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Evaluation of some biochemical parameters in Iraqi Patients with cardiomyopathy

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***Abstract*---**Cardiomyopathy is an affliction of the heart muscle that can result in heart failure.It comes in a variety of phenotypes, such as dilated, hypertrophic, and restricted. This study was aimed to investigate the level of physiological and biochemical parameters in Cardiomyopathy patients. Eighty two diagnosed cardiomyopathy adult patients with age range between (20-70) years, and thirty healthy with same range, were involved in this study during their attendance at Ibn Al-Bitar Center for Cardiac Surgery. The patients were diagnosed by an expert cardiologists based on ECG changes, Echocardiogram, chest x ray. The study was conducted from October 2020 to March 2021, and approved by ethical committees: Ref.: CSEC/0920/0052, September 15, 2020 of department of Biology, College of Science, University of Baghdad. Blood samples were collected the levels of biochemical parameters like troponin T, creatine kinase - MB (CK-MB), C-reactive protein (CRP), lactate dehydrogenase (LDH), Urea creatinine and electrolytes (Na^+, Ca^{++}, K^+ and Mg^+) were determined for the patients and control. The levels LDH, CRP) and CK-MB showed a highly significant ($P<0.01$) increase in patients compared with control, While the level of Troponin T showed non-significant ($P\geq 0.05$) differences. The level of urea showed highly significant increase ($P<0.01$) and level of creatinine showed a significant ($P\leq 0.05$) increase in patients compared with control. Referring to the electrolytes results, the levels of Mg+ and K+ showed highly significant ($P<0.01$) increase in patients, While, the levels of Ca^{+2} and Na^+ showed non-significant ($P \geq 0.05$) differences. It can be concluded that the patients with

cardiomyopathy suffer from different physiological problem because the changes that occur in many biochemical parameters.

***Keywords*---**Cardiomyopathy, biochemical parameters, Troponin T and CK-MB.

Introduction

Cardiomyopathies are heart muscle illnesses, a word coined in 1957 to describe a group of cardiac disorders that are not caused by coronary artery disease. Other known causes of myocardial dysfunction, such as systemic hypertension, valve disease, and ischemic heart disease, have been eliminated from the definition, which now refers to structural and/or functional abnormalities of the myocardium (Price *et al.,* 2016).

Dilated cardiomyopathy (DCM), which is characterized as LV dilation and systolic dysfunction in adults in their third and fourth decades of life, is a leading cause of heart failure. It is the most common reason for heart transplantation in the world. Chamber volume dilation and thin walls are common features of DCM, which diminish contractile force and lead to systolic heart failure (Ntusi *et al.,*2011; Tayal *et al.,*2017).

Hypertrophic cardiomyopathy has a wide range of clinical symptoms. Exertional dyspnea, weariness, palpitations, lightheadedness, syncope, unusual chest pain, and sudden cardiac death (SCD) can all be symptoms of HCM, which are caused by ventricular diastolic dysfunction, cardiac arrhythmias, and left ventricular outflow track obstruction (LVOTO), as key pathophysiologic factors (Marian and Braunwald, 2017; Maron *et al.,* 2018).

Restrictive cardiomyopathy is a cardiac condition caused by increased myocardial stiffness, which causes ventricular filling to be impeded. Until late in the disease, biventricular chamber size and systolic function are usually normal or near-normal. RCM, which can affect one or both ventricles, can lead to signs and symptoms of left or right heart failure. Arrhythmias and conduction abnormalities are very common (Muchtar *et al.,* 2017).

Troponin is a heterotrimeric protein found in human cardiac striated muscle and made up of three subunits: a $Ca2^{+}$-binding subunit called troponin C (TnC), a tropomyosin-binding subunit called troponin T (TnT), and an inhibitory subunit called troponin I (TnI) (Johnston *et al.,* 2018) .

The myocardium is the primary location of localization for cardiac-specific troponin proteins (cTnI, cTnT), allowing them to be used as specific biomarkers for detecting cardiac muscle changes (Chaulin and Duplyakov, 2020). The troponin complex, which is responsible for myocardial contractility, contains the majority of troponins (approximately 95%) of the overall number. (Duplyakov, 2020). Because they are the most sensitive and cardiac-specific laboratory measurements of myocardial injury now available, cardiac troponin I (cTnI) and cardiac troponin T (cTnT) are the biomarkers of choice for the diagnosis of

myocardial injury (Thygesen *et al.,* 2010). Cardiac troponins are sensitive and specific myocardial damage markers (Connelly 2016).

Lactate Dehydrogenase usefulness as a clinical diagnostic marker stems from its differential expression. The predominant isozyme found in heart tissue is LDH-1, which has four heart subunits (4H). LDH-2 is the primary isozyme of the reticuloendothelial system and RBCs, with three heart and one muscle subunit (3H1M). Lactate Dehydrogenase isozyme testing, in addition to determining the concentration of LDH in samples, also aids in determining the kind, location, and severity of tissue injury (Farhana and Lappin, 2020).

Creatine kinase CK is a dimeric molecule that is made up of two subunits, M and B. The isoenzymes CK–MM, CK–MB, and CK–BB are formed by combining these subunits. The myocardium contains a high concentration of the CK–MB isoenzyme, and the development of elevated CK–MB levels in serum is highly specific and sensitive for myocardial cell wall damage. Serum CK–MB normal reference levels vary from 3 to 5% (percentage of total CK) or 5 to 25 IU/L (C. Daniel Cabaniss, 2009). Creatine kinase-MB, an essential cardiac biomarker, is commonly employed in AMI diagnosis and prognosis (Seo *et al.,* 2017).

Material and Methods

This cohort study was performed on eighty two adults dignosed cardiomyopathy diagnosed patients , with age range of (20-70) years and the mean age was 47.78 ± 1.35 years during their attendance to Ibn Al-Bitar Center for Cardiac Surgery, Baghdad, Also thirty healthy subjects with same age range and mean of 48.53 ±1.64 years were enrolled in this study.

The study was conducted from October 2020 to March 2021, written informal consent was obtained from all patients and the study was approved by ethical committees :Ref.: CSEC/0920/0052, September 15, 2020 of department of Biology, College of Science, University of Baghdad.

The blood sample were collected and placed in a clean, dry plain plastic tube and allowed to clot for 5-10 minutes at 37 °C before centrifugation at 3000 rpm for 10-15 minutes for serum separation. After ensuring that there was no hemolysis in the serum, the clear serum was transferred to clean plastic tubes by micropipette, and kept at -20 o C for biochemical measurements. Measurement of Troponine T, Creatine kinase- MB (CK-MB), C-Reactive Protein (CRP), Serum Creatinine (Cr), lactate dehydrogenase (LDH) and Urea levels were carried out by a fully automated analyzer Rochee 411 (Germany) which is designed for determinations for a broad range of applications including hormones . Sodium (Na^{+}), Calcium (Ca^{+2}) , Potassium (K^{+}) and Magnesium (Mg^{+}) values were measured by automatic clinical chemistry analyzer Linear chromo plus (Spain). The Statistical Analysis System- SAS (2012) program was used to detect the effect of difference groups in study parameters. T-test was used to significant compare between means. Chi-square test was used to significant compare between percentage (0.05 and 0.01) probability in this study.

Result and Discussion

Levels of LDH, Troponin T, CRP and CK (MB) in cardiomyopathy patients and control

The levels of LDH, CRP and CK(MB) showed a highly significant (P<0.01) increase in patients with cardiomyopathy compared with control Level of Troponin showed non-significant (P≥ 0.05) differences in the patients with cardiomyopathy as compared with control table (1).

Table 1
Levels of LDH, Tn T, CRP and CK(MB) in cardiomyopathy and control

Group	Mean ± SE			
	LDH U/L	Troponin T (ng/ml)	CRP mg/L	CK(MB) U/L
Patients	336.98 ±9.98 a	0.287 ±0.01	11.58 ±0.86 a	19.58 ±0.57 a
Control	252 .56 ±5.91 b	0.286 ±0.02	2.051 ±0.18 b	10.33 ±0.48 b
T-test	33.56 **	0.0432 NS	2.866 **	1.975 **
P-value	0.0001	0.943	0.0001	0.0001
Means with the different letters in same column differed significantly ** (P≤0.01),				

In the present study, LDH, troponin T, CRP, and CK-MB were measured to evaluate whether cardiac abnormalities existed in patients with cardiomyopathy compared with control. LDH levels vary according on the metabolic needs of each tissue, as well as developmental, biological, and pathological factors (Joshi *et al.,* 2012).

There was a highly significant (P<0.01) increase in LDH level in patients with cardiomyopathy compared with control, this results in agreement with (Hamada *et al.,*2016). Moreover, in this study, the increase in LDH level was similar to the results of Piper *et al.* (2002), they found a greater serum LDH isozyme 1 in individuals with valvular heart disease and cardiomyopathy with volume and pressure overload.

Increased serum LDH may represent the severity of myocardial injury and reduced cardiac function, according to previous studies (Yamaguchi *et al.,* 2020). Following cardiac pump failure, LDH could signify metabolic alterations accompanied by a reduction in oxygen delivery. Low blood perfusion as a result of cardiac pump failure reduces oxygen delivery. The cardiac enzyme biochemical test is a useful tool for checking the heart muscle and preventing heart failure in patients (Hamzah, 2018).The cytosolic proteins CK and LDH are most prevalent in the heart, with CK-MB and LDH being the most abundant. As a result, prolonged elevations in serum CK-MB and LHD clearly reflect the presence of continuous myocardial damage, which could lead to myocardial cell death (Hamada *et al.,* 2016).

In this study, baseline CRP was shown to be higher in cardiomyopathy patients compared to controls. This increase is statistically significant, and it reflects the patient's baseline inflammatory condition. The result of the study similar with

(Zhang *et al.,* 2008, Hickman *et al.,* 2010) they reported that the elevated blood levels of myocardial damage biomarkers. There was a highly significant (P< 0.01) increase in current results also similar with Reynoso-Villalpando *et al.*2017, who recorded that CRP levels were considerably higher in acute myocardial infarction patients compared to patients without a personal history of ischemic cardiomyopathy. High sensitivity CRP is frequently used in both outpatient and inpatient departments to assess the outcome in patients with cardiac disease, such as myocardial infarction and acute myocardial infarction (De Servi *et al.,* 2005).

According to the results of this study, there was a highly significant (P<0.01) increase in CK-MB level in patients with cardiomyopathy compared with control, and this finding was according with previous and this finding was according with earlier researches of (Yang *et al.,* 2020, Inciardi *et al.,* 2020 and Aboughdir *et al.,* 2020).

Different levels of postmortem CK-MB were found in different sample sites. Because the chemical compounds secreted by the myocardium are first released into the cardiac blood and pericardial fluid, postmortem CK-MB levels in the pericardial fluid and serum from cardiac blood are higher than those in peripheral blood (Chen *et al.,* 2015; Cao *et al.,* 2019).

The muscle enzyme CK or CPK, which is found in the cytoplasm of myocytes and is mostly released into the bloodstream from necrosed myocardium, is the first biomarker to rise, because it is more selective to the myocardium, the CK-MB fraction swiftly superseded CK and is now regarded the gold standard. The CK is reported without clear cell death and sometimes with a reciprocal decrease of these markers in seemingly surviving cardiomyocytes under restricted ischemic circumstances or limited beta-adrenergic stimulation. Despite the fact that these investigations did not find cardiomyocyte death, it is likely that areas of cell death, particularly apoptosis, were missed by their histological exams.

With regard of Troponin level the results of current study showed non-significant difference between cardiomyopathy patients and control. This is in agreement with results of the Willeit's *et al.* (2017) who found that even troponin concentrations below 10 ng/L are predictive in terms of the development of cardiovascular disorders later on.

Troponin levels in blood serum are thought to be a sign of cardiac disease (Korff, 2006). Increased load, especially in hypertension, increased activity of the renin-angiotensin-aldosterone system, and activation of the sympathetic nervous system are thought to cause apoptotic death of myocardial cells, which may contribute to necrosis or increased permeability of cardiomyocyte cell membranes (Kociol *et al.,* 2010). A few studies on the effect of treatment on troponin levels have been reported. It's still unclear whether healthy people with high troponin levels can change their lifestyles to prevent the molecule from becoming further higher in blood serum (Hoshide *et al.,* 2013).

It may be due to Troponins are unable to detect myocardial ischemia in the absence of necrosis, making an early diagnosis impossible. Although troponin has

a higher sensitivity for detecting myocardial damage, its rise does not always indicate the development of ACS. Also, troponin levels are elevated in a range of additional clinical situations, including pulmonary embolism with acute right heart overload, heart failure, and myopericarditis. When compared to the more sustained elevation that occurs with acute myocardial damage, troponin elevations in these conditions are usually moderate (Chacko *et al.,* 2018).

Troponin is a powerful predictor of prognosis and has a high specificity and sensitivity for detecting myocardial necrosis. Troponin in the heart T and I are myocardial damage markers that are both sensitive and specific. In patients with dilated cardiomyopathy, this troponin can also predict a poor outcome. The low sensitivity of the traditional commercial assay technique, however, limits their clinical application (Anghel *et al.,* 2021).

Levels of kidney functions parameters in cardiomyopathy patients and control

The results of kidney functions parameters (blood urea and creatinine) are illustrated in table (2). The levels of urea showed highly significant (P<0.01) increase and level of Creatinine appeared significant (P≤0.05) increase in patients with cardiomyopathy compared with control.

Table 2
Levels of kidney functions parameters in cardiomyopathy patients and control

Group	Mean ± SE	
	Creatinine mg/dl	Urea mg/dl
Patients	1.006 ±0.06 a	43.88 ±1.36 a
Control	0.746 ±0.04 b	30.37 ±1.27 b
T-test	0.221 *	4.74 **
P-value	0.0210	0.0001

Means with the different letters in same column differed significantly.* (P≤0.05), ** (P≤0.01).

Blood urea nitrogen and creatinine are known indices of renal insufficiency and have been linked to the prognosis of patients with acute heart failure (AHF) (Kajimoto *et al.,* 2016; Palazzuoli *et al.,* 2016). Pre-renal acute kidney injury is caused by inadequate renal perfusion caused by ventricular systolic and/or diastolic dysfunction in patients with HF(Zhu *et al.,* 2020). This process lowers the glomerular filtration rate (GFR) while also increasing water and sodium re-absorption, lowering urea excretion (Smilde *et al.,* 2008).

Studies show that the affected neuro hormonal system is responsible for the reabsorption process in patients with acute heart failure (AHF)(Matsue *et al.,* 2017). Blood urea nitrogen is a marker for both renal function and neurohormonal activity, blood urea nitrogen levels have been linked to short, intermediate, and long-term prognoses in patients with cardiovascular illnesses such as heart failure (Kajimoto *et al.,*2016; Ren *et al.,* 2018) , myocardial

infarction (Horiuchi *et al.,* 2018; Richter *et al.,* 2019), and acute pulmonary embolism (Tatlisu *et al.,* 2017).

The heart and the kidney have a close bidirectional interaction. Cardio renal syndrome (CRS) is the clinical term for this interaction, which is defined as the occurrence of acute renal injury and dysfunction in patients suffering from severe cardiac disease (Zhu *et al.,* 2020).

Creatinine is not reabsorbed by the renal tubule, but blood urea nitrogen is partially reabsorbed in the renal tubule, making it one of the most relevant indicators for evaluating renal function. The renin-angiotensin-aldosterone system, sympathetic nervous system (SNS), and arginine vasopressin all have a role in reabsorption (Kazory, 2010). As a result, the BUN/Cr ratio could be a useful diagnostic for predicting the prognosis of patients with HF, as it reflects the activity of neuro hormones.

Levels of electrolytes in cardiomyopathy patients and control.

The results of electrolytes Sodium Calcium, Potassium and Magnesium, are illustrated in table (3). The levels of Mg^{+} and K^{+} showed highly significant ($P<0.01$) increase in patients with cardiomyopathy, While, the levels of Ca^{+2} and Na^{+} showed non-significant ($P \geq 0.05$) differences

Table 3
Levels of electrolytes in cardiomyopathy patients and control

Group	Mean ± SE			
	Na+ nmol/L	Ca+2 mg/dl	K+ mmol/L	Mg+ mg/dl
Patients	137.24 ±2.19	9.22 ±0.07	5.08 ±0.07 a	2.23 ±0.04 a
Control	139.10 ±1.08	9.31 ±0.05	3.72 ±0.11 b	1.77 ±0.09 b
T-test	7.449 NS	0.263 NS	0.269 **	0.190 **
P-value	0.622	0.516	0.0001	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01), NS: Non-Significant.				

With regard of potassium levels the results of current study showed highly significant increase, this contrasts with the findings of other HF real-world cohorts, which found that high-normal serum potassium levels were safe and had the same clinical outcome as normal potassium levels (Hoss *et al.,* 2016). This result is in agreement with retrospective studies by Ahmed *et al.,* (2007) and Ahmed *et al.,(*2010).

In "excitable membranes," such as those found in skeletal muscle, cardiac muscle, smooth muscle, and nerve cells, this gradient allows the development of functional transmembrane voltage gradients and the establishment of action potentials (Sterns *et al.,* 2016).

Myocardial infarction can impact electrolyte levels. Electrolyte ions, primarily sodium and potassium, are required for the formation and conduction of cardiac impulses and are constantly exchanged between intracellular and extracellular

areas via passive and active diffusion. Myocardial infarction damages the heart muscle cell membranes, causing sodium and potassium channels, as well as the sodium-potassium-ATPase pump, to malfunction. (Walim and Yatiraj, 2014; Faraj, 2015).Extracellular potassium elevation affects myocardial electrophysiology in a number of ways, contributing to intra cardiac conduction abnormalities (Dépret *et al.,* 2019).

Rapid fluctuations in plasma concentration, the gradient of potassium across the myocardial cell membrane, the action of other ions (i.e., sodium, calcium), and underlying heart illness all influence the electrocardiographic symptoms of hyperkalemia. Patients with hyperkalemia and aberrant ECG findings had a greater mortality rate, according to retrospective data (Durfey *et al.,* 2017). Because the potassium pool is primarily intracellular, changes in cellular potassium absorption can play a significant role in hyperkalemia (Kovesdy *et al.,* 2017).

Asystole, ventricular fibrillation, and cardiac arrest are all risk factors for hyperkalemia (Goyal *et al.,* 2012). Hyperkalemia, on the other hand, was found to be associated with a subset of patients who had advanced disease and were receiving less intensive treatment than suggested by guidelines (Sarwar *et al.,* 2016). Magnesium in this study showed highly significant increase in cardiomyopathy patients compared with control. Urdal *et al.* (1992), found that mononuclear cell magnesium concentrations before the magnesium retention test were somewhat greater in patients with acute myocardial infarction than in healthy volunteers, indicating that the acute myocardial infarction group had no magnesium depletion.

Magnesium has an impact on cardiac metabolism, Ca^{2+} homeostasis, and endothelium-dependent vasodilation in the cardiovascular system. It has antihypertensive, antidysrhythmic, anti-inflammatory, and anticoagulant properties. Opening of L-type Ca^{2+} channels in the heart results in a long-lasting Ca^{2+} current, which corresponds to the second phase of the cardiac action potential. Mg^{2+} blocks these channels, preventing Ca^{2+} excess and cell death, and so protecting the myocardium (Fiorentini *et al.,* 2021). Other mechanisms that Mg^{2+} has on cardiomyocytes include its ability to compete with Ca^{2+} for binding sites in proteins including calmodulin, troponin C, and parvalbumin, to act as substrate in a complex with ATP for cardiac Ca^{2+}- ATP ases, and to affect the affinity of the Na^{+}- Ca^{2+} exchanger (Severino *et al.,* 2019).

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