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The Correlation of Oxidative Stress Markers and Biochemical Cardiac Enzymes in Iraqi Patients Diagnosed with Acute Myocardial Infraction

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Abstract:

A myocardial infarction (MI), is the irreversible death (necrosis) of heart muscle commonly known as a heart attack. Acute myocardial infarction (AMI) occurs when blood flow decreases or stops to the coronary artery of the heart, causing damage to the heart muscle. MI is associated with an intelligible imbalance in oxidative stress. After myocardial injury, many cardiac biomarkers become detectable in venous circulation such as cardiac enzymes. The study's main goals were to evaluate the clinical significant change in cardiac enzymes and investigate the positive and negative correlation with some serum oxidative stress markers total oxidative state (TOS), free amine and total antioxidant capacity (TAC) in patient and control groups. This study contained 120 subjects who were divided evenly into patients and control groups for the period between July and September 2022. The serum levels of oxidative stress markers were measured manually using spectrophotometer (model, Cecil, CE10N / England). The activity of cardiac enzymes and lipid profile were also determined by using Spectrophotometric kits supplied from Biolabo, France. The study showed that TOS had a significantly positive correlation with CK (r = 0.269*, p= 0.038) and ALT (r = 0.259*, p= 0.046), also for free amine, TnI (r = 0.287*, p= 0.026). Moreover, cardiac Troponin had highly positive correlation with oxidants and enzymes of the cardiomyocyte.

Keyword: Myocardial Infarction, Oxidative stress, TOS, Antioxidants

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1-Introduction

Cardiovascular disease (CVD) encompasses multiple disorders affecting the circulatory system, which includes the heart and blood arteries [1]. One American died every 40 seconds in 2010 from cardiovascular disease, contributing to a total mortality rate of 235.5 per 100,000 [2]. In 2018, the number of deaths caused by Coronary Heart Disease in Iraq amounted to 32,463, accounting for 18.92% of the total deaths. With an adjusted mortality rate of 230.27 per 100,000 people, Iraq is ranked 20th globally [2], [3]. The current MI prevalence rate is 1,653 per 100,010 people, with research predicting that this number will rise to 1,845 by 2030 [4].

A myocardial infarction (MI), is the irreversible death (necrosis) of heart muscle commonly known as a heart attack. Damage to the heart muscle, known as acute myocardial infarction (AMI), happens when blood flow to the heart's coronary artery reduces or stops [5]. Also for prolonged lack of oxygen supply (tissue death or infarction of the myocardium caused by ischemia), that is lack of oxygen delivery to myocardial tissue [6]. The primary cause of myocardial infarction is the rupture of an atherosclerotic plaque on a coronary artery that supplies blood to the heart muscle [7]. Plaque can rupture causing a blood clot to develop and obstruct the artery and that can happen in a matter of minutes. If an artery becomes obstructed, the tissue that relies on that artery for nourishment may undergo necrosis [8]. Metabolic mechanisms, together with advancing age, significantly contribute to the development of atherosclerosis. Specifically, dyslipidemia was recognized as a significant risk factor over fifty years ago. Smoking is responsible for approximately 38% of cases of coronary artery disease, whereas obesity is responsible for about 20% [9]. Stress-related reasons such as job stress, which account for roughly 3% of cases, are among the less prevalent causes [9],[10]. Another significant risk factor is hypertension, diabetes mellitus, elevated blood cholesterol levels, specifically high levels of low-density lipoprotein, low levels of high-density lipoprotein, and elevated triglycerides [11]. After myocardial injury, many cardiac biomarkers become detectable in venous circulation such as cardiac enzymes lactate dehydrogenase (LDH), Creatine kinase myocardial band (CK-MB), aspartate amino transferase (AST), troponin I (TnI), and many other inflammatory markers. The C-Tn, or cardiac troponin, is a trimeric complex consisting of three regulatory proteins: troponin C, troponin I, and troponin T. These

proteins play a crucial role in the process of muscle contraction [12]. C-TnI and enzymes are crucial indicators for diagnosing and assessing the risk of individuals with symptoms indicating acute MI. The levels of troponin increase during a period of 3 to 4 hours following the onset of damage and remain elevated for a duration of 4 to 7 days for troponin I or 10 to 14 days for troponin T [4]. CK-MB is an isoenzyme of the enzyme CK, which constitutes around 30% of the CK present in the myocardium. An increase of more than 5% in the overall CK activity indicates injury to the heart muscle [13]. A blood level of CK-MB first occurs 4–6 hours after the onset of chest discomfort, and reaches its maximum level 10–12 hours following a myocardial infarction [14]. Myocardial ischemia can also be diagnosed using lactate dehydrogenase (EC 1.1.1.27), which is present in the blood and rises 6-13 hours after an acute MI, peaks between 24-72 hours, and then returns to normal between 8-13 days [15]. Another biomarker that can help in the diagnosis of acute MI is AST (EC 2.6.1.1). Blood AST levels rise 3–5 hours following an acute MI, reach a peak at 15–28 hours, and then drop back down to baseline within 5 days [16]. Reactive oxygen species (ROS) are free radicals a kind of electrically charged species that have one or more unpaired electrons in their outer orbital. Any molecule containing highly reactive oxygen, for instance, has free radicals [17]. Cellular function is disrupted and a number of clinical illnesses result from oxidative stress, which occurs when the equilibrium between ROS production and antioxidant defense is disturbed [18]. ROS are involved in a number of human disorders, including cardiovascular disease, since they can damage or destroy cells by attacking proteins, carbohydrates, nucleic acids, and polyunsaturated fatty acids [19]. Free radicals possess the capacity to selectively attack and harm the peptide backbone as well as the amino acid side chains of proteins, leading to the creation of diverse radical protein derivatives [20]. In respect of cleavage of the peptide backbone, the reaction pathway free amine and carbonyl fragments. Antioxidants, like vitamin C, are substances that safeguard cells from the harm inflicted by free radicals through accepting or donating electron (s) to remove the unpaired radical [17],[21]. The study main goal where to investigate the significant positive and negative correlation of cardiac enzymes with myocardial oxidative cellular damage and antioxidant levels for early predict and treat ischemic heart attack (MI).

2-Material and methods

The research included 120 participants, 60 of whom served as healthy controls and 60 of whom were identified as having acute myocardial

infarction (AMI) according to patient history, symptoms, electrocardiogram (ECG), and positive cardiac troponin. The study included only men aged between 45-63 years and the healthy subjects were collected from Mustansiriyah University, as well as AMI patients were collected from Baghdad teaching hospital-medical city, Baghdad, Iraq between July and September 2022. Patients provided blood samples for the study (3-5 mL), which were collected from the brachial vein using sterile syringes and kept at room temperature for 10 minutes, then centrifuged for five minutes at a speed of 3000 rpm to separate the serum, after that the obtained serum were stored at -20ºC until the time of analysis. Patients with any associated disease were excluded. Cardiac troponin reader used for cardiac troponin I in the samples both before and after IgG depletion. The activity of AST, ALT, ALP, CK, and lipid profile was determined by using Spectrophotometric (model, Cecil, CE10N / England) commercial kit supplied from Biolabo, France. Spectrophotometric Erel method was used to determine TOS and TAC value in the samples [22]. The method of Zaia et al. was used for spectrophotometric measurement of free amino groups [4].

3-Statistical analysis

Statistical analysis values were explained as mean ± standard deviation (SD). The comparison of was performed using Independent-Samples student's t-test where the difference is considered as highly significant when ($p<0.001$), significant when ($p<0.05$) and nonsignificant when ($p>0.05$). In addition, Pearson's correlation analysis is carried out to determine the relationships between all study variables.

4-Result

The obtained results showed that the mean age of MI patients and control were (55.45 ± 6.93), (53.91 ± 5.7) with a non-significant ($p>0.01$). Also, weight, height, and BMI mean values were non-significant ($p>0.01$). These non-significant obtained results for age and BMI provide a unique opportunity to conduct a comparative study accurately. The study showed that serum TOS, free amine, TnI, and VLDL significantly increase ($P<0.05$) in AMI patients than those of control group as shown in Table (1).

Table (1): The statistical disparities between patients and controls with respect to the parameters.

	Group-A		Group-B		
Parameters	**Mean**	**SD**	**Mean**	**SD**	***P*-value**
Age (year)	53.91	5.70	55.45	6.93	0.183 **NS**

BMI (kg/m^2)	25.52	3.51	26.49	3.95	0.216 **NS**	T
TOS (µmol Eq. /L)	1.374	0.575	3.99	1.256	0.0491* **S**	OS
Free amine (mmol/L)	31.28	8.829	43.39	11.84	0.003* **S**	had a
TAC (µmol Eq. /L)	1.425	0.383	0.571	0.103	0.0002* **S**	signifi
TnI (ng/ml)	0.031	0.047	20.48	16.92	0.001* **S**	cantly
CK-MB (IU/L)	114.72	105.8	807.8	431.21	0.001* **S**	positi
AST (IU/L)	20.35	9.058	94.05	48.87	0.0005* **S**	ve
ALT (IU/L)	15.58	4.295	36.67	18.65	0.063 **NS**	correl
ALP (IU/L)	60.53	20.28	99.59	33.14	0.010* **S**	ation
Chol (mg/dl)	170.1	32.45	179.49	50.6	0.227 **NS**	with
TG (mg/dl)	134.35	59.11	171.08	94.7	0.012* **S**	CK (r
HDL (mg/dl)	32.575	11.58	32.92	9.71	0.858 **NS**	=
LDL (mg/dl)	111.84	29.98	115.04	37.133	0.604 **NS**	0.269
VLDL (mg/dl)	26.55	12.05	34.24	19	0.009* **S**	*, p=

***Significant at *P*<0.05, NS: Non-Significant.** 0.038) and ALT (r = 0.259*, p= 0.046), (Table-2 Figure-3), also for free amine, TnI (r = 0.287*, p= 0.026) (Table-2 Figure-1, 2). Moreover, cardiac TnI had highly positive correlation with CK, AST and Chol while, negative for TG, LDL and VLDL as shown in (Table-2 and Figure-4, 5).

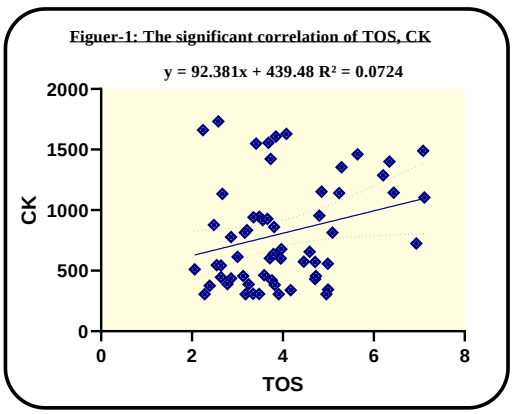
Table (2): The correlation coefficient (*r*) of cardic enzymes and oxidative markers.

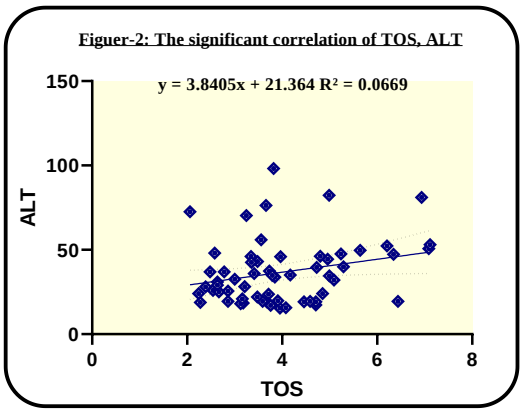
COR.	TOS	Free Amie	TAC	Trop oninI	VLD L
TnI	0.158	0.287 *	-0.090	1	-0.308 *
	0.229	0.026	0.494	-	0.017
CK	0.269 *	0.224	0.123	0.532 **	-0.227
	0.038	0.085	0.348	0.000	0.081
AST	0.163	0.197	-0.133	0.579 **	-0.266 *
	0.214	0.132	0.310	0.000	0.040
ALT	0.259 *	0.203	0.144	0.172	-0.194

	0.046	0.120	0.271	0.188	0.137
ALP	0.072	-0.012	0.241	-0.150	-0.048
	0.584	0.929	0.063	0.253	0.714
Chol	-0.181	-0.189	0.046	0.369**	0.453**
	0.167	0.149	0.724	0.004	0.000
TG	-0.078	-0.088	-0.012	-0.311*	1.00**
	0.555	0.504	0.927	0.015	0.000
HDL	0.145	0.079	0.163	0.028	-0.017
	0.268	0.548	0.215	0.832	0.895
LDL	-0.234	-0.217	-0.021	-0.268*	0.092
	0.072	0.096	0.874	0.038	0.483
VLDL	-0.079	-0.089	-0.015	-0.308*	1
	0.546	0.501	0.911	0.017	-

****Correlation is significant at the 0.01 level (2-tailed).**

***Correlation is significant at the 0.05 level (2-tailed).**





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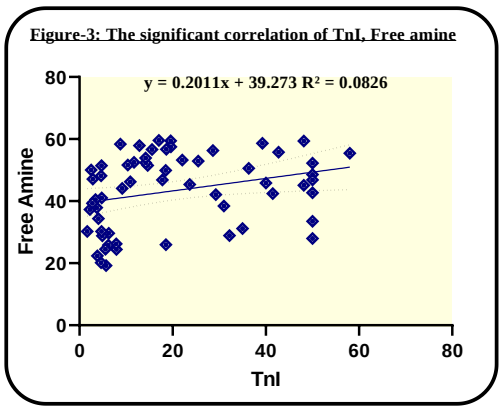

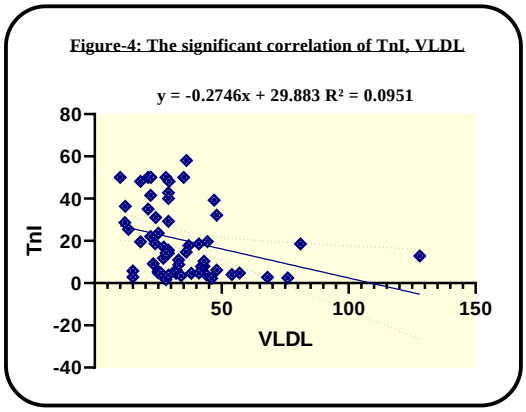

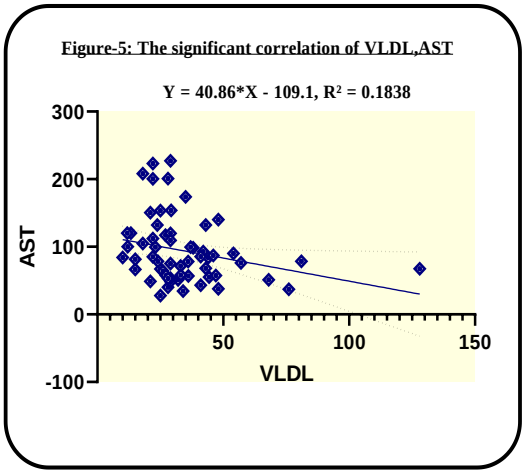

5-Discussion

In both underdeveloped and industrialized nations, myocardial infarction ranks high among the causes of death from cardiovascular disease. AMI is the main cause of mortality as the high death rate is almost epidemic [23]. Oxidative stress is a problem for the myocardium in any cardiac disease. Molecules undergo oxidative changes that quantify damage, these changes may serve as diagnostic and prognostic aids [24]. When antioxidants are outnumbered by oxidants, a condition known as oxidative stress sets up and damages cardiomyocytes. However, due of early detection and treatment, mortality has decreased over the previous three decades [25]. After myocardial injury many cardiac biomarker become detectable into venous circulation such as cardiac enzymes TnI, LDH, CK-MB, AST, and many other inflammatory markers. ECG changes, clinical symptoms and changes in cardiac enzymes, had used to diagnose AMI. The most extensively used approach for diagnosis is the electrocardiogram, but many times shows

inclusive pattern. In such cases, serum biochemical indicators of myocardial damage become critical in confirming the diagnosis, so the use of these parameters is very important in the study [26]. Therefore, there was a need to develop new parameters to increase the accuracy of the diagnostic process. The results demonstrate a notable elevation in serum free amine levels, consistent with multiple studies that establish protein oxidation as a key marker of heightened oxidative stress in pathogenic conditions [10]. This current study reveals that there is a significant positive correlation between oxidative stress markers and cardiac enzymes of cardiomyocyte. Free amine and carbonyl groups are an excellent biomarker for protein oxidation. The accumulation of oxidized protein relies on the equilibrium between pro-oxidant, antioxidant, and proteolytic activities [27]. The study believed that oxidative modification of proteins is implicated also in myocardial infarction and another cardiovascular diseases so, free amine and carbonyl are very important markers to determine the accumulation of oxidized protein in MI patients. The total antioxidant capacity of diet associate with lower risk of heart failure. The results are close to the findings of Demirbag et al and other studies in which they have reported significant low levels of TAC in AMI patients compared to normal people [22]. The TAC antioxidants protect cells from the necrosis caused by ROS due to their ability to neutralize these radicals and prevent them from causing damage through scavenging [28]. When antioxidants are present at low concentrations, oxidative stress arises, where there is an imbalance between antioxidants and oxidants [17]. Finally the positive correlation between cardiac enzymes and oxidants give an influential indication for the purpose of diagnosis and treatment.

6-Conclusions

In conclusion, serum oxidants and antioxidant levels may have a good diagnostic role in MI patients, with these data indicating that the positive correlation of TOS, Free amine, TAC with cardiac enzymes may serve for the early detection of AMI and treat.

7-Acknowledgments

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العلاقة بين علامات الاجهاد التأكسدي والانزيمات القلبية البيوكيميائية لدى المرضى العراقيين الذين تم تشخيص إصابتهم باحتشاء عضلة القلب الحاد

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المستخلص :
احتشاء عضلة القلب(MI)، هو تلف (نخر) في خلايا عضلة القلب المعروف باسم النوبة القلبية. يحدث احتشاء عضلة القلب الحاد(MI)عندما ينخفض أو يتوقف تدفق الدم إلى الشريان التاجي ، مما يتسبب في تلف عضلة القلب. يرتبط MI بخلل واضح في الاجهاد التأكسدي. بعد إصابة عضلة القلب ، اظهرت العديد من المؤشرات قابلة للاكتشاف في الدورة الدموية الوريدية مثل إنزيمات القلب. ان الاهداف الرئيسية للدراسة هي تقييم التغير السريري المهم في إنزيمات القلب والتحقق احصائياً من الارتباط السلبي والايجابي مع بعض علامات الاجهاد التأكسدي في الدم (TOS، الفري امين وTAC) في مجموعات المرضى ومقارنتها مع الاشخاص الاصحاء. تضمنت هذه الدراسة 120 شخصا تم تقسيمهم بالتساوي إلى مرضى واصحاء وتم جمع عيناتهم للفترة بين يوليو وسبتمبر(2022) وتم قياس مستويات علامات الاجهاد التأكسدي في المصل يدويًا باستخدام مقياس الطيف الضوئي (نموذج، Cecil، N10CE/إنجلترا). تم أيضا تحديد نشاط إنزيمات القلب ومستويات الدهون باستخدام كواشف المقياس الطيفي المقدمة من شركة Biolabo بفرنسا . أظهرت الدراسة أن TOS كان لها علاقة إيجابية بشكل ملحوظ مع CK (r=0.2369*) ، (p=0.038) و ALT(r=0.259*) (p=0.046)، وكذلك الفري امين، TnI(r=0.287*)، (p=0.026) بالاضافة الى ذلك ، كان للتروبونين علاقة إيجابية بشكل ملحوظ مع المؤكسدات والانزيمات في الخلية العضلية القلبية .

الكلمات المفتاحية: احتشاء عضلة القلب، الاجهاد التأكسدي، TOS، مضادات ألكسدة، أمراض القلب والاوعية الدموية، كواشف المقياس الطيفي.