [24].

Statistical analysis: The statistical software SPSS version 16 (Statistical Package for Social Sciences) and GraphPad Prism version 6.0 were used. An unpaired two-tailed Student's t-test was used to test the significance of the variables. Linear regression and correlation were used to evaluate the relationship between the two variables. Data are expressed as means ± S.E.M of measurements in the different experiments. Differences were considered statistically significant at $P<0.05$.

RESULTS

Subjects

Table (**3**) shows the baseline clinical characteristics of diabetic patients and non-diabetic subjects with and without coronary heart disease recruited for this study.

Table (3) *Baseline Clinical and Metabolic Characteristics of DM type 2 patients & ND individuals*

	Non-diabetic individuals		**DM Type 2**	
	Females	**Males**	**Females**	**Males**
Number (n)	17	18	40	27
Age	52.9±1.8	50.7±1.9	53.7±2	54.9 ±1.3
Duration of diabetes (years)	-	-	9.7±0.8	10.2±1.0
BMI (Kg/m^2)	31.1±1.8	26.9±1.2	31.8±0.7	29.5±0.9
Physical inactivity	11 (64.7%)	6 (33.3%)	29 (72.5%)	11 (40.7%)
Smokers (n)	0	11 (61.1%)	0	15 (55.6%)
Hypertension (n)	7 (41.2%)	8 (44.4%)	7 (17.5%)	1 (3.7%)
Coronary heart disease				
Absent	8 (47%)	3 (16.7%)	11 (27.5%)	10 (37%)
Present	9 (53%)	15 (83%)	29 (72.5%)	17 (63%)
Blood pressure				
Resting SBP	126.6±3.5	123.4±2.4	125.7±2.2	120.6±2.1
Resting DBP	77±2.1	77.2±2.1	77.5±1.5	74.4±1.4
Resting MBP	93.5±2.3	92.6±1.8	93.5±1.6	89.8±1.4
Exercise SBP	153.2±5.0	151.9±4.5	148.4±2.4	155.3±3.4
Exercise DBP	92.1±2.5	88.3±2.1	91.4±1.5	90.0±2.3
Exercise MBP	112.5±3.1	109.5±2.3	110.4±1.5	111.8±2.2
Diabetic neuropathy	-	-	9 (22.5%)	4 (14.8%)
Diabetic retinopathy	-	-	8 (20%)	5 (18.5%)
Peripheral vascular disease	-	-	3 (7.5%)	2 (7%)

1. The serum level of HbA_{1c} and FBS in diabetic and non-diabetic subjects

There is statistical significance in serum level of HbA_{1c} between females in non-diabetic (ND) and age-matched diabetic (D) groups (5.1±0.1 (n=17) *vs* 7.8±0.3 (n=40); ***P<0.0001). Correspondingly, males in both groups (ND and D) show statistical significance in serum level of HbA1c (5.4±0.1 (n=18) *vs* 8.1±0.3 (n=27); ***P<0.0001) as explained in figure (1A).

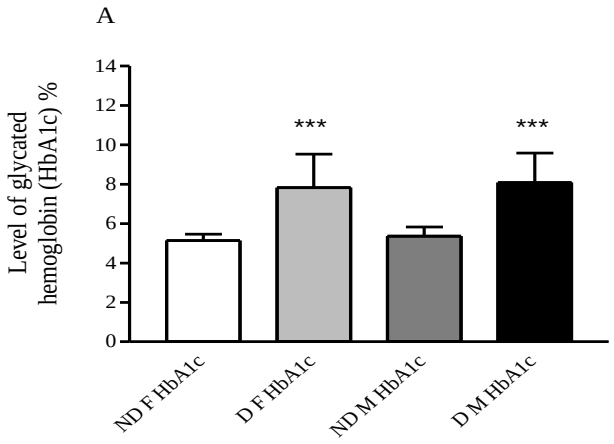

Figure (1A) *The age of DM type 2 (D) and Non-diabetic (ND) individuals in both genders expressed as (years old) show that the studied groups are age-matched. The age of females (F) in non-diabetic (ND) and females in diabetic patients (D) was (50.7±1.9 (n=17) vs 54.9±1.3 (n=40); P>0.07) which is similar to males (M) in both ND and D individuals (52.9±1.8 (n=18) vs 53.7±2 (n=27); P >0.7).*

The level of fasting blood sugar between non-diabetic and age-matched diabetic females and males (110.5±2.14 (n=17) vs 191.5±11.74 (n=40); ***P<0.0001) and (104.6±3.2 (n=18) vs 188.9±12.33 (n=27); ***P<0.0001), respectively as illustrated in figure (1B).

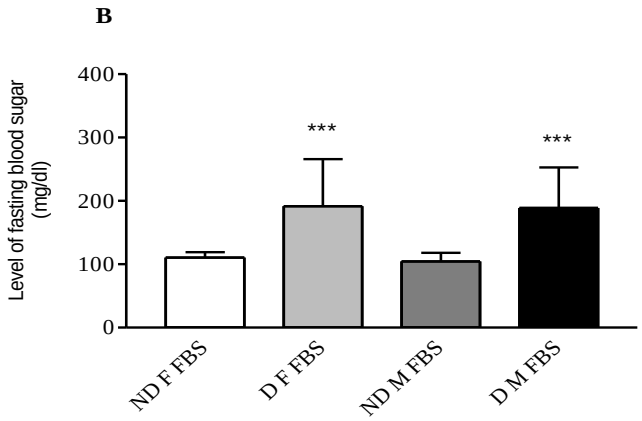

*Figure (**1B**) Body mass index (Kg/m^2) between females in non-diabetic (ND) and diabetic (D) groups (110.5 ± 2.1 (n=17) vs 191.5 ± 11.7 (n=40); P <0.0001) while in males in both groups (ND and D) show no statistical significance in body mass index as shown (104.6 ± 3.2 (n=18) vs 188.9 ± 12.3 (n=27); P< 0.0001). Data are presented as Mean ± S.E.M*

2. Serum lipid profiles in non-diabetics and diabetics in both genders:

There is no statistical significance in serum level of total cholesterol between females and males in non-diabetic (ND) and diabetic (DM2) groups (186.5±6.2 (n=17) *vs* 198.4±5.9 (n=40); P>0.2), and in males (ND and DM2) (174.8±9.2 (n=18) *vs* 190.2±8.9 (n=27); P>0.2), respectively as shown in **figure** (**2A**). Similarly, the levels of LDL were statistically insignificant between (ND and DM2) in females and males as well (112.7 ± 5.9 (n=17) *vs* 120.2 ± 5.0 (n=40); P > 0.3); (93.4 ± 5.0 (n=18) *vs* 106.4 ± 5.6 (n=27); P > 0.1), respectively as shown in **figure** (**2B**).

In addition, there is no statistical significance in the level of HDL in females and males in (ND) and (DM2) {44.7±1.3 (n=17) *vs* 42.9 ± 1.5 (n=40); P > 0.4; and 44 ± 1.9 (n=18) *vs* 39.6±1.8 (n=27); P>0.1). The ratio between LDL/HDL in females and males in ND and DM2 (2.5±0.14 (n=18) *vs* 3.2±0.26 (n=40); P=0.14), and (2.2±0.15 (n=18) *vs* 2.8±0.25 (n=27); P=0.053) respectively, as shown in **figures** (**2C** and **D**

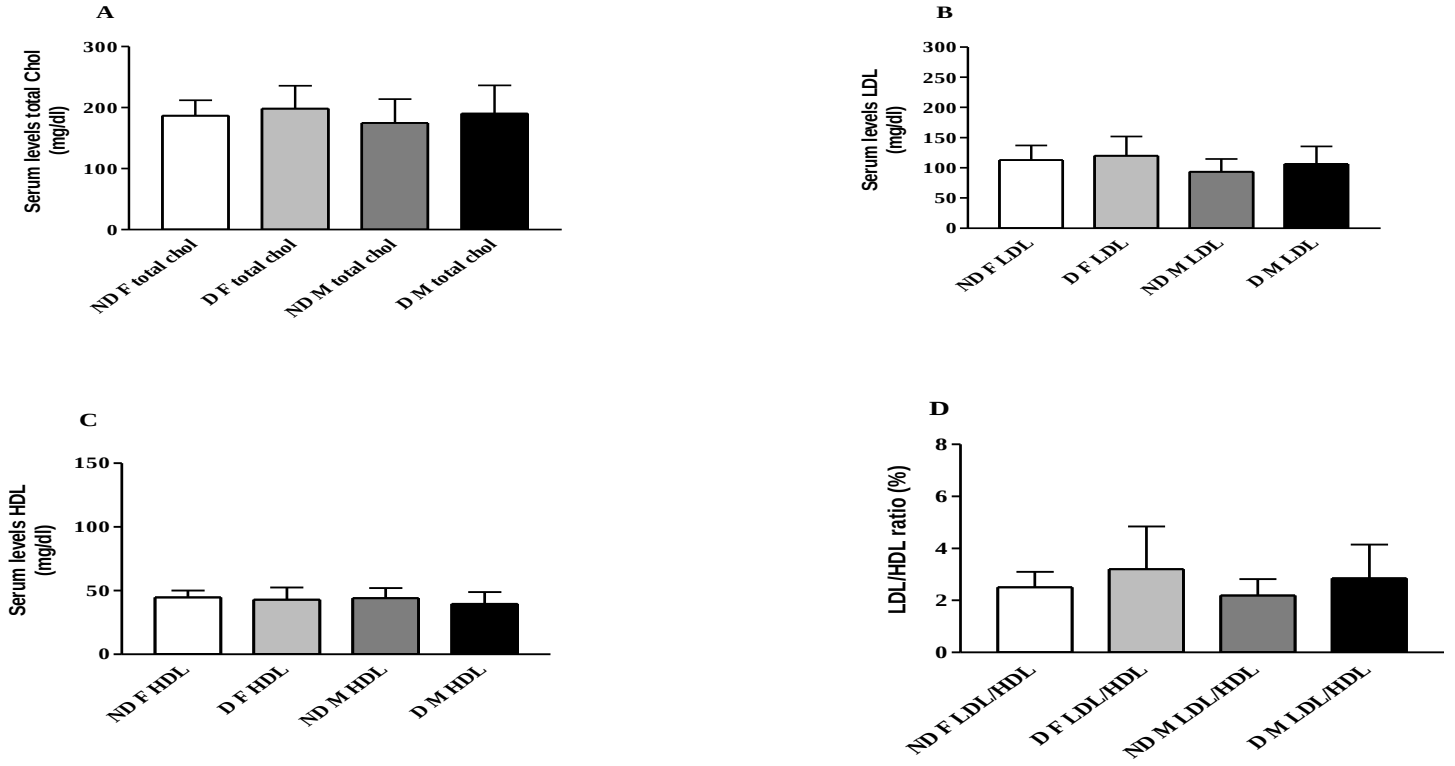

***Figure** (**2**) The data for serum lipid profile was compared between age-matched non-diabetic individuals and DM type 2 patients of both genders. Serum fresh samples were analyzed for total cholesterol (total chol) as shown in (**figure 2A**), low-density lipoprotein (LDL) as shown in (**figure 2B**), and high-density lipoprotein (HDL) as shown in (**fig 2C**), all data were expressed as mg/dl and LDL/HDL ratio as shown in (**figure 2D**) and expressed as a percentage (%). All the previous data did not show any statistical significance between all the groups.*

3. Triglyceride (TG) and Triglyceride Glucose Index (TyG) in non-diabetic and diabetic individuals in both genders

There is no statistical significance in serum level of Triglycerides (TG) in females between non-diabetic (ND) and diabetic (D) patients (149.6±10.4 (n=17) vs 172.8±12.9 (n=40); P>0.2) and also in males in (ND and D) groups (135±13.4 (n=18) vs 166.6±13.7 (n=27); P>0.1) as shown in **figure** (**3A**). However, there is strong statistical significance in Triglycerides Glucose Index (TyG) between females in non-diabetic (ND) and diabetic (D) groups (3.9±0.04 (n=17) vs 4.15±0.04 (n=40); P =0.0004) and similarly, males in both groups (ND and D) show statistical significance TyG (3.8±0.05 (n=18) vs 4.1±0.04 (n=27); P <0.0001) as shown in **figure** (**3B**).

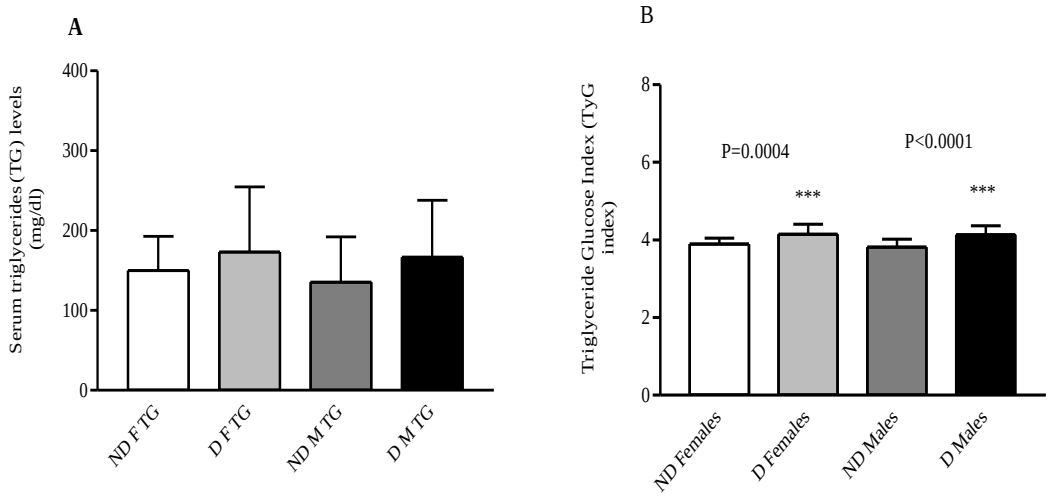

*Figure (3A) There is no statistical significance in serum level of triglyceride levels between ND and D females and males (P>0.2 and P>0.1), respectively. (**3B**) The data for triglyceride glucose index (TyG) between non-diabetic (ND) and diabetic (D) for females (F) and males (M). The TyG index was calculated as an Ln (fasting triglyceride level (mg/dl) x fasting glucose level (mg/dl)/2). The data expressed as mean ± SEM; ***P < 0.0004 and ***P<0.0001, respectively.*

However, the values of TyG index compared between non-diabetic and diabetic concerning BMI at 19-24.9 Kg/m^2 {4.7±0.07 (n=11) *vs* 5.09±0.09 (n=8); **P< 0.005}, and at BMI 25-29.9 Kg/m^2 {4.9 ± 0.05 (n=15) *vs* 5.1 ± 0.07 (n=17), **P <0.007} and at > 30 Kg/m^2 {4.9±0.05 (n=15) *vs* 5.1±0.04 (n=42); **P< 0.002} as shown in **figure** (**3C**).

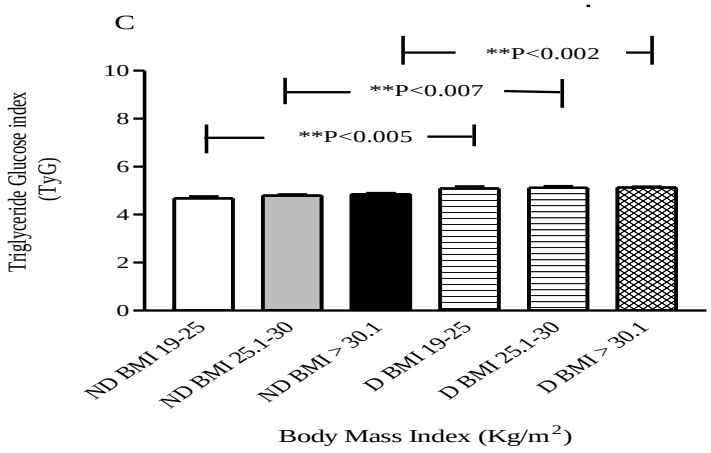

***Figure** (**3C**) The data for triglyceride glucose index (TyG) between normal, overweight and obese individuals according to BMI in (ND) and diabetic (D) for females (F) and males (M). There is a statistical difference between the TyG index and BMI of 19 to 25% showing (**P<0.005), BMI 25.1 to 29.9 (**P<007) and BMI > 30 kg/m^2 (**P<002), respectively.*

4. Serum level of cardiac enzymes in diabetics and non-diabetics in both genders:

There is statistical significance in serum level of troponin-T between females in non-diabetic (ND) and diabetic (D) groups (0.11±0.004 (n=17) *vs* 0.2±0.005 (n=40); ***P <0.0001). In addition, the serum level of troponin-T between males of non-diabetics and diabetics show strong statistical significance (0.11±0.004 (n=18) *vs* 0.15±0.006 (n=27); ***P <0.0001) as shown in **figure 4A**. Furthermore, there is an increased serum level of glutamic oxaloacetic transaminase (GOT) in diabetic patients compared to non-diabetic individuals in females and males (14.9±0.21 (n=17) *vs* 21.5±0.3 (n=40); ***P <0.0001) and (13.6±0.25 (n=18) *vs* 19.6±0.37 (n=27); ***P <0.0001), respectively as shown in **figure 4B**.

Additionally, there is a significant statistical difference in the serum level of lactate dehydrogenase between diabetic and non-diabetic females (336±15 (n=40) *vs* 271±17 (n=17); *P <0.02) and males (343.1±13 (n=27) *vs* 290.8±14 (n=18); *P <0.02) as shown in **figure** (**4C**) and also isoenzyme of creatinine phosphokinase (CK-MB) between diabetic and non-diabetic females (18.2±0.4 (n=40) *vs* 10.8±0.3 (n=17); ***P <0.0001) and males (21.5±1.0 (n=27) *vs* 12.0±0.32 (n=18); ***P <0.0001) as shown in **figure** (**4D**), respectively.

5. The correlation between left ventricular ejection fraction (LVEF) and duration of diabetes in both males and females

The percentage of left ventricular ejection fraction showed a very significant decrease with the duration of diabetes in males ($r = 0.48$; $*P < 0.012$) and females ($r = 0.399$; $*P < 0.012$) respectively as shown in **Figures** (**5A** and **B**). This data shows that the left ventricular ejection fraction is negatively correlated with the increased duration of diabetes mellitus.

6. Left ventricular Ejection Fraction (LVEF) detected with 2DE in non-diabetic and diabetic patients in both genders

The mean value of left ventricular ejection fraction detected by 2DE and expressed as a percentage in non-diabetic and diabetic patients in females and males shows no statistical significance. This is mainly explained due to small-sized data or only a few individuals who have suffered severe chronic myocardial ischemia or transmural myocardial infarction as shown in **figure** (**6**).

7. ST-depression detected by Ex-ECG in non-diabetic subjects and diabetic patients in both genders

There is statistical significance in ST-depression estimated by Ex-ECG between females in (ND) and (DM2) (-0.2 ± 0.01 ($n=17$) *vs* -0.28 ± 0.004 ($n=40$); $***P<0.0001$). Besides, there is a significant statistic between males of (ND) and (DM2) (-0.2 ± 0.007 ($n=18$) *vs* -0.33 ± 0.008 ($n=27$); $***P < 0.0001$) as shown in **figure** (**7**).

8. Relationship between ST-depression detected by Ex-ECG and duration of diabetes in both genders

The relationship between ST-depression expressed as mV detected by Ex-ECG and duration of diabetes in females ($r=0.39$; $*P <0.02$) and males ($r=0.46$; $*P <0.02$), respectively as shown in **Figures** (**5A** and **5B**). Therefore, there is a negative correlation between ST depression and the duration of diabetes.

9. The number of participants in medical and surgical therapy

The number of non-diabetic and diabetes mellitus type 2 who had coronary heart disease and are on medical therapy such as (anti-platelets, anti-hypertensive treatment, lipid-lowering agents, and anti-anginal therapy), and participants who undergo surgical procedures (coronary stents and coronary artery bypass graft) as demonstrated in Figure (8).

DISCUSSION

This study presents the critical role of Ex-ECG and 2DE in the diagnosis of coronary heart disease in DM2 and NDM individuals of matched age in both genders. Furthermore, this study explains some of the controllable and uncontrollable factors (i.e male gender, the elderly, ethnicity, and family history of CHD factors related to the increase in the onset of CVD. The age is matched between all groups, and the percentage of smokers present only in males with diabetes (55.6%) and those without diabetes (61.1%), physical inactivity for males and females with DM2 are (40.7% and 72.5%) and in NDM are (33.3% and 64.7%), respectively.

Physical inactivity is reflected by the presence of overweight and obesity in both groups. Though obesity and being overweight increase early inflammatory processes within coronary arteries, and they are closely related to concomitant diseases such as diabetes mellitus, hypertension, and hyperlipidemia. The severity of CHD is associated with being overweight and obesity as critical factors.

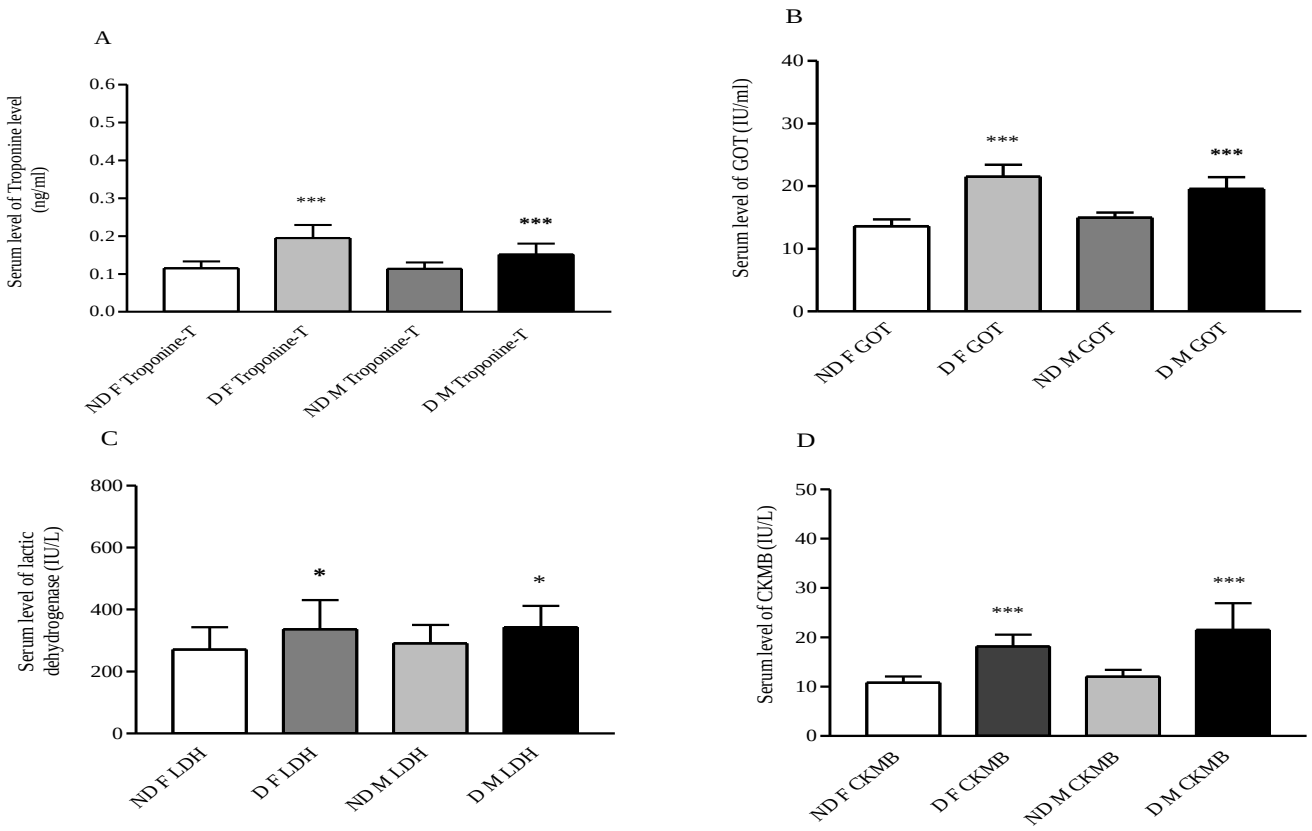

Figure (4) *Serum level of cardiac enzymes in non-diabetic and DM type 2 in both genders. The data for serum level of troponin-T and glutamic oxaloacetic transaminase (GOT) between non-diabetic and diabetic patients in both genders show statistically significant ***P < 0.0001, ***P < 0.0001 as shown in figure (**4A and 4B**), respectively. Similarly, there is statistical significance in both serum levels of lactate dehydrogenase with *P<0.02 **figure (4C)** and creatinine kinase isoenzyme (CK-MB) between diabetics and non-diabetics in both genders (***P < 0.0001as shown in **figure (4D)**). The data are expressed as mean ± SEM.*

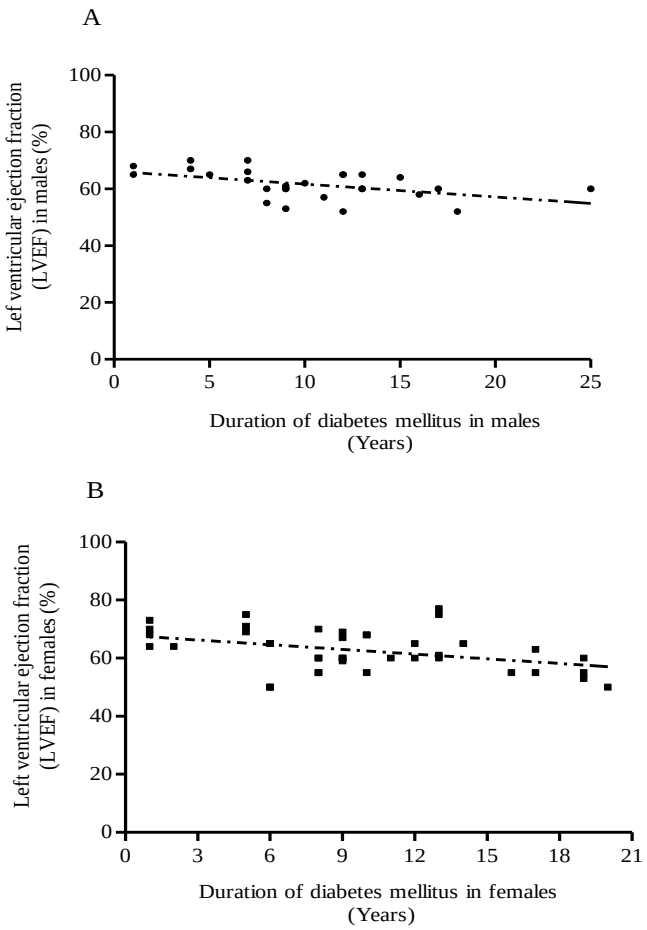

***Figure** (**5A**) The negative correlation between duration of diabetes mellitus (years) and left ventricular ejection fraction (EF) expressed as (%) in diabetic males (r = 0.48; *P < 0.02) and (**figure 5B**) in diabetic females (r=0.399; *P<0.02).*

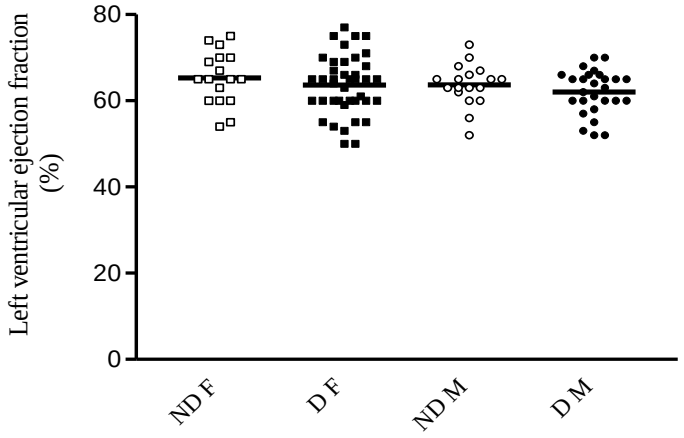

Figure *(**6**) The mean values of left ventricular ejection fraction (LVEF) expressed as (%) in non-diabetic (ND) and diabetic (D) females (F) and males (M) are lower in diabetic compared to non-diabetic of both genders. However, there is no statical significance between D and ND groups.*

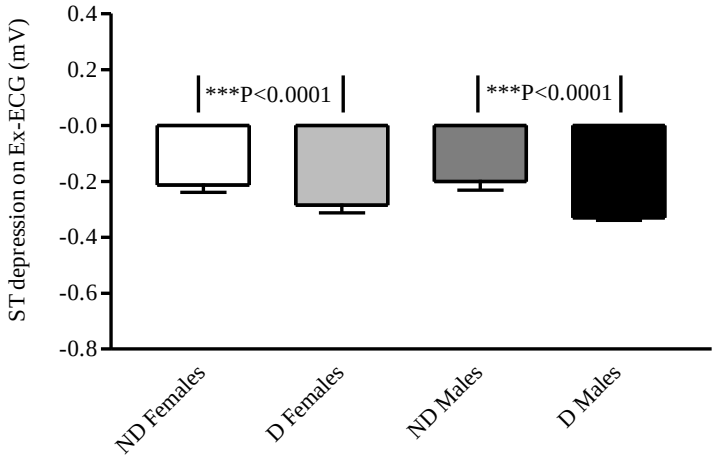

Figure *(**7**) There is statistical significance in ST-depression in non-diabetic and diabetic patients expressed as (mV) in both genders are ***P<0.0001, respectively. Data are expressed as mean ± SEM.*

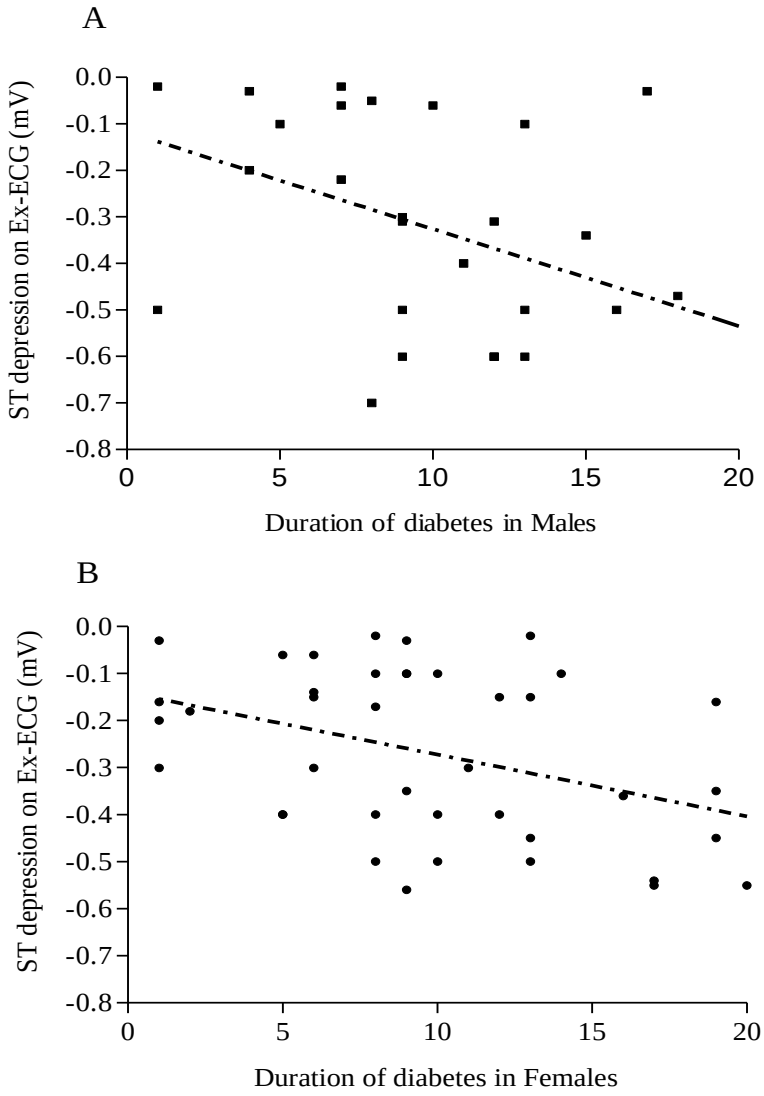

Figure (8A) *There is a negative correlation between the duration of diabetes mellitus (years) and ST depression in diabetic females (r* =0.39*; *P <0.02) and figure* ***(8B)*** *in diabetic males (r*=0.46*; *P <0.02).*

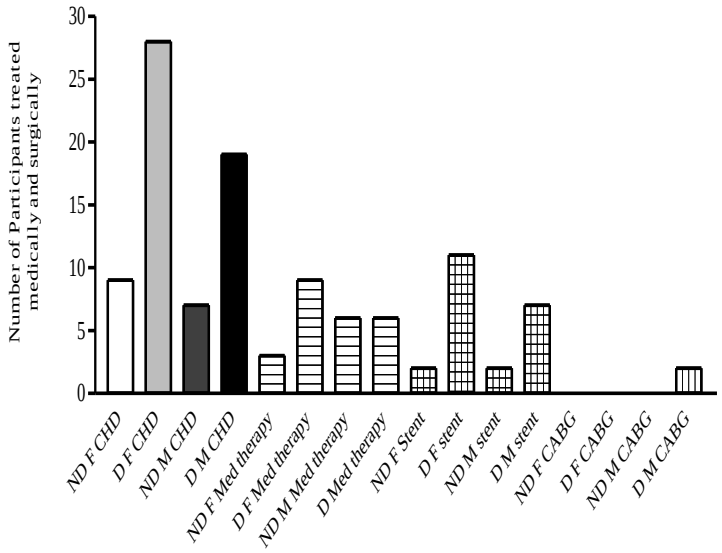

Figure (9) *The number of individuals (diabetic and non-diabetic) treated medically and surgically. The medical treatment consists of anti-hypertensive, anti-platelets, and lipid-lowering agents. Surgical therapy consists of coronary stents and coronary artery bypass grafts.*

Additionally, diabetic HbA_{1c} is a critical and more accurate standard for determining the severity of DM on fasting glucose levels [(25)]. HbA_{1c} levels provide a greater advantage by providing a consistent indicator of long-term blood sugar status, which correlates between two to three months of the average plasma glucose concentration [(26)]. Previous studies described high levels of HbA_{1c} and the degree of coronary heart disease (CHD) among diabetic patients and demonstrated that high HbA_{1c} was related to severe CHD [(27,28)]. In its recent position statement, the American Diabetes Association stated that HbA_{1c} reduction may be associated with a decrease in vascular and large vascular complications for diabetics [(29)]. Additionally, there is a potential use of HbA_{1c} as a vital sign of hyperlipidemia as well as a potential indirect indication of CVD risk in patients with DM type 2 [(30)].

Previous studies revealed that lipoprotein metabolism, not only in DM2 but also in impaired glucose tolerance (IGT) tends to show changes such as decreased HDL and increased triglyceride levels, which may be associated with increased insulin and increased insulin resistance [(31)]. Because high levels of triglycerides and fasting glucose are two components of metabolic syndrome, which is one of the most important risk factors for cardiovascular disease [(32)]. The triglyceride index (TyG) combines both triglyceride levels and fasting glucose, and its strong association with insulin resistance and a reliable mark of insulin resistance has been reported [(33)]. These results were similar to the data shown in this study. Although obesity is a risk factor for CHD [(34)], this study showed a strong relationship between BMI and the TyG index, which is an increased risk of CHD effect [(35)].

Increased duration of DM2 is associated with increased plasma HbA_{1c} levels and a decrease in the LVEF that increases the risk of mortality in patients with coronary heart disease supported by data from Sheng et al, 2019 in two main outcomes: (i) Patients with a DM duration of ≥ 10 years with higher HbA_{1c} levels Of plasma than those with a disease duration of fewer than 10 years and (ii) patients with DM who have been with STEMI, especially those with disease periods of ≥ 10 years, have a higher prevalence of lipid-rich plaques, a thin-covering fibroma (TCFA), plaque rupture from those without diabetes [(36,37)]. Furthermore, a study by Sacks et al., 2002 suggested the improved effect of pravastatin to improve HDL and triglycerides in patients with coronary artery disease who have low LDL concentrations [(38)].

Due to the risk of cardiovascular disease in diabetic patients, the target serum levels of LDL in secondary and primary prevention should not exceed 100 mg/dl as in secondary prevention for patients without diabetes [(39)].

The data in this study in both NDM and DM2 had a low level of average HDL concentration that may be due to family inheritance or physical inactivity and increased advanced glycation endproducts (AGE) in diabetic patients. Once more HDL has anti-inflammatory, anti-oxidant, anti-coagulant, and anti-apoptotic properties, which protect against coronary heart disease development [(40)].

Evliyaoğlu et al, 2011 concluded that increased glucose levels can damage liver cells and heart muscles. Monitoring blood glucose levels is a more valuable parameter than monitoring HbA_{1c} in the immediate assessment of serum LDH, CK-MB levels, and glutamic oxalacetic transaminase (GOT) especially in diabetics [(41,42)]. While this study examined the role of the TyG index in predicting cardiovascular events and compared the roles of fasting glucose, HbA_{1c}, the level of triglycerides, and the TyG index in predicting cardiovascular events in patients with DM2 during follow-up for 5.93 years. The results showed that fasting glucose and TyG index were associated with increased cardiovascular events, but HbA_{1c} was not associated with increased cardiovascular events. Moreover, our results showed that fasting glucose and the TyG index may improve predictability in DM2 patients due to insulin resistance.

A study by (Spiezia et al., 2018) found that patients with DM2 showed increased platelet reactivity compared to patients without diabetes, despite combined treatment with clopidogrel and aspirin. An increase in clopidogrel dose was not sufficient to reduce increased platelet reactivity in patients with DM2, highlighting the need for further investigation of other anti-platelet drugs in the studied population [(43)].

The right branch block (RBBB) or the left branch block (LBBB) caused by exercise is usually not specified unless it is associated with evidence of ischemia, i.e. angina, and then strongly suggests ischemia. Causes of the false-positive test include left ventricular hypertrophy (LVH), which is associated with decreased specificity of the exercise test, but sensitivity is not affected [(44)]. Digitalis causes exercise-induced ST-depression in 25% to 40% of ordinary people [(45-47)].

Numerous reports have demonstrated a lower diagnostic accuracy for exercise electrocardiography in women, in particular the occurrence of 1 mm of ST-segment depression. The average sensitivity and specificity for the exercise electrocardiogram are 61% and 69% [48-50].

Therefore, an integrated decision is needed with cardiologists and cardiac surgeons to improve medical treatments and pre-operative and post-operative outcomes for non-ST segment elevation in acute coronary syndrome patients who undergo coronary artery bypass graft (CABG).

To conclude, the Ex-ECG is non-invasive, convenient, and quick, affords diagnostic and prognostic value, and can also provide a reliable prediction of coronary heart disease and cardiac mortality especially if combined with 2DE and biochemical analyses related to cardiac risk factors. Also, they help give guidelines for patient therapy through physical rehabilitation and identify patients with potentially poor future outcomes.

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