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Study of some Hematological and Physiological Parameters and Electrolytes in Cardiomyopathy Iraqi Patients

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Abstract: Cardiomyopathy (CM) is a condition that affects the heart muscle and can lead to heart failure. It can be dilated, hypertrophic, or restricted. This study was aimed to investigate the level of physiological and biochemical parameters in CM. Sixty patients with age (40-70), and thirty healthy controls with the same age range, were involved in this study during their attendance to Iraqi Center for Heart Diseases, Ghazy Al-Hariri Hospital for Surgical Specialties in the Medical City in Baghdad. The patients were diagnosed by an expert cardiologist. The study was conducted from November 2021 to April 2022, and approved by ethical committees: Ref.:0CSEC/0121/0074 on October 20, 2021of Department of Biology, College of Science, University of Baghdad. Blood samples and data were collected to evaluate the level of complete blood counts (CBC), some biochemical parameters like Troponin T, creatine kinase - MB (CK-MB), C-reactive protein (CRP), Lactate dehydrogenase (LDH), and blood electrolytes like (Magnesium Mg++, Sodium Na^{+}, Potassium K^{+}, and Calcium Ca^{++}) for the patients and control. Results appeared that mean total WBC count, Lymphocyte, and Monocytes percentages were significantly ($P \leq 0.01$) increased in CM patients as compared with control, while there was a highly significant ($P \leq 0.01$) decrease in RBC, Hb, and HCT in CM patients as compared with control, the levels of CK-MB, LDH, and CRP in CM patients was a significant increase as compared with the control group. Referring to electrolytes results, the levels showed that there was a significant ($P \leq 0.01$) increase in the levels of both Mg+2 and k+ in patients with CM as compared with the control group, While the level of Na+ was decreased in CM patients. It can be concluded from the current results that the wide range of biochemical abnormalities play a major role in the pathogenicity of CM patients.

Keywords: Cardiomyopathy; biochemical parameters; Troponin T; CK-MB.

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Introduction

Cardiomyopathy (CM) is a diverse collection of illnesses of the myocardium, typically with inappropriate ventricular hypertrophy or dilatation. It is an anatomical and pathologic diagnosis connected to muscular or electrical malfunction of the heart. It frequently results in cardiovascular mortality or progressive heart failure-related impairment and may be heart-specific or a component of a more widespread systemic illness (1).

Dilated cardiomyopathy (DCM) is a nonischemic condition that affects the myocardium and has structural and functional abnormalities. The clinical features of DCM are if the arterial muscles of the heart are dilated or systole, resulting in valvular disease, genetically transmissible heart disease, or hypertension (2). Currently, DCM is the second most common heart failure phenotype and indication for heart transplantation and is also a feature of systemic disorders (autoimmune, endocrine, neuromuscular or infectious diseases, iron overload, and sarcoidosis) (3).

Hypertrophic cardiomyopathy (HCM) is in virtually every instance, this condition is hereditary and is

defined by an increase in the number of heart muscle cells. This disease is caused if any mutations occur in genes responsible for the coding of sarcomeres protein, and resulting myocyte disarray which is a characteristic of HCM (4).

Restrictive cardiomyopathy (RCM) is a myocardial disorder that usually results from increased myocardial stiffness that leads to impaired ventricular filling. Biventricular chamber size and systolic function are usually normal or near-normal until the later stages of the disease. The affecting either or both ventricles (5).

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) (6). 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 (7). Because they are the most sensitive and cardiac-specific laboratory measurements of myocardial injury they are the biomarkers of choice for the diagnosis of myocardial injury (8).

Lactate dehydrogenase is an enzyme located in the cytoplasm that is widely expressed in tissues. The enzyme converts pyruvate, which is the final product of glycolysis, to lactate when oxygen is in short supply, and it is detectable in the serum. Conditions that can cause increased LDH include tissue injury, necrosis, hypoxia, hemolysis, or malignancies Serum levels of the enzyme LDH are useful indicators of disease severity in a variety of tissues, making their measurement essential in clinical practice. LDH can be used as a marker for many different types of tissue injury thanks to its ubiquitous presence and specific isozyme form, LDH is released into the bloodstream by injured cells (9).

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 (10).

Material and methods

Sixty patients (men and women) with CM after being diagnosed by the physician and thirty healthy subjects with the same age range (40-70) were intricated in the study during their attendance at Iraqi Center For Heart Diseases, Ghazy Al-Hariri Hospital for surgical specialties in the Medical City in Baghdad. The patients were diagnosed by an expert cardiologist based on ECG changes, Echocardiogram, and chest x-ray. The study was conducted from November 2021 to April 2022 and approved by ethical committees: Ref.: CSEC/0121/0074 on October 20, 2021, of the Department of Biology, College of Science, University of Baghdad. Blood samples were gathered from all the subjects involved in the study. The blood sample were collected and divided into two parts, the first part was transferred to an EDTA tube for determination of CBC, and the second part was transferred to a gel tube and

allowed to coagulate. Serum was separated after centrifugation for 10 minutes at 3000 rpm and transferred to clean plastic tubes by micropipette and kept at -20C for biochemical measurements like Troponin, LDH, CRP, and CK-MB, electrolytes include Ca^{+2}, K^{+}, Na^{+} and Mg^{+}. The CBC measurement was done by automated digital counting equipment manufactured (BC-5000) by mindray which is 5-auto analyzer of the automatic differential part of hematology, while the measurement of Troponin T, CK-MB, CRP, and LDH levels were carried out by a fully automated analyzer Roche e411 (Germany) which is designed for determinations for a broad range of applications including hormone. Sodium Ca^{+2}, K^{+} and 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 different factors on study parameters. T-test was used to significantly compare between means. All results were expressed as mean ± SE (11).

Result and discussion

Total and differential counts of leukocytes in cardiomyopathy patients and control

The results of total and differential counts of leukocytes are illustrated in table (1). The mean total WBC count showed a highly significant increase ($P<0.01$) in CM patients as compared with control. Also, the percentage of Lymphocyte and Monocytes showed a highly significant increase ($P<0.01$) in CM patients as compared with control, while the percentage of Neutrophils, Eosinophils, and Basophils showed non-significant differences ($P\geq 0.01$) in the patients with CM patients as compared with control.

Table (1): Total and differential counts of WBC in cardiomyopathy patients and control.

Group	Mean ± SE					
	WBC $10^3/mm^3$	Lymphocyte %	Monocytes %	Neutrophils %	Eosinophils %	Basophils %
Patients	8.57 ±0.32	34.00 ±1.78	8.44 ±0.73	51.39 ±1.98	4.83 ±2.01	1.34 ±0.85
Control	6.10 ±0.33	28.60 ±1.66	6.24 ±0.23	60.32 ±1.76	4.37±0.33	0.470 ±0.05
T-test	1.028 **	5.295 **	2.098 **	6.120 NS	2.640 NS	2.404 NS
P-value	0.0001	0.0028	0.0016	0.0938	0.733	0.473
** ($P\leq0.01$), NS: Non-Significant.						

In the present study, the WBC count for CM patients was highest than in the control group. This is in agreement with the results of Barron *et al.* (2000) who discovered that an elevated WBC is linked to an increased risk of HF in patients who had a myocardial infarction(12). In human DCM patients with significant left ventricular dilatation, the WBC count upon hospital admission predicts mortality and is thus an independent predictor of mortality in these individuals, while physiological stress is linked to leukocytosis in humans, relative leukocytosis in human HF is thought to be part of a larger inflammatory response (13). Leukocytes play a key role in the early inflammatory response with a healing function, favoring the creation of a scar following an acute myocardial

infarction. It is self-evident that infarcts of greater size are more likely to develop consequences of HF, and mortality (14).

The highly significant (P<0.01) increase of Lymphocyte and Monocytes in cardiomyopathy patients' agreement with the study done by Wrigley *et al*. (2011) who showed that patients at risk of readmission to the hospital for worsening HF and there is accumulating evidence to suggest the crucial role of inflammatory cells, particularly monocytes and macrophages, in the pathophysiology of HF (15). Leukocytes and their subsets (neutrophils, monocytes, and lymphocytes) have been implicated in the onset and progression of cardiovascular illnesses in numerous investigations (16). Monocytes have been implicated in the etiology of hypertension and cardiac remodeling (17). Classical monocytes, also known as CD14, and CD16 in humans, have been linked to inflammation, the bone marrow, and extramedullary sites of hematopoiesis, such as the spleen, release these cells (18).

Table (2): Blood parameters level in Cardiomyopathy patients and control.

Group	Mean ± SE			
	RBC 10^6/µL	**Hb g/dl**	**HCT %**	**PLT 10^3/mm^3**
Patients	4.65 ±0.09	10.39 ±0.36	34.12 ±0.94	240.52 ±11.2
Control	5.08 ±0.10	13.37 ±0.20	40.29 ±0.65	253.83 ±24.1
T-test	0.312 **	0.761 **	2.268**	46.179 NS
P-value	0.0072	0.0079	0.0035	0.568
** (P≤0.01), NS: Non-Significant.				

Blood parameters level in cardiomyopathy patients and control

The mean of RBC, Hb, and HCT showed a highly significant (P<0.01) decrease in patients with CM patients as compared with control, while the mean PLT appeared to be non-significant differences (P≥ 0.01) in patients with CM as compared with control as shown in table (2).

Red blood cell transfusion practices in critically sick patients are driven by hemoglobin level thresholds, with other patient characteristics such as increased age, the severity of illness, gastrointestinal bleeding, concomitant cardiac disease, and sudden myocardial infarction all having an impact (19).

Patients in the current study presented with lower RBC count, Hb, and HCT, the result of the study is similar to Cho *et al.* (2014) which showed that LV enlargement was linked to increased anemia severity, as measured by decreased RBC counts and Hb, as well as qualitative RBC abnormalities (20). Severe iron deficiency anemia has been reported to play a pivotal role in the development of HF through left ventricular dysfunction and myocardial damage, however, the pathogenesis of cardiomyopathy associated with anemia is unknown due to the limited number of affected patients (21).

Anemia is prevalent comorbidity in individuals with chronic heart failure, and it's linked to greater all-cause and cardiovascular mortality, decreased exercise capacity due to decreased oxygen carrying and storage capacity, lower quality of life, and a higher chance of hospitalization (22). Iron deficiency anemia, in particular, has been implicated in the development of cardiomyopathy (23).

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, While the level of Troponin T showed non-significant (P≥ 0.01) differences table (3).

Table (3): Levels of CK-MB, CRP, LDH, and Troponin T in cardiomyopathy patients and control.

Group	Mean ± SE			
	CK-MB U/L	CRP mg/L	LDH U/L	Troponin T ng/ml
Patients	22.50 ±1.21	10.92 ±0.86	310.08 ±10.80	0.262 ±0.01
Control	9.99 ±0.48	2.052 ±0.18	201.36 ±8.95	0.282 ±0.02
T-test	3.472 **	2.457 **	32.915 **	0.049 NS
P-value	0.0001	0.0001	0.0001	0.421
** (P≤0.01), NS: Non-Significant.				

In the present study the levels of CK-MB, LDH, CRP, and troponin T were measured to evaluate whether cardiac abnormalities existed in patients with CM compared with control. According to the results of this study, there was a highly significant (P<0.01) increase in CK-MB level in patients with CM compared with control, and this finding was according with research of Aboughdir *et al*. (24). The CK-MB, which is located 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 (24). However, the CK-MB fraction quickly superseded CK and is now considered to be the gold standard(25). For decades, it was the most effective early detection marker. The ideal time for detection is between 6 and 48 hours after the event has occurred(26).

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(27).

Cardiomyopathy patients were found to have higher levels of CRP compared to controls. The patient's preexisting inflammatory state can be seen reflected in this statistically significant increase. The findings are consistent with those of Feng *et al*. (2022), who also found elevated CRP levels in DCM (28).

Patients with DCM who have left ventricular systolic dysfunction and larger right ventricular and left atrial diameters are more likely to have elevated CRP (29). Recent study done by Akhtar and Elliott, (2019) suggested that C-reactive protein is a marker of inflammation, and significantly higher levels have been shown to be present in DCM patients dying within 5 years of hospitalization compared to survivors (30). All of these results suggest that the CRP value is a useful biomarker for predicting the outcome of DCM patients (31).

There was a highly significant (P< 0.01) increase in LDH level in patients with CM compared with control, this results in agreement with (32). According to a recent study, an elevated serum LDH level may indicate how severe the damage to the myocardium is as well as a decreased level of cardiac function (33).

The biochemical test for cardiac enzymes is a helpful tool for evaluating the health of the heart muscle and reducing the risk of HF in patients (34).

Piper *et al*. (35) also identified an increase in serum LDH isozyme in people with valvular heart disease and cardiomyopathy due to volume and pressure overload, which is consistent with the findings of the present study(35).

With regard of Troponin T 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 (36).

The result of this study is also similar to the finding of Al- Otaiby *et al*. (37). Troponin is a powerful predictor of prognosis and has a high specificity and sensitivity for detecting myocardial necrosis (37). 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 (38).

Levels of electrolytes in cardiomyopathy patients and control.

The results of electrolytes are illustrated in table (4). The levels of Mg+2 and k+ showed a highly significant (P<0.01) increase in patients with CM compared with control. while the levels of Na+ showed a highly significant (P<0.01) decrease in patients with CM as compared with control, and the level Ca+2 showed a non-significant (P ≥0.01) difference in CM patients compared with control.

Table (4): Levels of electrolytes: Magnesium, Potassium Sodium, and Calcium, in cardiomyopathy patients and control.

Group	Mean ± SE			
	Mg+2 mg/dl	K+ mmol/L	Na+ nmol/L	Ca+2 mg/dl
Patients	2.19 ±0.04	4.67 ±0.11	129.45 ±2.60	9.28 ±0.09
Control	1.83 ±0.09	3.85 ±0.12	140.62 ±1.09	9.27 ±0.06
T-test	0.187 **	0.358 **	7.503 **	0.276 NS
P-value	0.0002	00001	0.004	0.908
** (P≤0.01), NS: Non-Significant.				

Both high and low electrolyte levels are related to unfavorable cardiovascular outcomes, implying that a delicate balance of electrolytes crucial in regulating cardiovascular excitability is required, without which arrhythmias and sudden death may occur (39).

Magnesium in this study showed a highly significant increase in cardiomyopathy patients compared with control. The findings of this study are similar to Cheungpasitporn *et al.* (2015). 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(40). 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 (41). 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 (42).

Potassium levels in the current study showed a highly significant increase in CM patients compared with control, this contradicts the results of other investigations, which discovered that high-normal serum K+ levels were harmless and produced the same clinical outcome as normal K+ levels (43). Hyperkalemia and hypokalemia, two types of abnormalities in serum potassium, are common in the HF population and are frequently associated with adverse outcomes (44).Serum Na+ showed a highly significant difference between cardiomyopathy patients with lower serum Na+ compared with control, this result agrees with Ali *et al*. (2016) that reported (hyponatremia) low Na+ is common in patients hospitalized with HF, similar finding observed by Hamaguchi *et al*. (2014) (45-46). Sodium is thought to be one of the most powerful prognostic indicators in both acute and chronic settings and has aroused a lot of interest in determining its role as a potential therapeutic target in HF (47,48,49). Many studies in the field of HF and CM have focused on sodium, the fundamental element of fluid balance and a significant regulator of extracellular volume in HF (50,51). Hyponatremia is one of the most common electrolyte abnormalities encountered in cardiomyopathy and HF (49).

Conclusion

Together all of these data indicate that patients with CM have a wide range of biochemical abnormalities, and it can be concluded that they have a variety of physiological issues. the strength of evidence, based on an assessment of prior supporting research offers a clearer risk profile for individuals with CM. Additionally, hematological, physiological parameters, and electrolytes can be used to identify high-risk individuals who require closer monitoring and more intensive treatment.

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