Original Article

Correlation of Coenzyme Q10 with MDA in Iraqi Patients with Myocardial Infarction

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Abstract

Background: Myocardial infarction (MI) is the leading cause of morbidity and mortality in the worldwide. A high level of oxidative stress is linked to myocardial infraction, which results in induced damage by free radicals, lipid peroxidation, and deficient energy production. Coenzyme Q10 is essential for the ATP production process. It is therefore necessary for all energy-dependent mechanisms in cardiac cells, which are highly sensitive to CoQ10 insufficiency caused by cardiovascular events. With CoQ10 enhancing cellular bioenergetics as well as its antioxidant activity, it may play a role in the prevention and treatment of heart diseases. In this study, we measured serum levels of enzymatic markers of tissue damage including High-Sensitivity Cardiac Troponin (hs-cTnT) and Creatine Kinase MB (CPK-MB) and the markers of oxidative stress including Coenzyme Q10 (CoQ10) and Malondialdehyde (MDA).in addition to lipid profile in 50 patients with MI and 45 control subjects. We also studied correlations between CoQ10 with the above biomarkers. This study found that serum CoQ10 levels (nmol/L) were lower in MI patients than in control group (10.38 vs 77.33). The levels of MDA (ng/mL) were significantly higher in MI patients than in control group (1847 vs 398.3). There was a significant increase in serum levels of hs-cTnT (pg/mL) and CPK-MB(IU/L) in MI patients than in control group (1406 vs 3.143) (107.9 vs 11.46). Serum MDA levels significantly increased in patients with MI in comparison to healthy subjects and the coenzyme Q10 levels were significantly decreased in patients with MI than in controls.

Keywords: Myocardial Infarction, Oxidative Stress, Coenzyme Q10, Malondialdehyde, Heart Diseases.

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INTRODUCTION

Myocardial infarction (MI) is described as the occurrence of myocardial cell necrosis as a result of substantial and sustained ischemia (Mendes et al, 2011). It is also termed a heart attack due to the sudden blockage of blood flow in the coronary arteries. It is distinguished by chest pains or discomfort that may spread to the shoulder, arm, back, neck, or jaw (Khadse, Wankhda & Gaiki, 2020). Oxidative stress is a condition that results from an imbalance in the production and elimination of reactive oxygen species (ROS), which causes cellular damage (Wassmann, Wassmann & Nickenig, 2004).Coenzyme Q10 (CoQ10) is a lipid soluble ubiquinone that is present in large concentrations in the mitochondria of the heart and other tissues, where it plays a critical role in cellular respiration (Martelli et al, 2020).CoQ10 is an important antioxidant that inhibits lipid peroxidation in cell membranes. In addition to its anti-oxidative activity, it also functions as an electron carrier in the mitochondrial electron transport chain, transporting electrons from complex I or II to complex III (Pastor-Maldonado et al, 2020).

Due to the greater metabolic requirements of cardiac myocytes, coenzyme Q10 is essential for myocardial bioenergetics. As a result, the level of CoQ10 in heart tissue declines, especially in patients with cardiovascular disease (CVD) and in conditions of severe oxidative stress (Sue-Ling, Abel & Sue-Ling, 2022). Reduced CoQ10 levels have been associated with a higher risk of mortality in chronic heart failure, according to a study. COQ10 deficiency was found to be related to disease severity. As a result, CoQ10 deficiency may be a major pathological mechanism linked to higher risks in this situation. (Molyneux et al, 2008).

Lipid peroxidation is the mechanism that occurs when oxygen interacts with lipids to produce lipid hydroperoxides. It is considered to be the main process of cell membrane damage and deterioration (Conrad et al, 2018). Malondialdehyde (MDA), a breakdown product produced by lipid peroxidation, has been considered as a biomarker of oxidative stress. It has been widely utilized in clinical studies and assessments of oxidative stress (Cui et al, 2018).

The main goal of this study was to determine the serum levels of CoQ10 and MDA in Iraqi MI patients and controls

and to explore the relationship between CoQ10 with MDA and some parameters that help in diagnosing myocardial infraction.

Material And Research Methods

Material

This study involved fifty patients with MI, admitted to Al-Ramadi Teaching Hospital (Al-Anbar Governorate) during the period from November 2021 to April 2022. age range of 41-68 years. The patients were diagnosed to have myocardial infarction based on positive troponin tests in addition to ECG findings and clinical symptoms of myocardial infarction. Our control group consisted Forty healthy controls had the same gender and age as the patient groups and consisted of chosen individuals without ischemic heart disease who also had no history of smoking or drinking alcohol.

A venous blood sample was collected from all the subjects; the samples were centrifuged for 5 minutes at 4000 rpm. Separated into various parts using Eppendorf tubes, and stored at -20 °C until biochemical analysis. The following parameters were measured using commercial kits from Roche, Switzerland: hs-cTnT, CPK-MB, total cholesterol (T.C), HDL, LDL and TG. while serum levels of coenzyme Q10 and MDA determined by using an enzyme linked immunosorbent assay (ELISA) kit (Melsin China) for CoQ10 and (ELISA) kit (elabscience) for MDA.

Statistics

We examined our data using GraphPad Prism 7. The values of the mean, standard error of the mean (SEM), and standard deviation (SD) were used to present the data. A students' t-test was used to evaluate how different means differed from one another. Bivariate associations were examined using Pearson correlation coefficients. The area under the ROC curve was used to assess the investigation's accuracy. At P 0.05, the significance level was established.

Result

Table 1 shows the standard experimental characteristics of the subjects, had serum CoQ10 levels (nmol/L) were lower in MI patients than in control group (10.38 vs 77.33) with p-value less than 0.0001 as shown in figure 1. while the serum levels of MDA (ng/mL) were significantly higher in MI patients than in control group (1847 vs 398.3) as shown in figure 2.

Table 1. Clinical and Biochemical Parameters of MI patients and controls.

	Healthy controls			MI patients			
Parameter	**Mean**	**SD**	**SEM**	**Mean**	**SD**	**SEM**	**p-value**
CoQ10 nmol/L	77.33	18.11	2.864	10.38	4.411	0.6239	<0.0001
MDA ng/mL	398.3	165.4	26.15	1847	348.2	49.24	<0.0001
hs-cTnT pg/mL	3.143	0.8289	0.1311	1406	472.5	66.82	<0.0001
CPK-MB IU/L	11.46	3.24	0.5123	107.9	45.82	6.48	<0.0001
T. Cho. mg/dL	168.2	32.13	5.08	173.3	34.76	4.916	0.4747
TG mg/dL	117.1	35.55	5.621	144.4	60.2	8.514	0.0129
HDL mg/dL	44.33	7.116	1.125	38.36	7.116	1.006	0.0002
LDL mg/dL	100.9	26.45	4.183	103	27.71	3.918	0.7105
VLDL mg/dL	23.4	7.14	1.129	28.88	12.04	1.703	0.0128
LDL/HDL	2.313	0.6711	0.1061	2.777	0.9036	0.1278	0.0083
T. Cho./HDL	3.847	0.7956	0.1258	4.657	1.209	0.171	0.0004

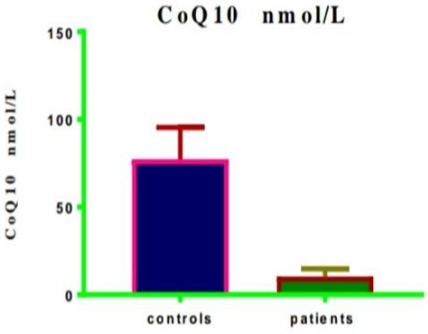

Figure 1. Mean+S.D. for CoQ10 in control and patients

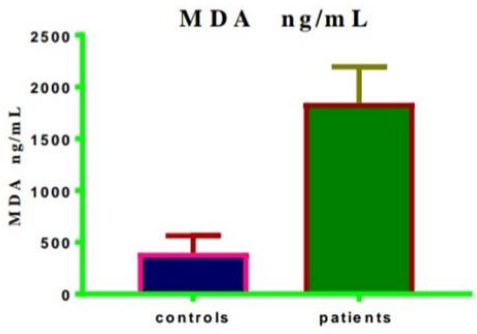

Figure 2. Mean+S.D. for MDA in control and patients

Also Results of this study showed a significant increase ($p < 0.05$) in serum levels of hs-cTnT (pg/mL) and CPK-MB(IU/L) in MI patients than in control group (1406 vs 3.143) (107.9 vs 11.46) respectively, as shown in figure (3,4).

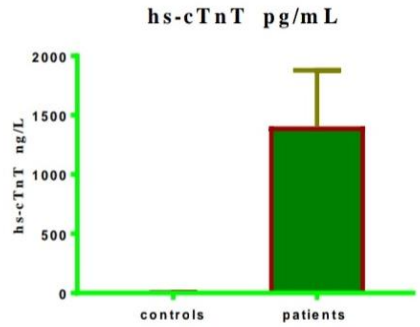

Figure 3. Mean+S.D. for hs-cTnT in control and patients

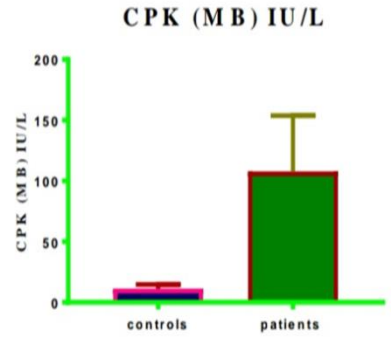

Figure 4. Mean+S.D. for CPK in control and patients

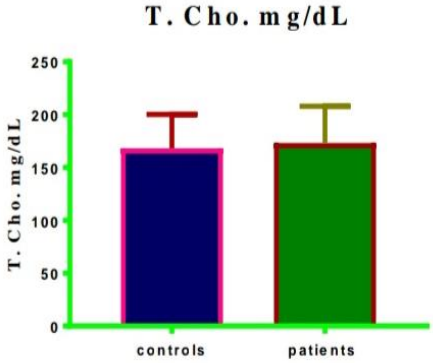

Figure 5. Mean+S.D. for T.Cho. in control and patients

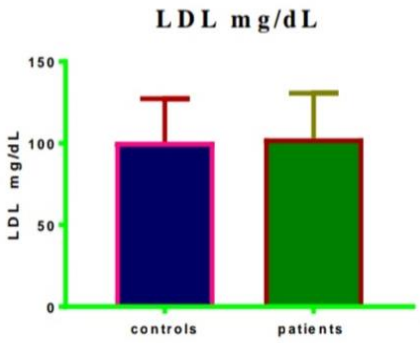

Figure 6. Mean+S.D. for LDL in control and patients

It was observed that the levels of TG significantly ($p < 0.05$) increased in patients group than the control (144.4 vs 117.1) mg/dL, figure 7. Also there is a significant increase in VLDL level in patients group compared with control (28.88 vs 23.4) figure 8. HDL levels were significantly decreased in patients group than control (38.36 vs 44.33) mg/dL figure 9. The results of this study also showed that there was a significant difference ($p< 0.05$) in the levels of T. Cho. /HDL and LDL/HDL (4.657vs 3.847) (2.777vs 2.313) respectively, in the patient group compared to the control, figures (10,11).

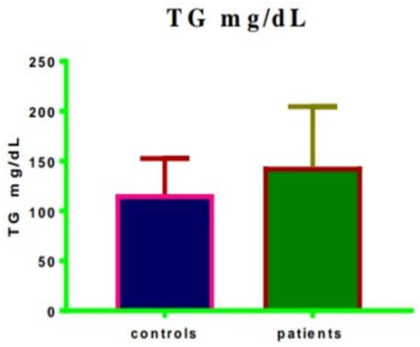

Figure 7. Mean+S.D. for TG in control and patients

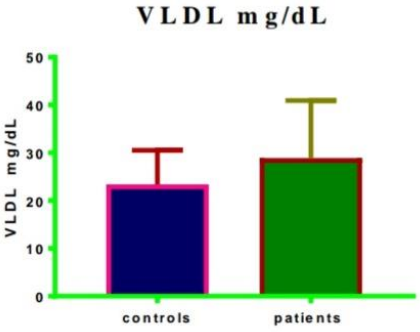

Figure 8. Mean+S.D. for VLDL in control and patients

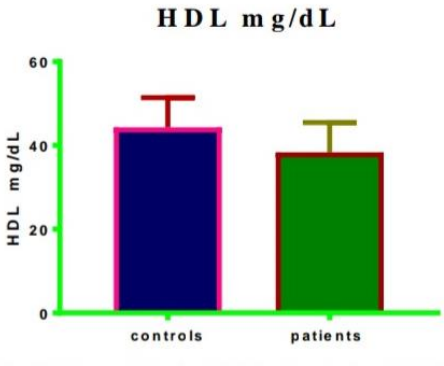

Figure 9. Mean+S.D. for HDL in control and patients

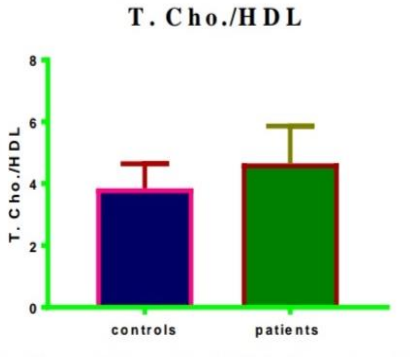

Figure 10. Mean+S.D. for T.Cho.\HDL in control and patients

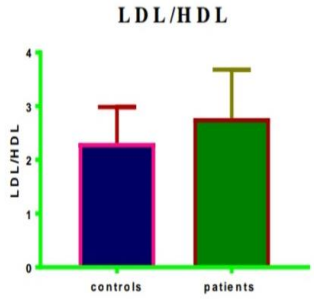

Figure 11. Mean+S.D. for LDL\HDL in control and patients

In this study, the correlations of CoQ10 and other variables are investigated and the results obtained are given in table 2.

Table 2. Correlation of COQ10 with other Variables in Study.

Parameter	r (CoQ10 nmol/L)	p-value
MDA ng/mL	-0.871	<0.0001
hs-cTnT pg/mL	-0.843	<0.0001
CPK-MB IU/L	-0.771	<0.0001
T. Cho. mg/dL	-0.158	0.137
TG mg/dL	-0.268	0.011
HDL mg/dL	0.324	0.002
LDL mg/dL	-0.138	0.194
VLDL mg/mL	-0.269	0.011
LDL/HDL	-0.319	0.002
T. Cho. /HDL	-0.376	<0.0001

The results of this study shown non-significant correlations between COQ10 with T. Cholesterol, TG, LDL and VLDL. While Significant negative correlations were detected of COQ10 with MDA, hs-cTnT and CPK-MB (r= -0.871, p <0.0001) (r= -0.843, p <0.0001) (r= -0.771 p <0.0001) respectively, as shown in(Table2) and (figures 12-14) while a positive correlation of COQ10 with HDL (r= 0.324 p 0.002) was detected. also, as shown in (Table2) there was negative correlations of COQ10 with LDL/HDL and T. Cho. /HDL (r=-0.319 at p 0.002) (r= -0.376 at p <0.0001) respectively.

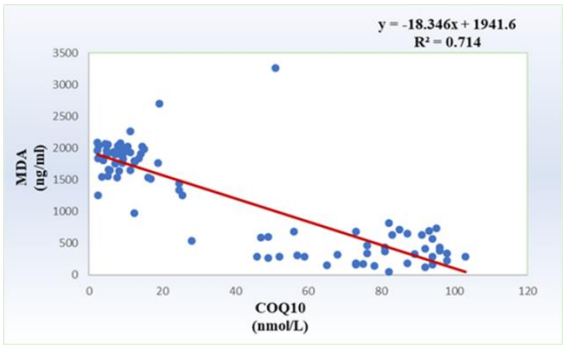

Figure 12. Correlation between Coenzyme Q10 with MDA

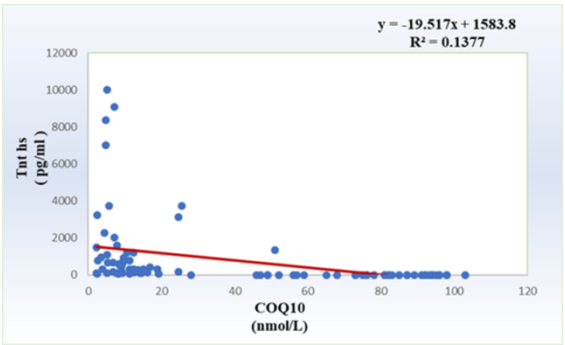

Figure 13. Correlation between Coenzyme Q10 with hs-TnT

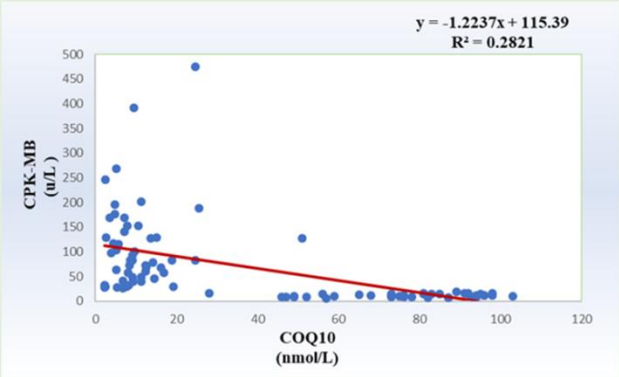

Figure 14. Correlation between Coenzyme Q10 with CPK-MB

Receiver Operating Characteristic Curve Analysis

The ROC curve is a statistical tool used to assess the diagnostic accuracy of a test or biomarker that has a continuous range of test results. The ROC analysis's area under the curve (AUC) identifies the best cut-off values, allowing for the dichotomization of continuous values. It is possible to conclude that the speculative AUC result is significant if the test value is greater than the Table value (0.5), and all parameters evaluated had some significance for predicting MI.

Table 3. Standard of ROC Curves for Tested Variables in MI Patients

Parameter	AUC	Std. Error	95% confidence interval	P-value
Troponin-T pg/mL	1	0	1 to 1	<0.0001
CPK-MB IU/L	1	0	1 to 1	<0.0001
T. Cho. mg/dL	0.5378	0.06149	0.4172 to 0.6583	0.5398
TG mg/dL	0.6285	0.05841	0.514 to 0.743	0.0369
HDL mg/dL	0.7213	0.05279	0.6178 to 0.8247	0.0003
LDL mg/dL	0.5305	0.06168	0.4096 to 0.6514	0.6204
VLDL mg/dL	0.6295	0.05836	0.5151 to 0.7439	0.0355
MDA ng/mL	1	0	1 to 1	<0.0001
CoQ10 nmol/L	1	0	1 to 1	<0.0001

The parameters CoQ10, MDA, hs-cTnT and CPK-MB were among the standards with the highest validity and displayed an excellent strategy for discriminating between healthy people and patients with MI, with a value [AUC= 1 P < 0.0001, 95% Confidence Interval (CI): 1 to 1 and SE: 0] for all above parameters, While TG value is a very important parameter with a value of [AUC = 0.6285 P = 0.0369 and SE: 0.05841], as well HDL [AUC = 0.7213 p = 0.0003, 95% Confidence Interval (CI): 0.6178 to 0.8247 and SE: 0.05279] and VLDL [AUC = 0.6295 p = 0.0355, 95% Confidence Interval (CI): 0.5151 to 0.7439 and SE: 0.05836].Finally, T. cholesterol and LDL, were among the factors with the lowest predictive validity for MI [AUC = 0.5378 P = 0.5398, 95% Confidence Interval (CI): Between 0.4172 and 0.6583, SE: 0.06149], [AUC = 0.5305, p = 0.6204 95% Confidence Interval (CI): Between 0.4096 and 0.6514, SE: 0.06168] respectively, (Table3) and (figures 15-23).

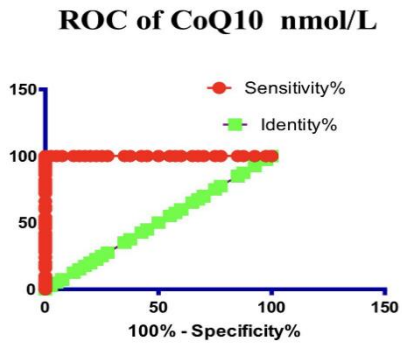

Figure 15. Area under Curve of CoQ10 in MI Patients.

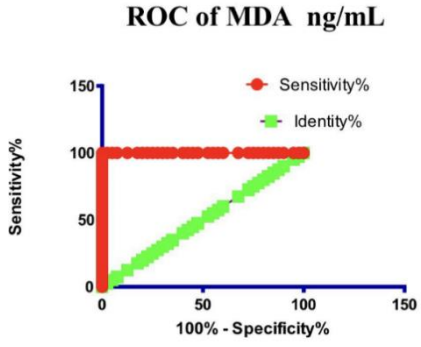

Figure 16. Area under Curve of MDA in MI Patients.

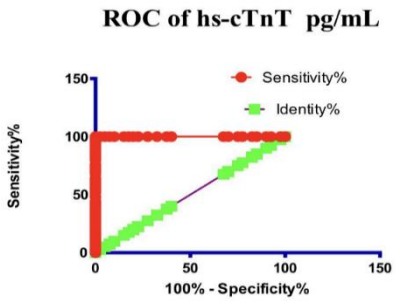

Figure 17. Area under Curve of hs-cTnT in MI Patients.

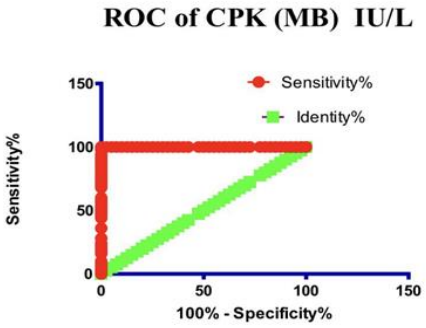

Figure 18. Area under Curve of CPK-MB in MI Patients.

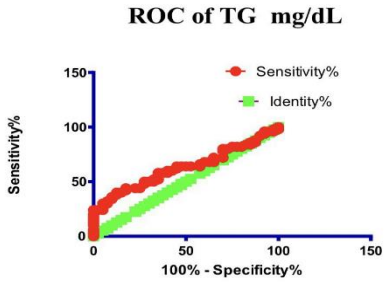

Figure 19. Area under Curve of TG in MI Patients.

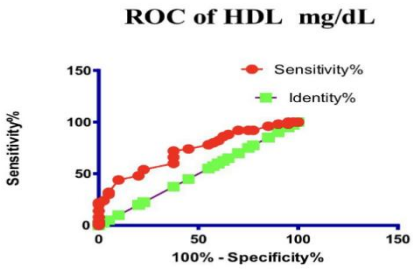

Figure 20. Area under Curve of HDL in MI Patients.

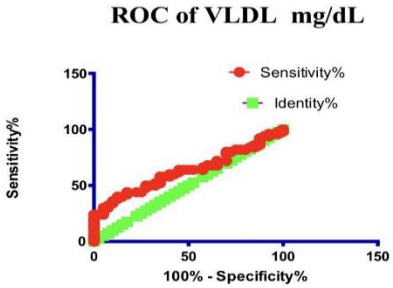

Figure 21. Area under Curve of VLDL in MI Patients.

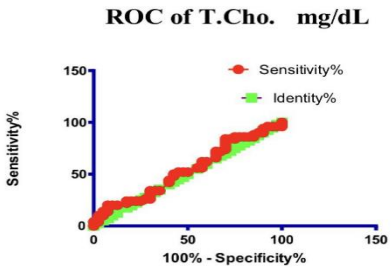

Figure 22. Area under Curve of T. Cho. in MI Patients.

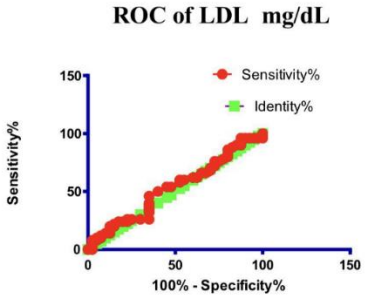

Figure 23. Area under Curve of LDL in MI Patients.

DISCUSSION

Oxidative stress is considered to be an important contributor to the development of cardiovascular disease (CVD) (Pignatelli et al, 2018). CoQ10 is a crucial oxidative damage inhibitor. CoQ10's antioxidant activity inhibits the development of lipid peroxidation in membranes either directly or by recycling other antioxidants like vitamin E or ascorbate (Artuch et al,2009). In addition, CoQ10 inhibits the atherosclerosis process and reduces inflammation by limiting the oxidation of low-density lipoprotein (LDL). (Shah et al, 2021).Patients with ischemic heart disease have been reported to have significantly lower blood levels of CoQ10 than healthy people (Kumar et al, 2009).The present study has demonstrated that serum CoQ10 levels were reduced in patients with MI as compared to control subjects, this result is similar to the results of a study on patients with coronary artery disease, which observed that the patients had significantly decreased plasma coenzyme Q10 levels compared to healthy controls (Lee et al, 2012). Plasma concentrations of CoQ10 were significantly lower in patients with ischemic heart disease and dilated cardiomyopathy compared to healthy individuals (Langsjoen et al, 1990). The level of polyunsaturated fatty acid damage is determined by measuring MDA levels. Thus, one of the crucial parameters to assess the oxidative damage occurring in myocardial infarction is MDA, which is end product of lipid peroxidation (Ismail et al, 2018). The results of this study shown significantly increase in MDA levels in MI patients, our results are in agreement with those of numerous other studies that have observed an increase in MDA levels in MI patients. These results could refer to the increased production of lipid peroxidation products in MI patients (Chatterjee & Rahaman, 2017; Bashar & Akhtar, 2014). Additionally, MDA levels were significantly higher in patients with coronary heart disease, which was a sign of high oxidative stress. Lipid peroxidation may alter the characteristics of membranes due to chemical alterations in oxidized lipids or because it causes the polymerization of membrane constituents (Kamruzzaman et al, 2019).There was a strong negative correlation between coenzyme Q10 and MDA levels (Table 2. Figure 12.) Results in Table 2 also showed that hs-cTnT and CPK-MB had negative, highly significant correlations with serum CoQ10 levels. Myocardial infarction causes the release of a variety of proteins into the bloodstream, including cardiac troponin I (cTnI) and T (cTnT), creatine kinase (CK), myoglobin, and others. Cardiac troponins are now considered the gold standard for diagnosis due to their high specificity and sensitivity (Solecki et al, 2015). Our findings are in agreement with those of another study, which found that AMI patients had significantly higher levels of troponin I and creatine kinase-MB than control subjects (Zrari & Mohammed, 2016). Our study showed no significant difference in T. Cholesterol and LDL levels and there was a significant increase in TG, VLDL levels and significant decrease in HDL levels in patients group than control.

CONCLUSIONS

The current study found that the patients with MI have low levels of CoQ10 and high levels of MDA. CoQ10 has been shown to have a significant cardio-protective effect against coronary artery disease (CAD), and its deficiency has been linked to disease severity. Thus, CoQ10 supplementation has the potential to be extremely useful in improving health by preventing oxidative stress, which is linked to myocardial infarction. The current data demonstrated that serum MDA levels were higher in MI patients; this finding clarified the importance of this biomarker and its impact for myocardial infarction pathophysiology. This finding explains the significance of lipid peroxidation and its effects on the pathophysiology of MI. High levels of MDA are linked to the development of MI. Therefore, we can conclude that high levels of oxidative stress play a significant role in the progression of myocardial infarction, which may be the reason for the various complications during the disease course. As a result, evaluating lipid peroxidation biochemical markers may be useful.

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