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Original Article

Evaluation of Cardiac Myosin Binding Protein-C3 (cMyBP-C3) as Potential Risk Factor of Acute Coronary Syndrome in Diabetic Patients

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ABSTRACT

Background: Recent years, the prevalence of Type 2 Diabetes Mellitus (T2DM) has increased annually. The major complication of T2DM is Cardiovascular Disease (CVD). Cardiovascular disease is the main cause of death in T2DM patients, particularly those with comorbid Acute Coronary Syndrome (ACS). The present study aims to determine the cardiac Myosin Binding Protein-C3 (cMyBP-C3) levels in patients with Type 2 Diabetes Mellitus (T2DM) and to examine the relation of cMyBP-C3 levels with the Acute Coronary Syndrome (ACS). **Materials and Methods:** Eighty diabetic patients with T2DM who are free from cardiovascular conditions were included in the study, with ages ranging from 35 to 65 years. The T2DM patients were categorized into three subgroups based on their glycemic control, determined by their Hemoglobin A1c (HbA_{1c}) levels. Additionally, forty healthy individuals were included as the control group. The cMyBP-C3 and insulin levels in serum samples were measured using the ELISA Kit. The lipid profile results and fasting serum glucose test were measured using an automated chemical analyzer. The HbA_{1c} levels were determined using the HPLC method. **Results:** The study showed that the serum concentration of cMYBP-C3 in the group with T2DM was significantly higher in comparison to the healthy subjects ($p<0.05$). There were significantly substantial association between the levels of cMYBP-C3 and three variables: Malondialdehyde (MDA), insulin, and baseline HbA_{1c}%. There was an excellent area under the curve (AUC=0.963, $p=0.0001$). **Conclusion:** That circular cMyBP-C3 may serve as a prognostic indicator for the progression of ACS and declining cardiac function in patients with T2DM. Additionally, it was verified that there was a strong correlation between cMyBP-C3 levels and poorly controlled glycemia.

Keywords: cMyBP-C3, Type 2 diabetes, HbA_{1c}, Acute Coronary Syndrome, Cardiac complications of diabetes.

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INTRODUCTION

The most challenging medical conditions of the twenty-first century is diabetes mellitus.[1] Type 2 Diabetes Mellitus (T2DM) has a higher cardiovascular morbidity and mortality as well as a disproportionate amount of Cardiovascular Disease (CVD).[2] Furthermore, the metabolic disturbance associated with T2DM increases the risk of developing diabetic cardiomyopathy and CVD. These circumstances can result in heart failure through multiple pathways, such as myocardial infarction and persistent pressure excess.[3]

A high blood glucose level, which is an independent cardiovascular risk factor, increases the risk of Acute Coronary Syndrome (ACS).[4-6] The main causes of ACS incorporate unstable angina pectoris, acute non-ST segment elevation myocardial infarction, tear of coronary atherosclerotic plaques, and following occlusive thrombosis.[7] ACS leads to significant healthcare expenditures and is a primary contributor to both illness and death on a global scale.[8-11] In patients with type 2 diabetes, the prospect of ACS could be estimated by using some biomarkers such as sarcomeric proteins.[11]

A sarcomeric controlling protein called cardiac Myosin Binding Protein-C (cMyBP-C) regulates the heart contractile activity.[12-14] cMyBP-C contains eight immunoglobulin-like domains, three fibronectin type III domains, a M domain, and a proline-alanine-rich region located between C0 and C1.[15] Sarcomeric shape and function in the heart are regulated by cMyBP-C, an assembly protein and myosin stabilizer.[16-19] A growing body of research indicates that cMyBP-C is essential for controlling myosin function and heart contraction.[19,20] The MYBPC3 provides instructions for making cardiac MyBP-C, which is found in heart

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(cardiac) muscle cells. Based on a recent study, cMyBP-C may serve as a potential biomarker for Myocardial Infarction (MI) due to its release into the bloodstream post-MI in individuals and in a rat model, facilitated by proteolysis and dephosphorylation.[13]

Furthermore, in comparison to the currently recommended diagnostic biomarkers, cMyBP-C is a sensitive and early cardiac-specific biomarker of MI. As such, it has the potential to be a very helpful tool for ACS patients in terms of quick and precise point-of-care diagnosis and therapy.[15] Recent study showed the prevalence of ACS and its consequences in individuals with type 2 diabetes mellitus. Studies reveal that compared to the general population, diabetics are 2-3 times more likely to acquire ACS.[21] No studies have investigated the potential association between cMYBP-C3 and ACS in individuals diagnosed with type 2 diabetes. This is in consideration of the impact of cMYBP-C3 levels on ACS. Also, no previous study has investigated the role of serum cMyBP-C3 in T2DM patients as a predictor of Acute Coronary Syndrome (ACS). In this research, we evaluated the special effects of the levels of cMYBP-C3 in patients with T2DM and healthy individuals. Moreover, we study the correlation between cMYBP-C3 levels and the severity of diabetes mellitus type 2 patients (defined by Hb1Ac level).

MATERIALS AND METHODS

Diabetic Patients

Eighty individuals diagnosed with T2DM and without any history of heart diseases, aged between 35 and 65 years, were included in the study. The T2DM patients were categorized into three subgroups based on their glycemic control determined by their HbA_{1c} levels. The first subgroup pertained to those with well-controlled glycemia, aiming for an HbA_{1c} level of less than 7%. The second subgroup comprised individuals with inadequate glycemic control, with HbA_{1c} levels ranging from 7% to 8%. Finally, the third subgroup consisted of patients with poorly controlled glycemia, characterized by an HbA_{1c} level exceeding 8%.[22]

Healthy Subjects

Forty individuals without any health conditions were selected to participate in the study, ensuring that their ages fell within the range of 35 to 65 years and that both males and females were represented. The control group's average age was 60.85 ±1.14 years. The criteria employed by the physician to select the control group included absence of a history of alcohol or tobacco use, non-diabetic and non-hypertensive status, as well as the absence of acute illness symptoms.

Sample Collection

Each patient and member of the control group had 10 mL of blood extracted during the morning hours between 8 and 11, following a fast of 12 to 15 hr. The blood samples were divided into two parts. The first part had Ethylene Diamine Tetra Acetic acid (EDTA) (1.5 mg/mL) added to assess HbA_{1c} within 3 hr, while the second part was placed in a gel tub tube and left to coagulate at room temperature (22°C) in order to collect serum. Subsequently, the sample was centrifuged at 3000 rpm to separate the serum.

Evaluation of the Homeostasis Model Evaluation (HOMA-IR)

In this study, the most widespread method for valuing Insulin Resistance (IR) was applied, which was the calculation of Homeostasis Model Assessment (HOMA). The equation below shows that this account used glucose (mg/dL) and insulin (U/mL). Insulin resistance is a crucial area of investigation due to its impact on the regulation of various metabolic processes.[23]

$$\text{HOMA-IR} = [\text{glucose (mg\dL)} \times (\mu\text{U/mL})] / 405$$

Valuation of the traditional risk factors oxidative stress in groups under study to assess the risk of ACS

The molar ratio of the logarithm of triglyceride to high-density lipoprotein was applied to compute the Atherogenic Index of Plasma (AIP).[24] The TC/HDL-C, and LDL-C/HDL-C concentration ratios were calculated.[24] The amounts of Malondialdehyde (MDA) and Nitric Oxides (NO) were measured using an Enzyme-Linked Immunosorbent Assay (ELISA) plate reader.

Clinical Laboratory Analysis of Groups

The cardiac myosin binding protein C3 (cMYBP-C3) kit (My BioSource, USA) and insulin kit (My BioSource, USA) were measured using an ELISA plate reader. An automated chemical analyzer (COBSe 411, Germany) was used to evaluate the lipid profile and fasting serum glucose testing. Additionally, the determination of HbA_{1c} was performed using the HPLC method.[25]

Statistical Analysis

Statistical analysis for the current study was done using SPSS version 25. The mean and standard error of the numerical variables with normally distributed data were calculated, and the frequency and percentage of the categorical variables were calculated. The study utilized independent t-tests and ANOVA tests to examine potential significant differences between the numerical variables. A significance level of 0.05 was employed for this analysis. The t-test and Pearson correlation were used to determine the significance of the correlation between the two quantitative variables. Using a Receiver Operating Characteristic (ROC) curve technique, the value of cMYBP-C3 as a disease screening or diagnostic marker was assessed.

RESULTS

Anthropometries and biochemical markers in healthy individuals and T2DM patient groups

The age distribution of T2DM patients (54.57 ± 1.35) and healthy people (50.05 ± 2.10) is displayed in Table 1, with a *p*-value of 0.06 for each group. Additionally, there was a statistically significant increase ($p<0.05$) in the mean of Hip Circumference (93.64 ± 3.54) of patients when compared to the healthy group (55.47 ± 2.91). Also, the metabolic risk factor (FSG, Insulin, HOMA-IR, HbA1C) shows a statistically significant increase ($p<0.05$) in the mean of patients (217.06 ±10.57), (311.51 ±19.61), (3.23 ±0.24) (10.61± 2.40) and that of healthy subjects (110.17 ±2.48), (55.84 ±7.53), (0.309.47 ±0.04), (5.42 ±0.07) respectively. The lipid profile (TC, Triglyceride, VLDL, and LDL) demonstrated significant increase between patients and control group (191.02 ± 7.55), (198.67 ±15.37), (86.32 ±11.16), (100.56 ± 6.01), (164.50 ± 4.15) (105.25 ± 4.27), (21.35 ± 0.80), (96.57 ± 4.07) respectively. Similarly, the mean MDA appearance showed a statistically significant increase in patients (150.62 ± 6.47) compared to healthy subjects (74.08 ±2.48). Conversely, the presence of NO showed a statistically significant decrease in the average of patients (137.96 ± 10.66) compared to healthy subjects (176.85 ±3.05). The mean AIP and TC/HDL levels of patients with T2DM show a notable increase (0.548 ±0.02), (4.02 ±0.16) when compared to the healthy group (0.35 ± 0.02), (3.63 ±0.12) respectively. Conversely, no statistically significant difference ($p>0.05$) was observed in the mean of Waist, BMI, Troponin-I of T2DM patients (41.69 ± 2.12), (30.21 ±0.99), (1.52 ±0.08), when compared to healthy subjects (39.35 ±1.92), (28.85 ±0.91), (1.78 ±0.07) respectively.

Table 1: Characteristics of study subjects in patients and control groups.

Variables	Patients (80) Mean ±SE	Control (40) Mean ±SE	*p*-value
Age (year)	54.57 ±1.35	50.05 ±2.10	0.0637 NS
Hip Circumference/Cm	93.64 ±3.54	55.47 ±2.91	0.0001 **
FSG (mg/dL)	217.06 ±10.57	110.17 ±2.48	0.0001 **
Insulin (Pg/mL)	311.51 ±19.61	55.84 ±7.53	0.0001 **
HOMA-IR	3.23 ±0.24	0.309 ±0.04	0.0001 **
HbA1C (%)	10.61 ±2.40	5.42 ±0.07	0.0001 **
Cholesterol (mg/dL)	191.02 ± 7.55	164.50 ±4.15	0.0001 **
Triglyceride (mg/dL)	198.67 ±15.37	105.25 ±4.27	0.0001 **
VLDL (mg/dL)	86.32 ±11.16	21.35 ±0.80	0.0001 **
LDL (mg/dL)	100.56 ± 6.01	96.57 ±4.07	0.0001 **
HDL (mg/dL)	50.18 ± 1.94	46.50 ±1.52	0.124 NS
MDA (ng/mL)	150.62 ± 6.47	74.08 ±2.48	0.0001 **
Nitric Oxide µmol/L	137.96 ±10.66	176.85 ±3.05	0.0117 *
Troponin-I (pg/mL)	1.52 ±0.08	1.78 ±0.07	0.7 NS
AIP	0.548 ±0.02	0.352 ±0.02	0.0001 **
TC/HDL	4.02 ±0.16	3.63 ±0.12	0.01*
LDL/HDL	2.18 ±0.13	2.12 ±0.09	0.753 NS
Waist/Cm	41.69 ±2.12	39.35 ±1.92	0.476 NS
BMI (kg/m^2)	30.21 ±0.99	28.85 ±0.91	0.382 NS
S.B.P (mmHg)	13.08 ±0.20	12.62 ±0.12	0.133 NS
D.B.P (mmHg)	8.67 ±0.14	7.85 ±0.14	0.0004 **
Smoking (No, %)	Yes: 9 (11.39%) No: 70 (88.61%)	Yes: 0 (0.00%) No: 40 (100%)	0.0052 **
Disease period/Month	80.28 ±10.08	---	---
Family History (No, %)	Yes: 57 (72.15%) No: 22 (27.85%)	---	---

* ($p\leq0.05$), ** ($p\leq0.01$), NS: Non-Significant.

AI atherosclerosis index, AIP Atherogenic index of plasma, TG triglyceride, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, TC total cholesterol, BMI body mass index, FBG fasting blood glucose, HDL-C high-density lipoprotein cholesterol, VLDL-C very low-density lipoprotein cholesterol.

Table 2 displays the subgroup results: diabetic patients with good glycaemia (n=16) who have HbA_{1c} target of less than 7%, patients with inadequate glycaemia (n=24) who have HbA_{1c} target of 7-8, and patients with poorly controlled glycaemia (n=40) who have HbA_{1c} greater than 8%. No significant differences were observed in the levels of cholesterol and HDL-C among the study groups. Nevertheless, the triglyceride, LDL, VLDL, FBG, HbA_{1C} (%), and HOMA-IR levels showed a significant increase in T2DM patients across the three groups compared to the healthy group. Also, Table 2 shows the traditional risk factors in term of (AIP, TC/HDL, LDL/HDL) that increase the risk of ACS in T2DM patients. There is a predicted substantial increase (p 0.001) in AIP, TC/HDL, LDL/HDL, and MDA in T2DM groups relative to the healthy group.

There is a significant difference (p<0.01) between patients (three subgroups) and control group in oxidative stress marker (MDA and NO) as can be seen in Table 3.

Serum cMYBP-C3 in Healthy Subjects and T2DM Groups

In comparison to the healthy subject group (0.230 ±0.001 ng/mL), the serum level of cMYBP-C3 was significantly higher (3.69 ± 6.31 ng/ml) in T2DM patients (p< 0.05). As illustrated in Figure 1A, B, the level of serum cMYBP-C3 was substantially greater in patients with poor control glycaemia (T2DM) (5.27 ± 0.02 ng/mL) than in the inadequate glycaemia (2.93 ± 0.01 ng/mL) and good glycaemia patients' group (2.88 ± 0.02 ng/mL) (p< 0.05).

Multiple Regression Analysis

The multiple linear regression model was used to determine how a group of explanatory variables affected the baseline serum cMYBP-C3 level. Initially, all potential explanatory variables were included in the model. The equation for the analysis can be found in Table 4 reveals a positive connection between cMYBP-C3 and three variables: insulin, MDA, and baseline HbA_{1c}%. The estimated variability of the response variable is 89%. A statistically significant result was obtained for the resulting equation (p= 0.001).

ROC Curve Analysis T

The effectiveness of blood cMYBP-C3 level to distinguish T2DM patients from healthy people was investigated using ROC curve analysis (Table 5; Figure 2). Larger validity (high specificity and high sensitivity) was implied by the T2DM Receiver Operator Curve (ROC), which was much higher than that of the diagnostic test. The Area Under the ROC Curve (AUC) indicated a high likelihood of accurately predicting poorly controlled blood sugar levels in individuals diagnosed with T2DM, with a value of 0.963 (p=0.001).

Table 2: Characteristics of study subjects in Control and Patients with three groups.

(good glycaemia), (inadequate glycaemia), (poorly control glycaemia)						
Variables	**Control (40)**	**Patients (40) (poorly control glycaemia)**	**Patients (24) (inadequate glycaemia)**	**Patients (16) (good glycaemia)**	**LSD**	***p*-Value**
Cholesterol(mg/dL)	164.50 ±4.15	222.57 ±12.30	161.37 ±6.21	154.33 ±7.74	44.534	0.305 NS
Triglyceride (mg/dL)	105.25 ±4.27 c	225.02 ±27.07 a	176.29 ±16.88 b	164.20 ±21.57 bc	55.54	0.0001 **
HDL (mg/dL)	46.50 ±1.52	49.55 ±1.83	48.60 ±3.07	54.40 ±7.69	33.18	0.801 NS
LDL (mg/dL)	96.57 ±4.07 a	126.55 ±9.06 a	77.19 ±6.95 b	66.71 ±9.39 b	22.35	0.0138 *
VLDL (mg/dL)	21.35 ±0.80 b	46.30 ±5.08 a	37.00 ±3.62 ab	34.26 ±4.38 a	45.02	0.0002 **
FSG (mg/dL)	110.17 ±2.48 b	271.27 ±15.50 a	182.73 ±7.03 ab	126.80 ±8.69 b	59.99	0.0244 *
HbA_{1c} (%)	5.42 ±0.07 b	10.69 ±0.28 b	7.72 ±0.08 b	6.68 ±0.63 a	9.31	0.0024 **
Insulin (Pg/mL)	55.84 ±7.53 b	283.41 ±27.11 a	311.34 ±34.20 a	386.76 ±46.89 a	74.73	0.0001 **
HOMA-IR	0.309 ±0.04 b	3.87±0.42 a	2.82 ±0.29 ab	2.21 ±0.31 a	78.59	0.0053 **
AIP	0.347 ±0.02 b	0.575 ±0.04 a	0.544 ±0.04	0.468 ±0.05 a	0.118	0.0062 **
TC/HDL	3.64 ±0.12 b	4.53 ±0.20 a	3.70 ±0.33 b	3.15 ±0.22 b	0.662	0.0278 *
LDL/HDL	2.12 ±0.09 ab	2.59 ±0.18 a	1.89 ±0.26 bc	1.53 ±0.22 c	0.556	0.0002 **
Troponin-I	1.78 ±0.07	1.65 ±0.16	1.35 ± 0.06	1.42 ± 0.09	0.397	0.077 NS

Significant differences were between the means of having different letters in the same row.* p<0.05. * p<0.001 *** p<0.0001 NS: Non-Significant. a indicates significant between control and poorly control glycaemia groups.b indicates significant between control and inadequate glycaemia groups.
c indicates significant between control and good glycaemia groups.

Table 3: Oxidative Stress Marker in Control and Patients with three groups (good glycaemia), (inadequate glycaemia), (poorly control glycaemia).

Variables	Control (40)	Patients (40) (poorly control glycaemia)	Patients (24) (inadequate glycaemia)	Patients (16) (good glycaemia)	LSD	*p*-Value
MDA (ng/ml)	74.08 ±2.48 b	175.95 ± 6.86 a	152.60 ± 12.12 a	79.91 ± 3.75 ab	36.01	0.0006 **
Nitric Oxide (µmol/L)	176.85 ±3.05 a	131.22 ±14.82 b	132.60 ±17.96 b	164.66 ± 28.21 ab	43.56	0.0375 *

Significant differences were between the means of having different letters in the same row.* $p<0.05$. * $p<0.001$ *** $p<0.0001$ NS: Non-Significant.a indicates significant between control and poorly control glycaemia groups.b indicates significant between control and inadequate glycaemia groups.c indicates significant between control and good glycaemia groups.

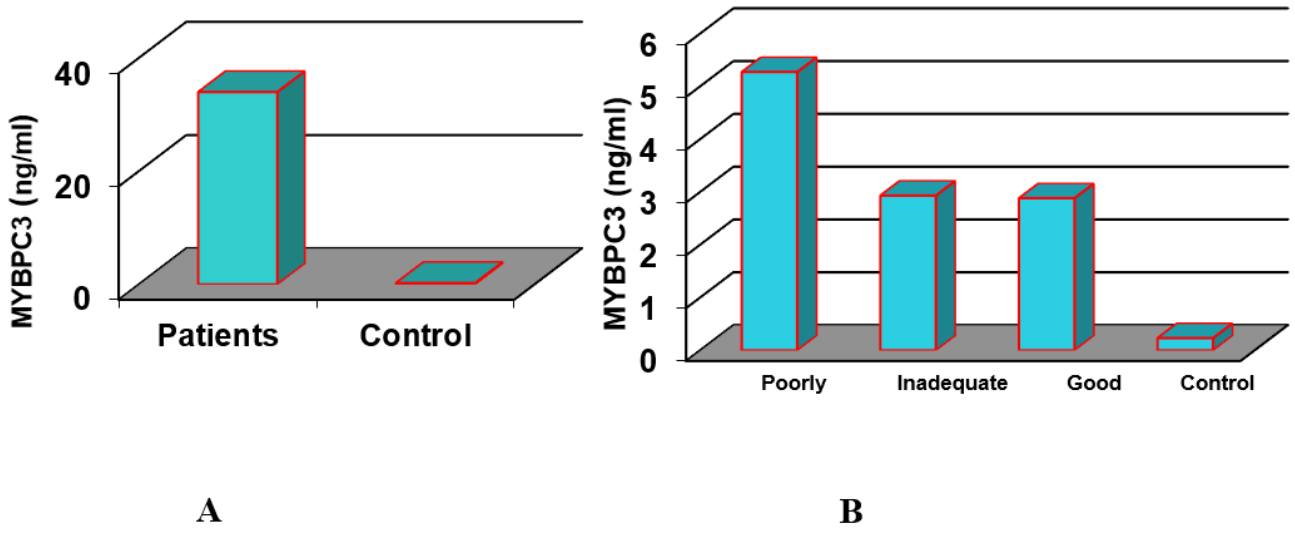

Figure 1: A Comparison of serum MYBPC3 among T2DM (*n*=80) patients and healthy subject (*n*=40). B The serum MYBPC3 among poorly glycaemia (*n*=40) inadequate glycaemia (*n*=24), and good glycaemia (16).

DISCUSSION

Myosin binding protein C, a protein associated with thick filaments, has complex regulatory functions during cardiac contraction. It controls the dynamics of sarcomere contraction, actomyosin gliding, and cross bridge kinetics by binding various thin and thick filament constituents.[26] Prior studies also described the effective role of cardiac Myosin-Binding Protein C (cMyC) as a diagnostic biomarker for Acute Myocardial Infarction (AMI). They show that cMyC has a greater dynamic range in AMI patients and matches the diagnostic performance of hs-cTn assays.[27] Moreover, variants in MYBPC3, the gene encoding cardiac myosin-binding protein C (cMyBP-C), are the leading cause of HCM. Concerning Insulin Resistance (IR), T2DM is a form of diabetes that results in both beta-cell dysfunction and IR. The first step in maintaining normal glucose levels is a compensatory increase in insulin production. As the disease progresses, beta cells undergo changes, and the secretion of insulin becomes insufficient to regulate glucose levels, resulting in hyperglycemia.[28] Previous research identified Insulin Resistance (IR) and Cardiovascular Disease (CVD) as significant public health risks. A proven causal relationship exists between IR and CVD.[29] To our knowledge, the primary complication of T2DM is Cardiovascular Disease (CVD), which is the leading cause of death in T2DM patients, especially those with comorbid ACS. We examined serum cMyBP-C3 in T2DM and compared it to the healthy group. The findings demonstrated a significant rise in cMYBP-C3 serum levels when compared to the reference control group. Moreover, we investigated the relationship between serum cMYBP-C3 levels insulin, HbA_{1c}, and MDA in individuals with T2DM. Govindan's prior research demonstrated that in a study involving patients with ACS and MI, the substantial release of cMyBP-C proved to be a valuable cardiac-specific biomarker for MI.[15] Sadayappan's research indicates that the plasma cMyBP-C level, present in both fragment and full-length peptide forms, may be a valuable clinical diagnostic tool and a more dependable and precise indicator of myocardial infarction.[30]

In addition, we investigated higher serum levels of cMYBP-C3 in patients with poorly glycaemia (4.86 ± 0.210) than patients with inadequate glycaemia (2.93 ± 0.012) and patients with good controlled glycaemia (0.230 ± 0.000) with ($p < 0.001$). It is commonly known that individuals with diabetes, have a higher risk of Cardiovascular Disease (CVD) when their HbA_{1c} levels

Table 4: Simple linear regression analysis between serum cMYBP-C3 level (µg/dl) as the dependent variable and the studied independent variables in diabetic independent variables β Standardized β *P*-value.

Independent Variables	B	β Standardized	*p*-value
FSG	0.003	0.155	0.200
INSULIN	0.002	0.188	0.002
HOMA	-0.016-	-0.018-	0.803
HBA_{1C}	0.403	0.482	0.000
TC	-0.002-	-0.045-	0.726
TG	-0.005-	-0.301-	0.092
VLDL	0.022	0.285	0.120
HDL	0.004	0.029	0.631
LDL	-0.001-	-0.025-	0.820
NO	0.010	-0.021-.	0.705
MDA	0.001	282	0.000

Table 5: An examination of the cardiac Myosin Binding Protein C3 (cMYBP-C3) in the studied groups using a Receiver Operator Curve (ROC).

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
0.963	0.021	0.000	Lower Bound	Upper Bound
			0.922	1.000

The test result variable(s): Serum cMYBP-C3 has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.a. Under the nonparametric assumption.b. Null hypothesis: true area = 0.5.

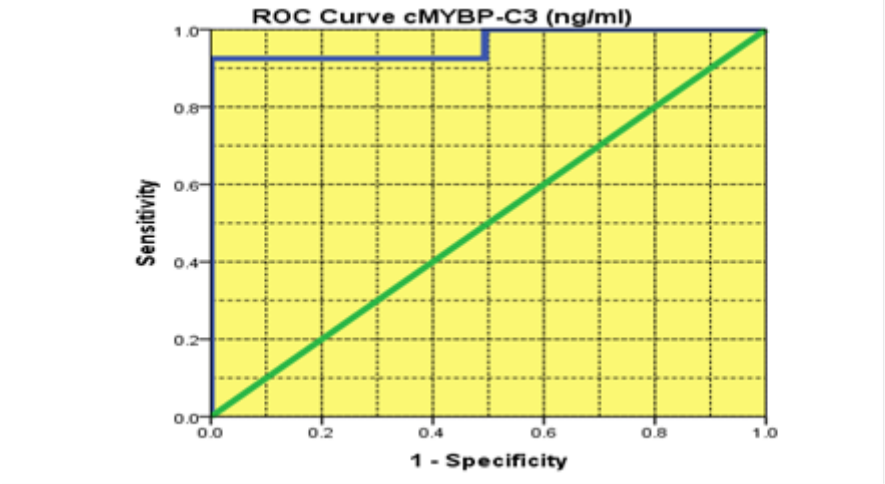

Figure 2: ROC curve analysis of serum cMYBP-C3 concentrations in continuing T2DM patients (*n*=80) against healthy participants (*n*=40)

are elevated.[31] Consequently, Patients with poorly controlled blood glucose levels who have higher levels of cMYBP-C3 are at a significantly higher risk of developing heart disease.

The multiple regression model suggests a connection between cMYBP-C3 and insulin, HBA_{1C}, and MDA. These findings point to a correlation between serum cMYBP-C3 levels and T2DM and ACS. Furthermore, receiver operator curve analysis for serum cMYBP-C3 showed an AUC value of 0.963. The atherogenic index of plasma is a strong predictor of atherosclerosis and coronary heart disease, and it effectively illustrates the association between protective and atherogenic lipoproteins.[32] Also, AIP was linked to a higher frequency of Major Adverse Cardiovascular Events (MACEs) among patients with type 2 diabetes and high CVD risk, according to a secondary analysis of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) research.[33] Previse research proved that obesity, hypertension, diabetes mellitus, insulin resistance, and metabolic syndrome were all strongly associated with AIP.[34,35] Also, it has been proposed that AIP serves as a valid predictor of atherosclerosis and related cardiovascular problems. In comparison to the CAD group, Cai *et al.* found a statistically significant reduction in the Atherogenic Index of Plasma (AIP) in the control group.[36] In this study, we examined

the statistically significant difference ($p < 0.001$) in AIP levels between subgroups of patients and healthy individuals.

Hyperglycemia in Type 2 Diabetes Mellitus can cause individuals to experience oxidative stress conditions, accompanied by a decrease in antioxidant activity in protecting cellular components against the attack of Reactive Oxygen Species (ROS). Reactive oxygen species oxidized lipid components can produce Malondialdehyde (MDA). Evaluation of MDA can be used as a marker Oxidative stress which can indirectly describe the effects of ROS because ROS compounds are reactive.[37] In comparison to the control group, the MDA level increased significantly ($p < 0.001$) in patients' group. Kumawat *et al.*[38] discovered considerably higher ($p< 0.001$) levels of MDA in T2DM patients compared with the healthy group, which may corroborate this study's finding. Therefore, it can be concluded that the metabolic regulation of diabetes determines the degree of oxidative stress and the development of problems in T2DM. Mishra's study revealed a substantial positive correlation between MDA, FPG, and HbA_{1c}, indicating that hyperglycemia plays a contributing role in glucose autoxidation, free radical production, creation of hazardous ROS, and genesis of oxidative stress. Shalash reported that Malondialdehyde is a non-invasive biomarker that can be used to distinguish T2DM cases from healthy controls and to identify diabetic patients who are at high risk of developing Cardiovascular Disease (CVD).[39]

Our report highlights several favorable aspects. Initially, we matched the three groups based on age. Subsequently, it is well-established that elevated glycaemia is a significant factor contributing to diabetes complications. In our study, we included patients with both well-controlled and poorly-controlled glycaemia. This phenomenon may be attributed to the secretion of serum cMYBP-C3 at various diabetes stages, with a notable correlation observed in patients with poorly-controlled glycaemia. Lastly, individuals with T2DM are not afflicted by cardiovascular diseases. This study has a limitation. To gain a deeper understanding of the role of cMYBP-C3 and its potential as a diagnostic or therapeutic target, researchers should thoroughly analyze cMYBP-C3 levels from the time of diagnosis until the continuation of T2DM treatment.

CONCLUSION

In conclusion, our research indicates a strong association between serum cMYBP-C3 levels and poor glycemic control in patients. This suggests that serum cMYBP-C3 may be a valuable biomarker for distinguishing diabetic patients from healthy individuals. The multiple regression model and receiver operator curve analysis were obtained to prove the important role of cMYBP-C3 as a novel risk factor for ACS in people with type 2 diabetes.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethics Committee of the Baquba Teaching Hospital and the National Center for Training and Human Development of the Iraqi Ministry of Health. Prior to their inclusion in the study, all participants provided informed written consent, and the research was carried out in accordance with the Helsinki Declaration.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

T2DM: Type 2 diabetes mellitus; **CVD:** Cardiovascular Disease; **ACS:** Acute coronary syndromes; **cMYBP-C3:** Cardiac Myosin binding protein C3; **HbA_{1c}:** Hemoglobin A1c; **MDA:** Malondialdehyde; **NO:** Nitric oxide; **TC:** Total Cholesterol; **TG:** Triglycerides; **HDL:** High-density lipoprotein; **LDL:** Low-density lipoprotein; **VLDL:** Very Low-density lipoprotein; **FBS:** Fasting Blood Sugar; **AIP:** Atherogenic Index of Plasma; **ELISA:** Enzyme-Linked Immunosorbent Assay.

SUMMARY

Cardiovascular disease is the main consequence of T2DM. For patient with T2DM, CVD is the primary cause of death, especially when combined with concomitant ACS. In the present study, we have shown that cMyBP-C3 deteriorating heart function in T2DM patients. Furthermore, substantial association between cMyBP-C3 levels and poorly regulated glycemia was confirmed.

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