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Evaluation of Myostatin Protein in Serum of Cardiac Patients

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ABSTRACT

In order to assess the significance of myostatin protein with some biochemical parameters in the blood serum of myocardial infarction and atherosclerosis patients. The study included 60 samples of heart patients (30 samples of myocardial infarction patients and 30 samples of patients with atherosclerosis) whose ages ranged from 35 to 65 years, in addition to 30 samples of healthy people of the same age group. Results revealed a marked rise in the level of myostatin protein in the myocardial infarction and atherosclerosis patients in comparison to healthy group, and rise in troponin protein in myocardial infarction patients. According to the findings, total cholesterol, triglycerides, low-density lipoproteins, and very-low-density lipoproteins were all significantly higher in the two patients groups than in healthy group, whereas high-density lipoprotein levels were significantly lower in both patients groups. The results indicated that calcium level had significantly decreased in myocardial infarction patients, but no change in phosphate level between groups. The findings revealed a significantly lower of glutathione and a significantly higher of malondialdehyde in the two patients groups as compared to the healthy group. In conclusion, the obtained data were directly aligned with the study hypothesis, showing significant elevation of myostatin and associated biochemical changes relevant to the pathophysiology of myocardial infarction and atherosclerosis, thus supporting the study objective. Results suggest myostatin as a potential supplementary biomarker and highlight useful biochemical alterations for patient assessment; however, lack of established diagnostic cut-offs, limited routine availability of myostatin testing, and small sample size may limit immediate clinical application.

Keywords: Myostatin, Troponin, Lipids profile, Myocardial infarction atherosclerosis.

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Introduction

Myostatin, also known as growth and differentiation factor, is one of the main regulators of skeletal muscle growth. The myostatin gene is highly conserved among mammalian species, and works in an almost unique way to reduce muscle size. Animals deficient in myostatin show an increase in skeletal muscle mass known as paired muscles. Mutations in myostatin have also been described in many species including dogs, sheep, and cattle. Myostatin is expressed in many tissues (including the mammary gland). but most prominently in skeletal muscle [1].

The function of myostatin has been revealed through genetic studies which have shown that mice with the deletion have myostatin skeletal muscle mass has increased significantly across the body as a result of the mutation, with individual muscles increasing to nearly twice their usual size. Later research revealed that the myostatin gene had undergone substantial conservation since the mature myostatin's amino acid sequence was the same in many animals including humans. Targeted or spontaneous alterations, as well as myostatin's role as a negative regulator of skeletal muscle hypertrophy, have all been acknowledged. After myostatin was discovered, a significant effort was made to study the cellular and molecular processes behind myostatin function with the long-term objective of creating methods to interfere with the therapeutic signaling pathway [2].

Elevated myostatin levels have been implicated in various pathological conditions beyond cardiovascular disease. In metabolic disorders such as type 2 diabetes mellitus and obesity, increased circulating myostatin is associated with insulin resistance, chronic low-grade inflammation, and reduced muscle mass, which may exacerbate metabolic dysregulation [3,4]. In chronic kidney disease, higher myostatin concentrations are linked to protein-energy wasting and sarcopenia, contributing to poor patient outcomes [5]. In neuromuscular disorders, including muscular dystrophy and cachexia associated with cancer or chronic illness, excessive myostatin activity promotes muscle atrophy [6].

Moreover, experimental and clinical studies suggest that myostatin plays a role in the pathophysiology of heart failure and post-myocardial infarction remodeling, potentially influencing cardiac muscle fibrosis and function [7,8]. These correlations demonstrate myostatin's versatility as a biomarker and possible target for treatment in a variety of illnesses involving chronic inflammation, oxidative stress, and muscle metabolism.

This study aims to assess the clinical significance of serum myostatin levels in patients with myocardial infarction and atherosclerosis and to explore their relationship with various biochemical parameters, including cardiac injury markers (troponin), lipid profile

components, calcium and phosphate levels, and oxidative stress/antioxidant status (malondialdehyde and glutathione). The objective is to determine whether myostatin can serve as a supplementary biomarker for the diagnosis, prognosis, and risk assessment of cardiovascular diseases, as well as to provide insight into the underlying biochemical alterations associated with these conditions.

Materials and Methods

Samples Collection

The study included 60 blood samples of people with cardiac diseases, and they were divided into two groups: patients with myocardial infarction and patients with atherosclerosis, and their ages ranged from 35 to 65 years. The study also included 30 samples of healthy people of the same age. Samples were collected from patients attending Azadi Teaching Hospital for the period between 2/15/2023 to 4/29/2023.

Blood Collection

Blood samples were collected by drawing 5 ml of venous blood using a sterile medical syringe, and placed in Plain tubes with a tight-fitting cover free of anticoagulant, and the tubes were left at room temperature (25 °C) until coagulation was completed, after that placed In a centrifuge 10-minute period at a pace of 704 xg, then withdraw the solution with a micropipette and divide the obtained serum into five parts with an Eppendorf tube to avoid decomposition of samples during the process of repeated thawing and freezing of the sample and keeping the serum in the freezer at -20ºC until the required examinations are carried out in the study.

Biochemical Parameters

The concentration of myostatin protein and troponin were estimated utilizing the method enzyme-linked immunosorbent assay (ELISA) technique, according a proven method in a kit prepared by Bioassay Technology Laboratory (BT LAB), China, with codes E0403Hu and E0416Ca respectively. Cholesterol, triglycerides, high-density lipoprotein cholesterol, calcium and phosphate were determined using a spectrophotometer, according a proven method in a kit prepared by Bio Maghreb. Serum MDA activity was measured by thiobarbituric acid (TBA) reaction method described by and Shah and Walker's based on TBA, the method is based on the reaction between lipid peroxides, mainly MDA, and TBA in an acidic medium and produces a colored product is measured at 532 nm [9]. Reduced glutathione was determined in serum using the modified Sedlak and Lindsay method (180). The method relies on the use of Ellman's reagent, which contains 5-5-Dithio bis-2-Nitrobenzoic acid (DTNB), which reacts rapidly with glutathione and is reduced by the sulfhydryl group of glutathione to produce a yellow compound with the highest absorbance at 412 nm [10].

Statistical Analysis

Analysis performed using GraphPad Prism version 7. Results were expressed as mean ± standard deviation. ANOVA analysis was used to determine significant differences among three group means for quantitative data, a probability level of $p \leq 0.05$ was considered statistically significant to calculate the mean and standard deviations (S.D).

Results and Discussion

The findings in Table 1 are representative of the mean ± the SD of the levels of myostatin protein and troponin in the two patients and healthy (control) groups. The results show that there is a significant increase in the level of myostatin protein in myocardial infarction patients group compared to the healthy group, and there is no significant difference between the two groups of atherosclerosis patients and the healthy group. The outcomes also show that there has been a notable rise in the degree of troponin protein in myocardial infarction patients group compared to the healthy group, while the atherosclerosis group did not show any difference with the healthy group.

Table 1. Mean ± SD of Myostatin protein and Troponin in the three groups.

Parameters	Control (n=30)	Myocardial infarction (n=30)	Arteriosclerosis(n=30)
Myostatin (ng/L)	108.277±31.186b	115.412±32.681ab	128.668±31.558a
Troponin (ng/ml)	0.0324±0.007b	20.078±2.169a	0.019±0.001b

* Different letters a,b mean difference significant at P≤ 0.05.

Table 1 shows that the concentrations of hepcidin and iron in thalassemia patients were 1539.846 ± 601.945 ng/ml and 40.673 ± 7.352 µmol/L respectively, while it was 531.048 ± 211.343 ng/ml and 21.587 ± 3.3152 µmol/L respectively in the healthy people. Results showed that the concentrations of hepcidin and iron increased significantly ($p \leq 0.05$) in the thalassemia patients compared to healthy people, as evidenced by figures 1 and 2.

The findings of the present investigation agree with the findings of the researcher Kesik et al [11]. who found an increase in the myostatin protein during the stages of cardiac disease, while in a study conducted by the researcher Elisabet Zamora et al. [12] they found that there was a decrease in the levels of myostatin in cardiac diseases patients compared to with healthy people.

The study's findings, which revealed a notable rise in the amount of troponin in patients with myocardial infarction, agree with Al-Duhaimi et al. [13] and Sandoval

et al [14], where acute heart disease occurs due to the death of heart muscle cells. This leads to the release of different proteins into the bloodstream. Cardiac troponin (cTns) is released from damaged muscle cells and reach circulation quickly, followed by a rapid peak in blood troponin levels in the first few hours [15].

The results of Table 2 show the levels of lipids in the study groups, which indicate a total cholesterol, triglycerides, low-density lipoproteins, and very low-density lipoproteins all increased significantly in the two groups of when patients are compared to the healthy group, there is a noticeable drop in high-density lipoproteins in the two patient groups compared a sound group.

Table 2. Mean ± SD of lipid profile in the three groups.

Parameters	Control (n=30)	Myocardial infarction (n=30)	Arteriosclerosis(n=30)
Cholesterol	161.599±30.627c	180.788±41.098b	203.640±38.060a
Triglycerides	134.758±22.596c	171.692±35.249b	200.314±29.218a
HDL-C	52.203±9.314a	39.620±8.176b	38.737±11.085b
VLDL	26.951±4.519b	34.338±7.049b	40.062±5.843a
LDL-C	82.444±30.616c	106.829±39.981b	124.840±39.527a

* Different letters a,b,c mean difference significant at P≤ 0.05.

The findings of the present investigation concur with those of Nadir et al [16], Al–Zubaidi et al [17], and Obaidi et al [18]. The results indicated that there is a substantial drop in the high-density density level lipids in patients with myocardial infarction compared with the healthy group, as well as there is a substantial the proportion of patients having atherosclerosis in addition to the group that is in good health. This study agrees with the findings of Kulsoom and Hasnain [19] and Mohammed Jaber et al [20].

The outcomes also demonstrated a notable rise in the degree of triglycerides when patients have atherosclerosis and myocardial infarction patients against the group of healthy people. This study agrees with Zrari and Mohammed [21], as well as Rasmussen et al. [22].

The study showed an increase in low-density lipoproteins in heart patients against the group of healthy people, as this study agrees with the results of Yang et al. [23] and Karalis [24]. The study also indicated a significant increase in the level of very low-density lipoproteins in patients with atherosclerosis and myocardial infarction compared to the healthy group. The study agrees with the findings of Shirafkan, A et al. [25].

The study's findings also revealed that there was a substantial decline in level of calcium for myocardial infarction comparing sick to the healthy group, while the atherosclerosis group did not indicate any significant difference. The outcomes also showed that there was no discernible variation in the level of phosphate in the two patient groups compared to the healthy group, as shown in Figures 3 and 4 and Table 3 also.

Table 3. Mean ± standard deviation of calcium and phosphate in the three groups.

Parameters	Control (n=30)	Myocardial infarction (n=30)	Arteriosclerosis(n=30)
Ca (mg/dl)	10.969±1.611a	9.335±0.941b	10.637±0.788a
PO_4 (mg/dl)	4.621±1.731a	4.498±1.729a	5.093±1.998a

* Different letters a,b mean difference significant at P≤ 0.05.

As for the level of calcium, the results of the study may agree with the findings of Kurabayashi [26], the patient's body has an imbalance of calcium ions, which results in secondary hyperparathyroidism, which then causes atherosclerosis [27]. Also, the present study's findings support with Arjwan Abdul-Jabbar [28] concluded with regard to phosphate, as well as a study conducted by the researcher Ramadesikan [29] about measuring the concentration of phosphate in heart patients (myocardial infarction), where it was found that there is very little change in phosphates in patients with myocardial infarction.

The results of Table 4 refer to the results values of glutathione and malondialdehyde, which demonstrated a substantial drop in glutathione levels in the two groups of patients and a substantial rise in level of malondialdehyde in the two groups compared to the number healthy group.

Table 4. Mean ± standard deviation of glutathione and malondialdehyde in the three groups.

Parameters	Control (n=30)	Myocardial infarction (n=30)	Arteriosclerosis (n=30)
GSH(mmol/L)	0.462±0.046a	0.369±0.045b	0.363±0.054b
MDA(µmol/L)	1.622±0.334b	2.013±0.410a	1.969±0.553a

* Different letters a,b mean difference significant at P≤ 0.05.

Conclusion

The results indicate that myostatin may represent an adjunct biomarker that can be used to evaluate patients with myocardial infarction and atherosclerosis. Along with traditional markers such as troponin and blood lipids, changes in myostatin and oxidative stress markers could contribute to a better understanding of risk scores and improve early diagnosis. The results also demonstrated that elevated myostatin is a common factor in both myocardial infarction and atherosclerosis. The study also demonstrated an integrated visualization of biochemical changes associated with cardiac events through biochemical variables such as lipids and ions. Myostatin can also be considered a reliable marker in medical research. The small sample size may limit the generalizability of the results to the wider population. The lack of routine availability of myostatin testing in clinical laboratories hinders the widespread application of the results in daily practice.

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Ethical Approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with a patient s verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a Local Ethics committee Azadi Teaching Hospital / Kirkuk city/Iraq, and University of Samarra, according to the document number 986 and the date in 10/02/2023

Conflicts of Interest

There are no conflicts of interest in this work.

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