Evaluation Role of Coenzyme Q10 in Patients with Ischemic Heart Disease

Othman M. Ayob Alsaiegh[1]*, Ammar Lateef Husein[2], Mohammad Harith Mohammad[3], Zaid dhafer abdulnafa[4]
[1,2]Department of Biochemistry, College of Medicine University of Tikrit, Tikrit, Iraq.
[3,4]Lecturer at college of medicine/university of mosul
Email: Othmanalsaiegh@gmail.com

Abstract

Background: The Coenzyme Q10 has a potential role for prevention and treatment of cardiovascular diseases by improving cellular bioenergeticsAim of study: To evaluate the role of coenzyme Q10 and other biochemical parameters in ischemic heart disease (angina pectoris and myocardial infarction).Methods: A case control study conducted at Intensive Care Unit of Ibn-Sina Teaching Hospital and Al-Salam General Hospital in Nineveh Province, Iraq for the period of two months from 1st April to 1st June 2022. It included 90 adult participants divided into two groups: Case group included 60 patients admitted to the Intensive Care Unit and diagnosed with ischemic heart diseases (Myocardial infarction or angina pectoris) and control group included 30 healthy participants matched in age and gender with case group. Subsequent assay of lipid profile, CRP, CPK, troponin level, and serum coenzyme Q10Results: In this study, 81.7% of patients in case group were diagnosed as myocardial infarction. Means of S. LDH, CRP, CPK, and troponin were significantly higher; while means of coenzyme Q10, S. cholesterol and S. HDL were significantly lower in case group than that in controls. Statistically significant moderate negative correlation was detected between coenzyme Q10 level and age; while significant weak negative correlations were seen between coenzyme Q10 level and all of S. LDH, CRP, and troponin level. Conclusion: Patients with ischemic heart diseases had considerably low serum levels of coenzyme Q10 compared with control group. The highest mean of lipid profile except TG in patients with IHD compared with control group explain the role of cholesterol compounds in progression of IHD. No significant correlations between coenzyme Q10 with BMI, s. cholesterol, s. TG, s. HDL, and CPK. Negative correlation between coenzyme Q10 with age, s. LDH, CRP, and troponin

Keywords: Coenzyme Q10, cardiovascular diseases, biomarkers, ischemia, Iraq.

1. Introduction

Cardiovascular diseases cause approximately one-third of deaths worldwide [(1)]. Among cardiovascular illnesses, ischemic heart disease (IHD) ranks as the most prevalent. Indeed, IHD is acknowledged as an important threat to sustainable development in 21st century [(2)]. Also referred to as coronary artery disease (CAD) and atherosclerotic cardiovascular disease (ACD) The term "acute coronary syndrome" (ACS) encompasses a range of thrombotic coronary artery diseases, including unstable angina and both ST-segment elevation (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI). It manifests clinically as myocardial infarction and ischemic cardiomyopathy. An increasing number of individuals with non-fatal IHD live with chronic disabilities and impaired quality of life [(3)]. IHD is a very common diagnosis and a leading cause of death in both men and women. It accounts for 30% of deaths worldwide, including 40% in high-income countries and approximately 28% in developing nations [(4)]. The increasing incidence of IHD is expected to continue, due not only to the increased prevalence of obesity, diabetes, and metabolic syndrome but also to population aging. The past two decades have witnessed a steep rise in global population aging. Indeed, the United Nations estimates an increase in the population aged over 65 years from 9.01% in 2019 to 16.6% by 2050 [(5)]. Cardiovascular diseases remain among the second leading causes of death in USA since 1975 with 633,842 deaths or 25% of deaths, heart disease occupied the leading cause of death in 2015 followed by 595,930 deaths related to cancer. CVD is also the number one cause of death globally with an estimated 17.7 million deaths in 2015, according to the WHO [(6)]. The primary pathological process attributed to IHD is atherosclerosis, an inflammatory disease of the arteries associated with lipid deposition and metabolic alterations due to multiple risk factors. More than 70% of at-risk individuals have multiple risk factors for IHD, and only 2%-7% of the general population have no risk factors [(7)]. Thorough clinical history and physical exam directed but not limited to the cardiovascular system are the hallmarks for the diagnosis of CVD. Specifically, a history compatible with obesity, angina, decreased exercise tolerance, orthopnea, paroxysmal nocturnal dyspnea, syncope or pre-syncope [(8)]. For symptomatic patients, stress echocardiography can be used to reach the diagnosis for obstructive coronary artery disease. The use of echocardiography, stress cardiac imaging, and/or advanced non-invasive imaging is not recommended on patients who are exhibiting no symptoms and are otherwise at low risk for developing coronary disease [(9)]. The diagnosis of coronary disease underlying particular symptoms depends largely on the nature of the symptoms. The first investigation is an electrocardiogram (ECG), both for "stable" angina and acute coronary syndrome. An X-ray of the chest and blood tests may be performed [(10)] Several cardiac markers have been used in diagnosis and management of CVD. A lack of sensitivity and specificity to cardiac muscle necrosis continues to be the need to look for newer specific molecules. Cardiac biomarkers are of great importance in timely, accurate diagnosis and management of ACS as well as prognosis [(11)]. Co-enzyme Q_{10} (CoQ10) exists in two different forms: a reduced form, as Ubiquinol ($CoQ_{10}H_2$), and an oxidized form, ubiquinone. It is

doi.org/10.31838/hiv22.02.672 Received: 08. 04.22, Revised:21.05.22, Accepted: 14.08.22

endogenously produced, and converts between the two forms, as the reduced or antioxidant form, and as the oxidized form, as part of normal cellular enzyme functions. it is an antioxidant, its main role is as an integral part of the mitochondria respiratory chain for energy production and deficiencies in coenzyme Q10 impair energy production [12]. The CoQ_{10} has a potential role for prevention and treatment of cardiovascular diseases by improving cellular bioenergetics. In addition, it has an antioxidant, a free radical scavenging and a vasodilator effect which may be helpful in these conditions [13].

Aim of study

To evaluate the role of coenzyme Q10 and other biochemical parameters as LDH, creatinine kinase, troponin, cholesterol, triglyceride oxidized, and LDL in ischemic heart disease (angina pectoris and myocardial infarction).

Subjects & Methods

This was a case control study conducted at Intensive Care Unit of Ibn-Sina Teaching Hospital and Al-Salam General Hospital in Nineveh Province, Iraq for the period of two months from 1st November 2021 to 1st June 2022. This study included 90 adult participants divided into two groups:Case group: Included 60 patients admitted to the ICU and diagnosed with ischemic heart diseases (Myocardial infarction or angina pectoris).

- Control group: Included 30 healthy participants matched in age and gender with case group.Diagnosis of IHD was based on symptoms, electrocardiogram and biochemical markers of myocardial necrosis.The blood samples were drawn from the vein. After cleaning the venipuncture site with iodine, five milliliters (10 ml) of the blood sample were collected from each patient. Blood was drawn into Gel Tube. The specimen for Gel tube was separated by centrifugation at 3000 rpm for 10 minutes to get the serum. The separated serum stored at –20 °C for the subsequent assay ofLipid profile, CRP, and CPK by COBAS C 111 technique.Troponin level by COBAS C 411 technique.Serum Coenzyme Q10 by ELISA (Enzyme-Linked Immunosorbent Assay) kit.Verbal permission was obtained from each participant prior to collecting data, and information were anonymous. Names were removed and replaced by identification codes. All information kept confidential in a password secured laptop and data used exclusively for the research purposes.Official approval was granted from the Scientific Committee in the Department of clinical biochemistry which was later approved by the Council of the College of Medicine / Tikrit University. Letter of facilitation was obtained from Tikrit College of Medicine to Ibn-Sina Teaching Hospital and Al-Salam General Hospital, Nineveh Province**Statistical analysis**The data analyzed using Statistical Package for Social Sciences (SPSS) version 26. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Independent t-test (two tailed) was used to compare the continuous variables between study groups. Pearson's correlation test (r) was used to assess correlation between COQ10 marker level with certain parameters. A level of P – value less than 0.05 was considered significant.

2. Results

The total number of study participants was 90. They were divided into two groups: Case group included 60 patients diagnosed with IHD, and control group included 30 healthy participantsStudy participants' age was ranging from 18 to 100 years with a mean of 52.37 years and a standard deviation (SD) of ± 16.6 years. The highest proportion of study patients in case groups was aged ≥ 60 years (50%); while 50% of controls were aged < 40 years.In this study, the highest proportion of case and control groups were males (70% and 80% respectively), and employees (46.7% and 70% respectively).Regarding BMI level, 50% of case group were overweighed; while 66.7% of controls had normal BMI level We noticed that 43.4% of patients and 83.3% of controls were current smokers and 40% of patients and 53.3% of controls had positive family history of IHD.Regarding chronic medical disease, 48.3% of patients had both hypertension and diabetes mellitus; while the majority of controls didn't have chronic diseases (86.7%).As shown in figure (1), 81.7% of patients in case group were diagnosed as MI

Table1: Distribution of study groups by certain biochemical parameters

Variable	Study group		Total (%) n= 90
	Case (%) n= 60	Control (%) n= 30	
Cholesterol Level			
High	2 (3.3)	10 (33.3)	12 (13.3)
Normal	58 (96.7)	20 (66.7)	78 (86.7)
Triglyceride Level			
High	31 (51.7)	12 (40.0)	43 (47.8)
Normal	29 (48.3)	18 (60.0)	47 (52.2)
HDL Level			
Low	46 (76.7)	16 (53.3)	62 (68.9)
Normal	14 (23.3)	14 (46.7)	28 (31.1)
LDH Level			
High	43 (71.7)	2 (6.7)	45 (50.0)
Normal	15 (25.0)	28 (93.3)	43 (47.8)
Low	2 (3.3)	0 (0)	2 (2.2)
CRP			
High	60 (100.0)	0 (0)	60 (66.7)
Normal	0 (0)	30 (100.0)	30 (33.3)
CPK Level			
High	38 (63.3)	0 (0)	38 (42.2)
Normal	22 (36.7)	30 (100.0)	52 (57.8)
Troponin Level			
High	52 (86.7)	1 (3.3)	53 (58.9)
Normal	8 (13.3)	29 (96.7)	37 (41.1)

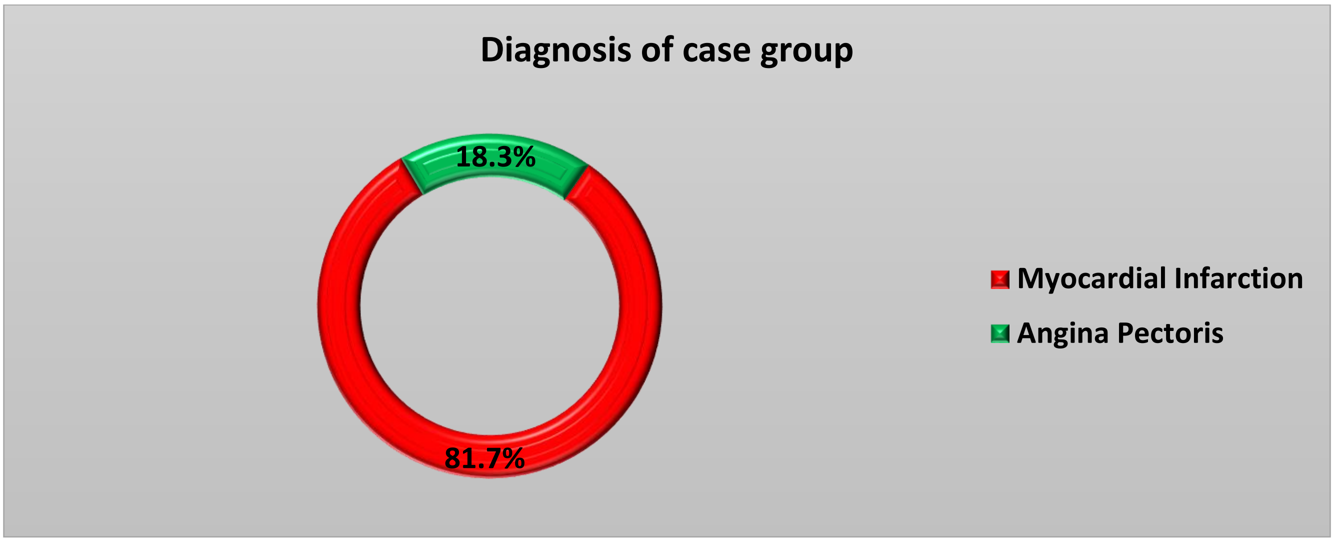

Figure 1: Distribution of case group by diagnosisThe distribution of study groups by certain biochemical parameters. In case group, 3.3% had high cholesterol level, 51.7% had high triglyceride level, 76.7% had low HDL level, 71.7% had high LDH level, all of them had high CRP level, 63.3% had high CPK level, and 86.7% had high troponin level.About healthy individuals, 33.3% had high cholesterol level, 40% had high triglyceride level, 53.3% had low HDL level, 6.7% had high LDH level, all of them had normal CRP, and CPK, and 3.3% had high troponin level Table 2 shows the comparison in certain biochemical parameters between study groups. We noticed that means of S. LDH, CRP, CPK, and troponin were significantly higher; while means of S. cholesterol and S. HDL were significantly lower ($P < 0.05$) in case group than that in controls. No statistical significant difference in mean of S. Triglyceride ($P = 0.36$) between study groups.

Table2: Comparison in certain biochemical parameters between study groups

Variable	Study group		P - Value
	Case Mean ± SD	Control Mean ± SD	
S. Cholesterol (mg/dl)	147.08 ± 35.8	182.96 ± 42.6	0.001
S. Triglyceride (mg/dl)	184.78 ± 103.2	163.16 ± 108.5	0.36
S. HDL (mg/dl)	33.08 ± 9.9	38.5 ± 6.8	0.003
S. LDH (IU/L)	496.85 ± 425.6	162.96 ± 34.1	0.001
CRP (mg/L)	32.7 ± 23.6	1.98 ± 1.2	0.001
CPK (U/L)	611.03 ± 733.0	94.73 ± 29.5	0.001
Troponin (ng/ml)	18.25 ± 22.7	0.016 ± 0.016	0.001

CoQ10 marker level

In case group, 65% of patients had low CoQ10 level; while all controls had normal level.Mean of CoQ10 Level was significantly lower in case group than that in controls (6.07 versus 12.41 mg/L, $P = 0.001$).

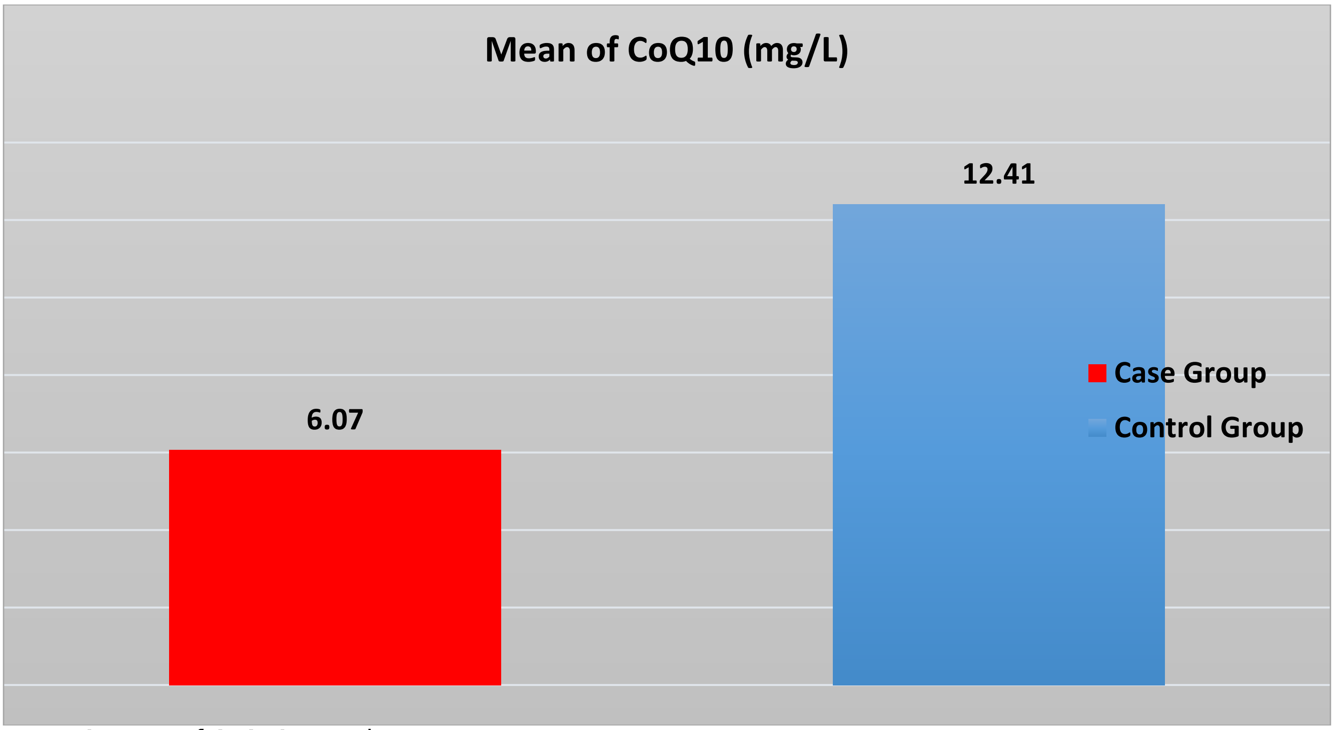

Figure 2: Mean of CoQ10 in study groups

Table 3: Comparison in CoQ10 Level between study groups			
CoQ10 Level (mg/L)	Study group		Total (%) n= 90
	Case (%) n= 60	Control (%) n= 30	
Normal	21 (35.0)	30 (100.0)	51 (56.7)
Low	39 (65.0)	0 (0)	39 (43.3)
	Mean ± SD	Mean ± SD	P - Value
	6.07 ± 1.6	12.41 ± 6.4	0.001

As shown in table (3) statistically significant moderate negative correlation was detected between CoQ10 level and age (r= - 0.409, P= 0.001); while significant weak negative correlations were seen between CoQ10 level and all of S. LDH (r= - 0.216, P= 0.04), CRP (r= - 0.337, P= 0.001, and troponin level (r= - 0.235, P= 0.026).No statistical significant correlations detected between CoQ10 level and all of BMI, S. Cholesterol, S. Triglyceride, S. HDL and CPK.

Table 4: Correlation between CoQ10 level and certain biological parameters		
Variable	CoQ10 level (mg/L)	
	r	P - Value
Age (Year)	- 0.409	0.001
BMI (kg/m2)	- 0.142	0.244
S. Cholesterol (mg/dl)	0.183	0.085
S. Triglyceride (mg/dl)	- 0.058	0.589
S. HDL (mg/dl)	0.2	0.059
S. LDH (IU/L)	- 0.216	0.04
CRP (mg/L)	- 0.337	0.001
CPK (U/L)	- 0.201	0.057
Troponin (ng/ml)	- 0.235	0.026

3. DISCUSSION

In the current study, 90 patients were enrolled, in which case group included 60 patients diagnosed with IHD, and control group included 30 healthy participants.In the present work, 81.7% of patients in case group were diagnosed as MI, which was higher than Khandelwal et al study in 2022, in which 70% of patients have MI [7]. Moreover, current study found in case group, that 3.3% had high cholesterol level, 51.7% had high triglyceride level, 76.7% with low HDL level, 71.7% had high LDH level, all of them had high CRP level, 63.3% had high CPK level, and 86.7% had high troponin level. About healthy individuals in this study, 33.3% had high cholesterol level, 40% had high triglyceride level, 53.3% had low HDL level, 6.7% had high LDH level, all of them had normal CRP, and CPK, and 3.3% had high troponin level.In 2022, Biradar and colleagues reported a different result, as found that 23.7% of patients with IHD were with high total cholesterol, 18.75% of patients with high and very high LDL cholesterol level, and 46.25% patients with low HDL cholesterol level. Moreover, number of patients with high / very high triglycerides level were 21.25% of patients enrolled in their study [18,19]. By comparison to other studies, Shabana et al study in 2021 found that Lipid abnormalities were prevalent in those with coronary heart disease. Among the cases, 50.7% had combined lipid abnormalities, i.e., the values of TC, LDL-C, TG and HDL-C were all deranged. Whereas 49.5% had TC more than normal (> 200 mg/dl), 51.6% had LDL-C > 100 mg/dl. Similarly, 80.4% of patients had TG levels more than upper normal range (> 150 mg/dl) and 64% had HDL values in moderate IHD group [9].In this study and by comparison between study groups, means of S. LDH, CRP, CPK, and troponin were significantly higher; while means of S. cholesterol and S. HDL were significantly lower (P < 0.05) in case group than that in controls. Moreover, no significant difference in mean of S. Triglyceride between study groups (P = 0.36). The results of Shabana et al study in 2020 contradict the current on in that, TG level was significantly increase in patients with IHD (P < 0.001), while other parameters agreed to the current results, in that mean TC, and LDL-C were significantly higher and HDL-C was significantly lower in the cases as compared to the controls[20]. Kamble and other co-authors published a results from study conducted in 2020, which differed from the current one, in that total cholesterol, LDL cholesterol, VLDL cholesterol and serum TG were significantly increased in those with IHD (P<0.05) [21]. Moreover, results in Ahmed et al study in 2020 observed a different finding, they found a significant increase in serum TC, TG, LDL-C, and VLDL in IHD group as compared to the controls (p= 0.001) [22]. Furthermore, Thabet and colleagues in a study in 2015, found that impact of HDL-C on in-hospital outcomes revealed that low HDL-C was associated with higher all in hospital morbidity and mortality, as in form of recurrent ischemic attacks (p=0.01), re-infarction (p =0.29) and cardiogenic shock (p=0.013) [23].Different sample size of each study, unhealthy food habits, poor physical activity, urbanization, economic growth, physical inactivity and increased stress, all these factors determined the differences observed among above mentioned studies.Abnormalities in the lipid profile, particularly hypertriglyceridemia and low levels of HDL-C have been reported to be a strong predictor to a variety of diseases as obesity, diabetes and cardiovascular diseases. It has been estimated that the risk of IHD decreases by 2-3% for every 1 mg/dL increase in HDL-C. Despite some controversy, high levels of triglycerides, fasting and non-fasting, also found to be an independent risk factor for IHD. Evidence from epidemiologic studies suggests that the co-occurrence of low HDL-C and elevated triglyceride levels is a strong risk factor for IHD, while an analyses of many studies have shown that patients with low HDL-C and high triglycerides have the highest rate of major coronary events. Whether an increased level of small dense LDL represents an independent risk factor remains somewhat controversial, but it is clearly associated with a high IHD risk [24-27]. Abnormalities in lipoprotein metabolism are important in atherogenesis, obesity, insulin resistance and DM; major areas of concern for public health, individual wellbeing and research [22].

4.4. CoQ10 marker level

In case group of the current study, 65% had low CoQ_{10} level; while all controls had normal level. Mean of CoQ_{10} Level was significantly lower in case group (P=0.001). Moreover, a significant moderate negative correlation was detected between CoQ_{10} level and age (r= - 0.409, P= 0.001);

significant weak negative correlations with S. LDH (r= - 0.216, P= 0.04), CRP (r= - 0.337, P= 0.001, and troponin level (r= - 0.235, P= 0.026). No significant correlations detected between CoQ_{10} level and all of BMI, S. Cholesterol, S. Triglyceride, S. HDL and CPK.In the concern of the role of CoQ_{10} in the assessment of IHD, multivariate Cox regression analysis, in Shimizu et al study in 2021, demonstrated that lower CoQ_{10} levels were associated with poor prognosis. Low serum levels during the acute phase of IHD were associated with long-term mortality in patients, suggesting the utility of low serum CoQ_{10} levels as a predictor and potential therapeutic target [28]. Accordingly, Yalcin and their colleagues in their study explore a relation exists between low plasma CoQ_{10} concentration and coronary artery disease. They observed that plasma CoQ_{10} concentrations in patients with IHD and controls were found as 0.77 and 0.41 micromol/l, respectively, with a significant relation ($P < 0.01$). Also, the ratio of CoQ_{10} to LDL was found significantly lower in patients with IHD ($P < 0.01$) [29].It had been reported that CoQ_{10} has been reported to have a wide range of therapeutic effects. The mechanism behind these therapeutic benefits are not yet fully understood. In addition to showing potential as an antioxidant and functioning as a cofactor in the mitochondrial respiratory chain, it has been suggested to have gene regulatory properties that might account for its effects on overall tissue metabolism [30-32].In fact, three out of four patients with CVD have low levels of CoQ_{10}. It was noticed that CoQ_{10}'s plasma levels in those with IHD and dilated cardiomyopathy are much lower than in healthy ones. Depending on the severity of cardiac injury circulating level of COQ_{10} decreases in direct proportion to disease progression [33]. There are several theories about the role of CoQ_{10}'s mechanism of action in cardiovascular disease.Firstly, as a result of its antioxidant effect as it was mentioned above. Ubiquinone should be reduced to ubiquinol to completely show its anti-oxidative function. It is obvious, that Reactive Oxygen Species (ROS) can lead to a serious cellular damage by means of reacting with cell membranes, DNA and protein centers [34]. Besides that, the products of oxidative stress and cytokines may cause hypertrophy since they trigger the growth of myocytes. Ubiquinol (reduced form of COQ_{10}) stops the initial process of lipid peroxyl radicals' formation. That is the reason why COQ_{10} is considered to be a very potent antioxidant against ROS and free radicals in biological membranes [35].Secondly, it plays a significant role in the heart's energetic needs. For example, the contraction of cardiac, which involves the release of Ca^{2+} from the sarcoplasmic reticulum and the following activation of the contractile proteins requires energy. There is a theory that myocardial failure may be caused by the reduced production of the energy in mitochondria. So, as it was mentioned before, COQ_{10} is the main component in the transport of electrons necessary for ATP production [6]. Furthermore, the anti-inflammatory effect should be taken in consideration, since different cardiovascular diseases, as heart failure are related to chronic pro-inflammatory state, supposing increased circulating levels of cytokines and adhesion molecules [36]. There are some new studies that establish anti-inflammatory properties of COQ_{10} possibly by means of nitric oxide's regulation, and that mechanism may be effective in heart failure treatment. Thus, the cytokines' and chemokines' secretion wouldn't induce myocardial fibrosis and lead to Heart Failure development [37]. On the other hand, CoQ_{10} has been reported to have a wide range of therapeutic effects. The mechanism behind these therapeutic benefits are not fully understood yet. In addition to showing potential as an antioxidant and functioning as a cofactor in the mitochondrial respiratory chain, CoQ_{10} has been suggested to have gene regulatory properties that might account for its effects on overall tissue metabolism. Despite reports of its safety, its efficacy in different disease states, and its deficiency in many conditions, CoQ_{10} supplementation is not widely prescribed in clinical practice. Potential reasons involve a lack of understanding about the critical role of CoQ_{10}, ignorance of the detrimental effects related to CoQ_{10} deficiency, and fact that CoQ_{10} is a nutraceutical rather than a patentable drug [31].This had been proved in Kumar et al study, in which observed a significant improvement in clinical and hemodynamic parameters and in exercise tolerance in patients given adjunctive CoQ_{10} in doses from 60 to 200 mg daily in the various trials conducted in patients of heart failure, hypertension, ischemic heart disease and other cardiac illnesses [33]. Another randomized study which involved diabetic patients with IHD supports the findings of the anti-inflammatory effect of COQ_{10} although didn't find any improvement of cardiometabolic markers. They concluded that CoQ_{10} intake after 8-weeks among diabetic patients with the stable IHD had beneficial effects on serum IL-6 levels, but did not alter other cardiometabolic markers [38].Despite these recommendations, research on CoQ_{10} absorption and bioavailability differs, and is dependent on the type of CoQ_{10} preparation used. Many formulations have been developed to improve CoQ_{10} solubility in the organism. Recent new formulations for CoQ_{10} are based on enhancing its water-solubility, as in the cases of Q-ter or Ubisol-Q_{10}. Ubisol-Q_{10} is a nano-miscelle formulation that appears to be water-soluble containing CoQ_{10}, where solubilization is achieved due to the amphipathic properties of polyetilenglycol-derivatized -tocopherol, which allows for the formation of stable and water-soluble nano-miscelle [39]. Q-ter is a supplement consisting of copovidone, which acts as a carrier, CoQ_{10}, and glycine, which works as a catalyst. This composition makes Q-ter 200-times more soluble than pure CoQ_{10} [40].

4. Conclusion

1. This study was approved the role of coenzyme Q10 in IHD were the patients had considerably low serum levels of coenzyme Q10 compared with control group.The highest mean of lipid profile except TG in patients with IHD compared with control group explain the role of cholesterol compounds in progression of IHD.No significant correlations between coenzyme Q10 with BMI, s. cholesterol, s. TG, s. HDL, and CPK.Negative correlation between coenzyme Q10 with age, s. LDH, CRP, and troponin.

5. References

1. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. circulation. 2015;131(4):e29-e322.Roth GA, Johnson C, Abajobir A, Abd-Allah F, Abera SF, Abyu G, et al. Global, regional, and national burden of cardiovascular diseases for 10 causes, 1990 to 2015. Journal of the American college of cardiology. 2017;70(1):1-25.Mohammed IJ, Sarhat ER, Hamied MA, Sarhat TR. (2021). Assessment of salivary Interleukin (IL)-6, IL-10, Oxidative Stress, Antioxidant Status, pH, and Flow Rate in Dental Caries Experience patients in Tikrit Province. Sys Rev Pharm.12(1):55-59.Sarhat E. S.A. Wadi, B.I. Sedeeq, Th.R. Sarhat and N.A. Study of histopathological and biochemical effect of *Punica granatum* L. extract on streptozotocin -induced diabetes in rabbits. *Iraqi Journal of Veterinary Sciences*, 2019; 33(2): 189-194. doi: 10.33899/ijvs.2019.125523.1045.Zbaar, S., Sarhat, E., khalaf, S. Association of C-Reactive Protein with Risk of Complications of diabetic nephropathy. *Egyptian Journal of*

Chemistry, 2022; 65(8): 181-186. doi: 10.21608/ejchem.2021.99957.4868.Sarhat ER, Rmaid ZJ, Jabir TH (2020) Changes of salivary interleukine17, Apelin, Omentin and Vaspin levels in normal subjects and diabetic patients with chronic periodontitis, Ann Trop Med & Pub Health; 23:S404. DOI: http://doi.org/10.36295/ASRO.2020.23118.*Sayran Sattar Saleh , Entedhar Rifaat Sarhat. Effects of Ethanolic Moringa Oleifera Extract on Melatonin, Liver and Kidney Function Tests in Alloxan Induced Diabetic Rats. Indian Journal of Forensic Medicine & Toxicology, 2019; 13(4): 1015-1016.*Khalid G. Washeel1Entedhar R.Sarhat , Talal H. Jabir. Assessment of Melatonin and OxidantAntioxidant Markers in Infertile Men in Thi-Qar Province. Indian Journal of Forensic Medicine & Toxicology, 2019; 13(4):1500-1504.AlMashhadani HA. Study the effect of punica granatum as oral antifungal on the corrosion inhibition of dental amalgam alloy in saliva. Journal of Materials and Environmental Science. 2018;9(2):662-71.Entedhar R. Sarhata, Moayad M. Al Anzy, Takea Shaker Ahmed. Study of oxidant-antioxidant status in cerebrospinal fluid of children with meningitis. Eurasian Chemical Communications, 2022, 4(9), 863-869. Link: http://www.echemcom.com/article_148799. htmlChacko S, Haseeb S, Glover BM, Wallbridge D, Harper A. The role of biomarkers in the diagnosis and risk stratification of acute coronary syndrome. Future Sci OA. 2017;4(1):FSO251-FSO.Barquera S, Pedroza-Tobías A, Medina C, Hernández-Barrera L, Bibbins-Domingo K, Lozano R, et al. Global overview of the epidemiology of atherosclerotic cardiovascular disease. Archives of medical research. 2015;46(5):328-38.Dunbar SB, Khavjou OA, Bakas T, Hunt G, Kirch RA, Leib AR, et al. Projected Costs of Informal Caregiving for Cardiovascular Disease: 2015 to 2035: A Policy Statement From the American Heart Association. Circulation. 2018;137(19):e558-e77.Sampasa-Kanyinga H, Lewis RF. Frequent use of social networking sites is associated with poor psychological functioning among children and adolescents. Cyberpsychology, Behavior, and Social Networking. 2015;18(7):380-5.Olvera Lopez E BB, Jan A. Cardiovascular Disease. In: StatPearls [Internet]. : Treasure Island (FL): StatPearls Publishing; 2022 [updated 2021 Aug 11; cited 2022 19 feb.]. Available from: https://www.ncbi.nlm.nih .gov/books/ NBK535419/.

2. Loder E, Weizenbaum E, Frishberg B, Silberstein S, Force AHSCWT. Choosing wisely in headache medicine: the a merican headache Society's list of five things physicians and patients should question. Headache: The Journal of Head and Face Pain. 2013;53(10):1651-9. Jacob R, Khan M. Cardiac Biomarkers: What Is and What Can Be. Indian J Cardiovasc Dis Women WINCARS. 2018;3(4):240-4 Oleck S, Ventura HO. Coenzyme Q10 and utility in heart failure: just another supplement? Current heart failure reports. 2016;13(4):190-5.Biradar MS, Rangaswamy. Lipid Profile Study in Patients Diagnosed with Acute Myocardial Infarction for First Time and Admitted in Tertiary Care Hospital Mysuru. The Journal of the Association of Physicians of India. 2022;70(4):11-2Neda Awni, Takea Shaker Ahmed. , Entedhar R. Sarhat, Nagham Hasan Ali. , Kasim Sakran Abass, Altered serum levels of melatonin, antioxidant enzymes and oxidative stress in individuals with diabetes mellitus Type 2.Revista Latinoamericana de Hipertensión.2022;17(N° 2): 2022:138-144.Al-Saadie KA, Abas HA, Almashhdani HA. Corrosion Protection of Iron Alloy Using Peganum harmala Extract as Inhibitor in Acidic Solution. Materials Sciences and Applications. 2015;6(11):1061.Shabana, Shahid SU, Sarwar S. The abnormal lipid profile in obesity and coronary heart disease (CHD) in Pakistani subjects. Lipids Health Dis. 2020;19(1):73KAMBLE PS. Association between apolipoprotein E polymorphism and lipid profile in patients of myocardial infarction. The Medical Journal of Basrah University. 2020;38(2):8-14.Ahmed HS. Assessment of ApolipoproteinsA1, E, and Insulin Resistance in Iraqi Male Patients with Acute Myocardial Infarction. Iraqi Journal of Community Medicine. 2020;33(2).Thabet NI HH, Kamal YM Study of High Density Lipoprotein Cholesterol among Patients with Acute Coronary Syndrome in Sohag University Hospital. . J Cardiol Curr Res. 2015;2(5):00073Entedhar Rifaat Sarhat. Acute Myocardial Infarction: Melatonin, Apelin, and Visfatin as Predictors of Disease . Diyala Journal of Medicine.2017; 13(2):11-17.Salim J.Khalaf, Gadeer Hatem Aljader, Entedhar R. Sarhat et al. Antidiabetic effect of Aqueous Extract of Medicago Sativa with Enhanced Histopathology of Pancreas in Alloxan Induced Diabetic Rats.P J M H S.2021;15(2): 492-492.Sarhat Entedhar Rifaat, Khalaf Salim Jasim, Hamad Mahde Salih. A Study of Some biochemical Parameters in blood Serum of Patientswith congestive Heart Failure. Indian Journal of Public Health Research & Development.2019: 10(5); 413- 418.Trialists CT. '(CTT) Collaboration, Baigent, C. et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet. 2010;376(9753):1670-81.Shimizu M, Miyazaki T, Takagi A, Sugita Y, Ouchi S, Aikawa T, et al. Low coenzyme Q10 levels in patients with acute cardiovascular disease are associated with long-term mortality. Heart and Vessels. 2021;36(3):401-717.

Yalcin A, Kilinc E, Sagcan A, Kultursay H. Coenzyme Q10 concentrations in coronary artery disease. Clinical biochemistry. 2004;37(8):706-9.Sarhat ER, Wadi SA, Awni N, Ali NA, Sarhat TR. Evaluation of Vimentin and Some Biochemical Parameters in the Blood of Acute Myocardial Infarction Patients.2022;339(65):1-2. DOI: 10.21608/EJCHEM.2021.80050.3943.Potgieter M, Pretorius E, Pepper MS. Primary and secondary coenzyme Q10 deficiency: the role of therapeutic supplementation. Nutrition Reviews. 2013;71(3):180-8.Sarhat ER, Siham A.W, Ayhan R. M. Effect of Ethanolic Extraction of Moringa oleifera on Paraoxonase and Arylesterase enzyme activity in High Fat Diet-induced Obesity in Rats. Research J. Pharm. and Tech.2018; 11(10): 4601-4.

3. Kumar A, Kaur H, Devi P, Mohan V. Role of coenzyme Q10 (CoQ10) in cardiac disease, hypertension and Meniere-like syndrome. Pharmacology & therapeutics. 2009;124(3):259-68.

4. Al-Mashhadani HA, Alshujery MK, Khazaal FA, Salman AM, Kadhim MM, Abbas ZM, Farag SK, Hussien HF. Anti-corrosive substance as green inhibitor for carbon steel in saline and acidic media. InJournal of Physics: Conference Series 2021 Mar 1 (Vol. 1818, No. 1, p. 012128). IOP Publishing.

5. Bergamini C, Cicoira M, Rossi A, Vassanelli C. Oxidative stress and hyperuricaemia: pathophysiology, clinical relevance, and therapeutic implications in chronic heart failure. European journal of heart failure. 2009;11(5):444-52.

6. 21.

Lim J-Y, Park SJ, Hwang H-Y, Park EJ, Nam JH, Kim J, et al. TGF-β1 induces cardiac hypertrophic responses via PKC-dependent ATF-2 activation. Journal of molecular and cellular cardiology. 2005;39(4):627-36.

7. Yang Y-K, Wang L-P, Chen L, Yao X-P, Yang K-Q, Gao L-G, et al. Coenzyme Q10 treatment of cardiovascular disorders of ageing including heart failure, hypertension and endothelial dysfunction. Clinica Chimica Acta. 2015;450:83-9.

8. Swarnakar NK, Jain AK, Singh RP, Godugu C, Das M, Jain S. Oral bioavailability, therapeutic efficacy and reactive oxygen species scavenging properties of coenzyme Q10-

loaded polymeric nanoparticles. Biomaterials. 2011;32(28):6860-74.

9. Mirhashemi SM, Najafi V, Raygan F, Asemi Z. The effects of coenzyme Q10 supplementation on cardiometabolic markers in overweight type 2 diabetic patients with stable myocardial infarction: A randomized, double-blind, placebo-controlled trial. ARYA atherosclerosis. 2016;12(4):158.

10. Muthukumaran K, Leahy S, Harrison K, Sikorska M, Sandhu JK, Cohen J, et al. Orally delivered water soluble Coenzyme Q10 (Ubisol-Q10) blocks on-going neurodegeneration in rats exposed to paraquat: potential for therapeutic application in Parkinson's disease. BMC neuroscience. 2014;15(1):1-11.

11. Fumagalli S, Fattirolli F, Guarducci L, Cellai T, Baldasseroni S, Tarantini F, et al. Coenzyme Q10 terclatrate and creatine in chronic heart failure: a randomized, placebo-controlled, double-blind study. Clinical cardiology. 2011;34(4):211-7.