RESEARCH ARTICLE

Relation between Acetyl-CoA Carboxylase with some Biochemical Variables in Iraqi Men with Acute Myocardial Infarction and Diabetes

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ABSTRACT

Background: Acute myocardial infarction (AMI) is a widespread cause of death in numerous parts of the world. Many factors raise the risk of myocardial infarction (MI). One of the most of it is atherosclerosis, caused by many factors such as Hyperlipidemia. Acetyl-CoA carboxylase (ACC) is the key regulatory enzyme in fatty acid synthesis. The disorder of lipid metabolism is one of the characteristics of diabetes, which is considered a risk factor for MI. Therefore, the activity ACC was estimated in patients with AMI and Diabetes.

Method: The study included estimation of ACC activity and correlated with other biochemical variables such as Troponin T(cTnT), C-reactive protein (CRP), glucose, lipid profile, electrolytes [Sodium (Na^+), Potassium(K^+), Chloride (Cl^-)], urea and creatinine (Crea.), and evaluation of body mass index (BMI) effect in serum of 60 patients with AMI and diabetes compared with 30 serum from apparently healthy individuals as a control group, both groups are of males with an average age (25–60 years).

Results and Conclusions: Results showed a significant increase in levels of ACC, cTnT, CRP, Glucose, and Lipid profile except for high-density lipoprotein – cholesterol (HDL-C) and urea, while a significant decrease with $Na^+$and K^+ also a non-significant variation was observed with Cl^- and creatinine in AMI and diabetes patients compared to control group.

Keywords: Acute myocardial infarction, Acetyl CoA carboxylase, Troponin T, Diabetes.

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INTRODUCTION

World Health Organization (WHO) assessments the yearly death from cardiovascular diseases (CVD) to be 17.9 million worldwide.[1] AMI is an acute kind of CVD. It is also the main reason for physical inability and death.[2] Hypertension, smoking, lifestyle, and diabetes among risk factors of MI.[3] Type 2 diabetes mellitus (T2DM) is related to a two-to four-fold raised risk of CVD.[4] Acetyl CoA carboxylase (ACC EC 6.4.1.2) is a key regulatory enzyme in the pathway of synthesis of free fatty acids (FFA). ACC stimulates the first step in the pathway of synthesis of long-chain free fatty acids. ACC contains biotin (Biotin), which stimulates the process of adding carboxyl radical to acetyl CoA(ACA) to produce Malonyl CoA (MCA), which is the basis for the synthesis of fatty acid (FA).[5,6] MAC is a strong inhibitor of Palmitoyltranseferasel (CPT1), which is a regulatory enzyme for fatty acid oxidation (FAO).[6] ACC has two isoenzymes that have been defined depending on the peculiar cellular distribution and physiological role, adipose tissues and liver cytosolic ACC1 (265KD) and ACC2 (280KD)) is a mitochondrial isoenzyme found in the heart and skeletal muscle.[7] Cardiac MAC levels increase in response to the stimulating conditions with the duration of glucose and insulin.[8] Studies have been conducted on ACC and MCA inhibition to reduce FA synthesis within the body and thus control on obesity, diabetes and heart disease,[9,10] beside other cardiac physiological markers such as myocardial necrosis marker cTnT,[11] inflammation CRP marker associated with the amplitude of cardiac injury in the acute stage of MI[12] finally the changes of Electrolytes like Na^+ and K^+ levels play an important role in increasing cardiovascular morbidity and mortality.[13]

MATERIALS AND METHODS

This study included 30 serum samples from apparently healthy males as a control group and 60 serums from a patient with AMI and T2DM males; both groups ranged from 25 to 60 years old. All samples were collected from Sulaymaniyah

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Cardiac Hospital in Sulaymaniyah city. Samples of smokers, alcoholics, and patients with other diseases that interfere were excluded. ACC activity and cTnT levels were estimated by using ELISA kits ready (HCUSABIO, America). Other biochemical parameters were measured by diagnostics kits (French company BIOLABO).

Statistical Analysis

Data were statistically analyzed using the statistical program (SPSS Version 24). The ANOVA test was used to analyze the variance between two groups at the probability levels $p \leq 0.01$ and $p \leq 0.05$. Duncan's polynomial test and the linear correlation coefficient (r) were calculated to find the correlation between ACC and other biochemical variables.

RESULTS AND DISCUSSION

The effect of age and BMI patients group compared with the control was shown in Table 1.

The results in Table 2 showed a significant increase at $p \leq 0.01$ in the activity of ACC in AMI-T2DM patients (25.04 ± 9.76 ng/mL) compared with control (6.12 ± 2.36 ng/mL), There are no previous studies that have evaluated the activity of ACC in patients with AMI-T2DM. However, many studies have been conducted to find out the role of the ACC in several diseases.[14-16] A study demonstrated that reduction of cardiac ACC2 led to a significant decrease in cardiac MCA, which is considered as a substrate for the synthesis of FA.[17] Inhibiting MCA production activates carnitine Palmitoyltranseferase 1CPT-1. It is a significant enzyme of fatty acids oxidation(FAO), thus increasing FAO.[18] Reducing ACC2 activity prevents intramyocellular lipid accumulation caused by high dietary lipids and insulin, which is improved by ACC2 inhibition,[19] that provided further evidence for the role of ACC2 as a potential target for T2DM treatments.[19,20]

The results showed a significant increase in cTnT level at $p \leq 0.01$ in AMI-T2DM patients (12.40 ± 2.2ng/mL) compared with in control (0.12 ± 0.059 ng/mL). These results agree with other studies.[21] cTnT levels increase due to cardiomyocyte necrosis after MI, occurs.[22]

The present results of this study showed a significant increase in CRP at $p \leq 0.01$ in serum of patients with AMI - T2DM (72.7± 27.5 mg/dL) compared with control (3.28 ± 1.67 mg/dL). This result was in agreement with Athab *et al*.[23] and Carrero *et al*.[24] Both Myocardial ischemia and diabetes causes a well-harmonious inflammatory response as recruitment of neutrophils and monocytes to the retaining myocardium and induction of healing,[25,26] also serum glucose level showed a significant increase at $p \leq 0.01$ in AMI-T2DM patients (209.21 ± 77.20 mg/dL) compared with control (107.20 ± 37.94 mg/dL), these results are in agreement with a previous study,[27] increase blood sugar causes cardiovascular dysfunction,[28] lack of blood flow and loss of ischemic ischemia[29] which leads to a decline in the performance of the myocardium.[30]

As it is known lipids have an impotent effect in vascular diseases, the results of the present study showed a significant increase at $p \leq 0.01$ in the total Chol., TG, LDL-C and VLDL-C in AMI-T2DM patients group (291 ± 99.5 mg/dL), (230.8 ± 98mg/dL), (182.9 ± 39.31mg/dL) and (43.20 ± 9.73 mg/dL) r espectively compared with (145 ± 16.1mg/dL), (120.8 ± 21.21 mg/dL), (90.7 ± 25.12 mg/dL) and (25.35 ± 4.84 mg/dL) respectively, while a significant decrease in HDL –C in patients group (22.68 ± 6.66 mg/dL) compared with control (38.77 ± 6.28 mg/dL). These results are in agreement with previous studies.[31,32] This could be explained by that the elevated levels of Chol. It can be attributed to the breakdown of LDL or the lack of efficiency of LDL-specific protein fraction receptors in tissues, as well as to the decreased activity of Acetyl cholesterol transferase the responsible enzyme for Chol. absorption.[33] Chol content of TG-rich lipoproteins is more probable to be the cause of atherosclerosis and CVD rather than raised TG in itself.[34] Lipoprotein-lipase (LPL) action at the surface of remnants, either within the intima or at the vascular endothelium, leads to emancipation, monoacylglycerols, free fatty acids, and other molecules, each of which could cause domestic injury and inflammation.[35] Regarding a decrease in the level of serum HDL-C, it can be attributed to the increase in TG and Chol. in the body, where an increase in these variables reduces

Table 1: Standard deviation of age and BMI in patients compared with control

	Control	*Patients*	
Variables	*Mean ± SD N = 30*	*Mean ± SD N = 60*	*p-value*
Age (years)	39 ± 8.94	47 ± 9.41	≤ 0.01
BMI	24.291 ± 1.498	29.39 ± 5.612	≤ 0.01

Table 2: The Mean ± SD of studied variables in patients compared with control

	Control	*Patients*	
Parameter	*Mean ± SD N = 30*	*Mean ± SD N = 60*	*p-value*
ACC(ng/mL)	6.12 ± 2.36	25.04 ± 9.76	≤ 0.01
cTnT(ng/mL)	0.12 ± 0.059	12.40 ± 2.2	≤ 0.01
CRP (mg/dL)	2.22 ± 1.32	72.7± 27.5	≤ 0.01
Glu (mg/dL)	107.20 ± 37.94	209.21 ± 77.20	≤ 0.01
Chol (mg/dL)	145 ± 16.1	291 ± 99.5	≤ 0.01
TG (mg/dL)	120.8 ± 21.21	230.8 ± 98	≤ 0.01
HDL-C (mg/dL)	38.77 ± 6.28	22.68 ± 6.66	≤ 0.01
LDL-C (mg/dL)	90.7 ± 25.12	182.9 ± 39.31	≤ 0.01
VLDL-C(mg/dL)	25.35 ± 4.84	43.20 ± 9.73	≤ 0.01
Na^+ (mmol/L)	139.94±5.27	130.64 ± 3.63	≤0.05
K^+ (mmol/L)	4.188 ± 0.68	3.08 ± 0.53	≤0.05
Cl^-(mmol/L)	96.72 ± 4.39	97.47± 2.11	NS
Urea (mg/dL)	33.4 ± 4.94	51.58 ± 7.22	≤0.05
Crea (mg/dL)	0.89 ± 0.31	1.29 ± 0.45	NS

*ACC: Acetyl Co A Carboxylase; cTnT: Troponin T; CRP: C-reactive protein; Glu: Glucose; Chol: Cholesterol; TG: Triglyceride; HDL-C: High-Density Lipoprotein- Cholesterol; LDL-C: Low-Density Lipoprotein-Cholesterol; VLDL-C: Very Low -Density Lipoprotein- Cholesterol; Na: sodium ion; K^+: Potassium ion; Cl^-: Chloride ion; Crea: Creatinine; NS: Non-Significant.

the efficiency of HDL-C in transporting Chol. from tissues to liver.[34] Decreased levels of serum HDL-C are associated with the risk of CVD, and elevated levels are a protective factor against CVD.[36] HDL-C molecules is believed to be anti-atherosclerotic, anti-inflammatory, antithrombotic, and antioxidant.[37] also, increasing Chol leads to decrease in the efficiency of LDL in transporting Chol from the liver to tissues inhibition of LDL receptors this leads to the accumulation of LDL particles in a high concentration in blood, synthesis of certain lipoprotein and high level of glucose and nonessential fatty acids might affect the regulation of the excretion of VLDL-C from the liver.[38] Diabetes also has a role in abnormal levels of lipids and lipoproteins.[39]

Electrolyte imbalance in CVD has been well studied. Table 2 showed a significant decrease at $p \leq 0.05$ in serum Na^+ and k^+ levels in AMI-T2DM patients (130.64 ± 3.63mmol/L) and (3.08 ± 0.53 mmol/L), respectively compared with control (139.94 ± 5.27 mmol/L) and (4.188 ± 0.68mmol/L) respectively, this result was an agreement with others studies.[40,41] Hypoxia and ischemia raise the cell of muscular sheath (sarcolemma) permeability of Na^+ [42] for individuals with MI have a rising rate of water retention, which leads to a decrease in sodium pressure of blood and hypo tonicity[43] and the decrease in serum k+ levels might be attributed to the sympathetic nervous system activation leading to an outflow of k+ from the extracellular to the intracellular fluid of body closets.[44,45] Non-significant changes at $p \leq 0.05$ in Cl^- levels in serum of AMI-T2DM patients (97.47± 2.11 mmol/L) compared with control (96.72 ± 4.39 mmol/L).

A common feature for imbalance in urea and crea. CVD patients as a result of a decrease in glomerular filtration rate (GFR).The results in Table 2 showed at $p \leq 0.05$ a significant increase in urea level (51.58 ± 7.22 mg/dL) in the patient's group compared with the control (33.4 ± 4.94 mg/dL). These changes might be due to the depressed output of the cardiac state of ventricular dysfunction.

Table 3: Correlation between ACC activity with other biochemical parameters

Parameters \ *ACC*	*r*
cTnT	-0.08
CRP	-0.075
Glu	0.584
Chol	-0.031
TG	0.76
HDL-C	-0.058
LDL-C	0.109
VLDL-C	0.024
Na+	-0.144
K+	0.024
Cl^-	-0.200
Urea	-0.227
Crea	0.062

Table 3 showed positive correlation between ACC and Glucose, TG, LDL-C, VLDL-C, and k+ and Crea. negative correlation with cTnT, CRP, Chol, Na+ , Cl^- and Urea. There is no previous study deals with the correlation between ACC and the variables in this study

CONCLUSION

The results showed a significant increase in ACC, cTnT, CRP, Glu, Urea, and Lipid profile except for HDL-C, while a significant decrease with Na^+ and K^+ at $p \leq 0.01$, $p \leq 0.05$, and non-significant variations was observed within Cl^- and Crea in sera of AMI -T2DM patients compared with control.

RECOMMENDATIONS

This study was conducted to find the correlation between ACC activity with other biochemical parameters in patients with AMI and Diabetes; more studies are needed to evaluate the relation of this enzyme with genders hormones in both men and women and to highlight the role of these associations in clinical diagnosis.

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