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Elevation of Serum Mitsugumin 53 Biomarker in ST-Elevation Myocardial Infarction Patients: A Case-Control Study from Southern of Iraq

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ABSTRACT

Background: *ST-elevation myocardial infarction (STEMI) is a medical emergency condition that causes permanent damage to the heart muscle as a result of persistent ischemia that needs a diagnosis and care right away. Mitsugumin 53 (MG53) is a muscle-derived myokine that plays a crucial role in repairing cell membrane damage and protecting tissues, including the heart, after injury such as myocardial infarction.* ***Objectives****: To evaluate the effectiveness of using Mitsugumin 53(MG53), in distinguishing STEMI from healthy controls and assessing their predictive ability in STEMI subtype.* ***Materials and methods:*** *The 46 patients diagnosed with STEMI in the emergency department and 82 healthy controls were included in this study. The levels of MG53 were analyzed using a sandwich-based Enzyme-Linked Immunosorbent Assay technique (ELISA), and other basic biochemical parameters of the study samples were analyzed using a enzymatic methods and a sandwich-based electrochemiluminescence immunoassay technique (ECLIA).* ***Results:*** *Serum levels of MG53 were significantly increased in STEMI patients compared to controls individual. Specifically, STEMI demonstrated higher MG53 concentrations (461.652±38.776 pg/mL vs. 373.232±7.061 pg/mL; P < 0.001). Furthermore, the MG53 biomarker demonstrates outstanding diagnostic performance in STEMI patients as reflected by its ROC curve metrics (cut-off > 381.5 pg/ml, 93.6 %sensitivity, 86.6% specificity, and 97.8 % AUC, p < 0.001).* ***Conclusion:*** *The study demonstrates that blood MG53 level was significantly increased in STEMI patients compared to healthy control. The present study indicates that MG53 is Highly diagnostic and sensitive novel biomarker for ST-elevation myocardial infarction.*

Keywords: ST-elevation myocardial infarction, Mitsugumin53.

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INTRODUCTION

Acute myocardial infarction (AMI) is the most common cardiovascular disease and one of the major causes of morbidity and mortality worldwide. Myocardial infarction is currently recognized as a component of a broader range of conditions known as acute coronary syndrome (ACS), which also encompasses unstable angina [1]. AMI occurs when a portion of the heart muscle (myocardium) undergoes necrosis as a result of ischemia, most often caused by the obstruction of a coronary artery by a thrombus. While the majority of myocardial infarctions involve the anterior or inferior walls of the heart,

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the posterior wall of the left ventricle can also be affected, leading to a posterior myocardial infarction [2]. Nearly half of the potentially salvageable heart muscle is lost within the first hour after a coronary artery becomes blocked, and two-thirds is lost within three hours of the onset of infarction [3]. A complete or partial blockage of a heart coronary artery can cause a heart attack. There are two subtypes of heart attack according to ST segment in electrocardiogram(ECG) findings: the first is ST-elevated myocardial infarction (STEMI), and the second is non-ST-elevated myocardial infarction (NSTEMI) [4]. STEMI is a medical emergency that needs a diagnosis and care right away, in which the culprit artery is complete occlusion and should be distinguished from NSTEMI, unstable angina, and stable angina [5]. Early detection of coronary artery disease can be achieved by assessing dynamic shifts in cardiac troponin levels, analyzing ECG results, and reviewing the patient's clinical symptoms [6].

Although cardiac troponins (cTns) are the gold-standard biomarkers for detecting acute coronary artery disease (CAD) due to cardiomyocyte necrosis, elevated cTn levels can also occur in non-ischemic myocardial injuries—such as myocarditis and cardiotoxicity—as well as in conditions involving multifactorial injury like congestive heart failure and pulmonary embolism. As a result, false-positive cTn results may pose a diagnostic challenge [7]. Electrocardiograms (ECGs) are a crucial tool for diagnosing acute myocardial infarction (AMI), but they have notable limitation [8]. ECGs may fail to detect certain types of AMI, such as infero-posterior infarctions, particularly during the acute phase, where abnormalities might not be evident on the initial reading [9]. Additionally, ECG changes such as ST-segment elevation or depression can occur in non-AMI conditions like early repolarization, hyperkalemia, left ventricular hypertrophy, or pericarditis, leading to diagnostic challenges [10]. Investigators have been examining other CAD biomarkers in the last few years that may be quickly identified in the circulatory system and result in a more precise diagnosis [11].

Mitsugumin 53 (MG53), also known as TRIM72, is a member of the tripartite motif (TRIM) protein family. It features a typical TRIM domain at its N-terminus, which includes a RING finger, a B-box zinc finger, and a coiled-coil region, while its C-terminus contains a SPRY domain [12]. MG53 has a dual function in the heart: it contributes to repairing the cell membrane, thereby preserving myocardial function, while also serving as an E3 ligase that promotes insulin resistance and cardiovascular complications [13]. Emerging studies indicate that MG53 levels may serve as a potential biomarker for cardiovascular diseases (CVD)[14]. In this study, we sought to investigate the levels of Mitsugumin 53 (MG53) in patients with ST-elevation myocardial infarction (STEMI) and assess the diagnostic and predictive potential of MG53 in this patient population.

MATERIALS AND METHODS

A total of 128 participants in a case-control study that included 46 patients (male 37, female 9) and 82 healthy controls (male 44, female 38) were all included in this study. The participants were selected from among those who were treated between September 2024 and January 2025 at the Basra Specialized Hospital for Cardiology and Heart Surgery and the Al-Sader Teaching Hospital in the Basra governorate. Everyone who participated had their blood sample taken, divided into two parts, and centrifuged to obtain serum. However, the initial sample was utilized to measure triglycerides, High density lipoprotein, Low density lipoprotein, total cholesterol, High sensitive troponin, and other tests that applied the exclusion criteria, such as liver function, urea, creatinin, and thyroid stimulation hormone. Mitsugumin 53 biomarker was identified by freezing the second sample at -20°C. A completely automated biochemistry analyzer (Cobas Integra 400 system, Cobas E411) and the

ELISA method (Shanghai Ideal Medical Technology Co., Ltd.) were used for determining all tests. A total of 46 patients were selected in accordance with the established exclusion criteria, the specified time frame, and the conditions prevailing at the sample collection center.

STATISTICAL ANALYSIS

Data were tabulated and analyzed using SPSS version 24. The Kolmogorov-Smirnov test was utilized to assess the normality of scale or continuous variables. Descriptive statistics were presented as frequencies, percentages, and mean ± standard deviation (SD). For group comparisons, the independent samples t-test was applied to normally distributed data, while the Mann-Whitney U test was used for non-parametric data to compare cases (STEMI) with controls. Categorical variables were analyzed using the chi-square (χ^2) test. Pearson's correlation coefficient was employed to evaluate the relationship between lipid profiles and the MG53 biomarker. The predictive value of Mitsugumin 53 for myocardial infarction was assessed using Receiver Operating Characteristic (ROC) curve analysis, with the area under the curve (AUC) reported. Youden's index was calculated to determine optimal cutoff values, sensitivity, and specificity. For all statistical tests, a P-value of less than 0.05 was considered statistically significant.

RESULTS

The study involved 46 individuals known to have myocardial infarction of ST elevation type. In addition, a counterpart of 82 healthy individuals were involved to as control group. Age was statistically comparable (P values >0.05). Sex distribution was different in cases as compared to control group with male patients were represented in a higher proportion in cases (80.4%). Cholesterol was also essentially identical in both groups. However, TG and LDL showed significantly higher levels in cases (p values <0.05), whereas HDL was significantly lower readings as shown in (**Table 1**).

Table 1: Basic characteristics in AMI cases and healthy control.

Items		Cases with STEMI (N =46)	Control (N=82)	P value
Age		56.41±10.81	55.89±10.76	0.793*
Sex	***Males***	37 (80.4%)	44 (53.7%)	0.03**
	Females	9 (19.6%)	38 (46.3%)	
Age	***35-45 years***	10 (21.7%)	13(15.9%)	0.844**
	46-55 years	13 (28.3%)	25(30.5%)	
	56-65 years	12 (26.1%)	25(30.5%)	
	66-77 years	11 (23.9%)	19(23.2%)	
Lipid profile	***Cholesterol***	177.46±50.85	173.61±23.46	0.560*
	TG	174.99±35.65	106.62±22.93	<0.001*
	HDL	32.09±11.64	44.22±6.28	<0.001*
	LDL	154.46±57.36	86.84±8.43	<0.001*

(*Student's t-test / Mann-Whitney's test **Chi-squared test)

Table 2 displays the biomarkers under study in the cases and control groups. STEMI cases exhibited markedly elevated serum levels of MG53 (461.652±38.776 vs. 373.232±7.061pg/ml, P < 0.001) and High-sensitivity troponin I (Hs-TnI) (377.85±532.68 vs. 6.0 ± 2.3 ng/L, P < 0.001) compared to controls.

Table 2: Biomarkers in STEMI and healthy control.

Items	STEMI (N =46)	Control (N=82)	P value*
MG53 (pg/ml)	461.652±38.776	373.232±7.061	<0.001
Hs-TnI (ng/L)	377.85±532.68	6.0 ± 2.3	<0.001

Student's t-test .

The correlation analyses between lipid parameters (cholesterol, TG, HDL, LDL) and biomarkers (Hs-TnI, MG53) in STEMI patients. Significant positive correlations were observed between cholesterol and TG (r = 0.343, p 0.02) , LDL (r = 0.850, p < 0.001) as well as HDL (r = 0.326, p < 0.027). No significant correlations were found between TG, LDL, HDL or MG53 and other biomarkers (p > 0.05). Notably, the strongest association was between cholesterol and LDL, indicating a robust linear relationship in the STEMI cohort. (See the **Table 3**).

Table 3: Correlation of Mitsugumin53 with lipids & Hs troponin in STEMI patients.

Items		TG	HDL	LDL	MG53	Troponin
Cholesterol	***Pearson Correlation***	0.343	0.326	0.786	-0.104	-0.179
	P value	0.020	0.027	<0.001	0.491	0.235
TG	***Pearson Correlation***		-0.198	0.198	0.085	-0.189
	P value		0.187	0.187	0.573	0.208
HDL	***Pearson Correlation***			0.211	-0.027	0.180
	P value			0.159	0.856	0.231
LDL	***Pearson Correlation***				0.046	-0.167
	P value				0.763	0.267
MG53	***Pearson Correlation***					-0.207
	P value					0.168

ROC curves were plotted for MG53 to examine the predictive ability of MG53 biomarker. the diagnostic performance of MG53 using ROC curve analysis (cut-off > 381.5pg/ml) achieved 93.6 %sensitivity, 86.6% specificity, and 97.8 % AUC (p < 0.001). MG53 biomarker demonstrated high accuracy (90.1%), supporting their utility as non-invasive diagnostic tools for STEMI **(Figure 1).**

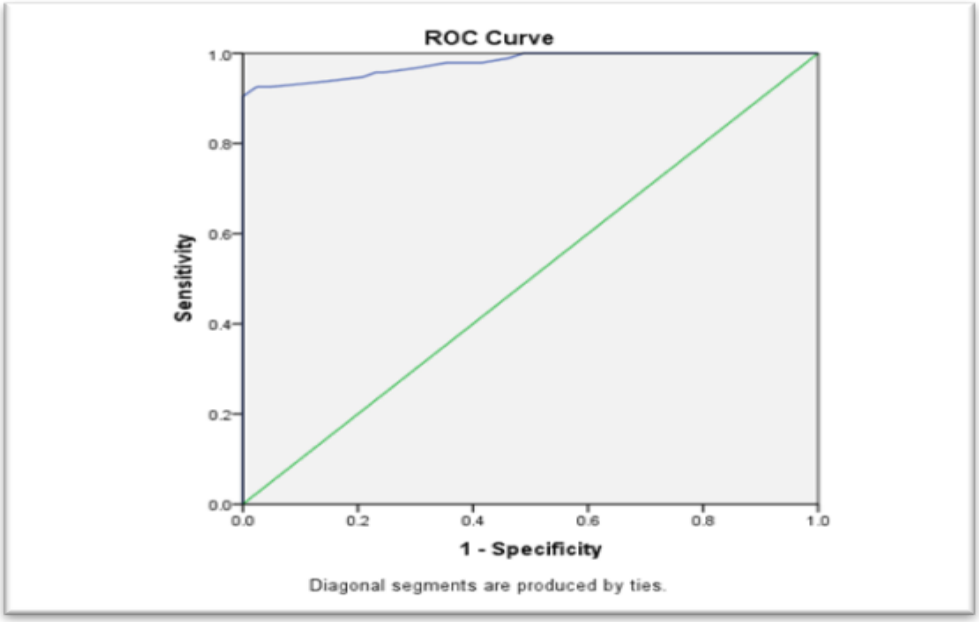

Figure 1: ROC curve of MG53.

DISCUSSION

AMI has been reported to happen ten years earlier in developing nations than in developed ones, where it typically strikes men in their mid-sixties and women in their early seventies [15, 16]. The current investigation determined the mean age of patients with AMI in southern Iraq to be lower (57.96 ± 9.63 years), aligning with prior regional studies in northern Iraq, Saudi Arabia and Iran, which revealed a lower mean age of AMI [17, 18]. This age discrepancy compared to developed nations may reflect differences in social welfare systems, cultural practices, lifestyle patterns, and access to preventive healthcare between high- and low-resource settings [18, 19].

The study findings indicate that males (69.1%) are significantly more likely than females (30.9%) to experience AMI. This observation aligns with previous research, which attributes the higher incidence in males to a combination of biological and lifestyle factors [20, 21]. Estrogen is thought to provide a protective effect against cardiovascular events in premenopausal women, reducing their risk of AMI. Furthermore, men tend to exhibit a higher prevalence of cardiovascular risk factors, including smoking, hypertension, and dyslipidemia, which contribute to their increased susceptibility to AMI [22].

Low-density lipoprotein (LDL) and triglyceride (TG) levels were observed to increase significantly in AMI patients compared to control individuals, consistent with prior studies highlighting elevated LDL and TG levels as key contributors to AMI [23, 24]. Atherosclerosis, the primary pathological process underlying AMI, is strongly associated with circulating LDL, one of the earliest recognized factors in its progression [25]. Genetic and epidemiological research has further identified elevated TG levels as a major residual cause of atherosclerotic cardiovascular diseases (ASCVD) [26, 27]. These findings underscore the complex interplay between lipid metabolism and cardiovascular risk in AMI patients.

Myokines are polypeptides or cytokines secreted from striated muscles during exercise [28]. It occurs because of both abnormal and typical physiological processes. Increasing evidence suggests that myokines are linked to the development of cardiovascular disease [29]. In this study, it was discovered that MG53 levels were remarkably higher in the serum of patients after a heart attack than in the healthy group, and they were shown to be reliable indicators for

diagnosing AMI. . In Parallel with these observations, a Chinese study that revealed individuals with STEMI had higher levels of MG53 than those in the control group[30]. Although the exact mechanism by which higher MG53 levels occur in AMI is unclear, prior studies has demonstrated that MG53 regulates inflammation [31], plays a crucial role in cell membrane repair [32], and maintains the mitochondrial integrity of cardiomyocytes during ischemia [33]. These findings can help refine the diagnostic and prognostic approaches for myocardial infarction and provide valuable clinical insights.

In patients with STEMI, the MG53 biomarker demonstrates outstanding diagnostic performance as reflected by its ROC curve metrics. A high AUC indicates excellent discrimination ability, meaning MG53 can almost perfectly differentiate AMI patients from non-affected individuals. The p-value < 0.001 confirms this finding is highly statistically significant, ruling out chance as an explanation for the observed diagnostic accuracy. The Sensitivity suggests MG53 effectively identifies the vast majority of true AMI cases, minimizing false negatives, which is critical in acute settings where missed diagnoses can be fatal. The Specificity of MG53 shows a strong capacity to correctly exclude those without AMI, reducing false positives and unnecessary interventions. Overall accuracy further supports MG53 as a reliable biomarker for AMI diagnosis. These combined values position MG53 as a promising tool for early and accurate AMI detection, potentially improving clinical decision-making and patient outcomes by balancing sensitivity and specificity optimally, as ROC curve analysis aims to achieve.

Study limitations and future directions

There were several restrictions on this study. Geographic diversity is restricted by two-center recruitment from the Basra Governorate, which raises concerns about its generalizability to larger populations. Furthermore, biomarker levels were assessed at a single time point, leaving out information on their temporal dynamics following AMI. In areas with low healthcare resources where the burden of cardiovascular disease is still substantial, more validation through multicenter studies is necessary to verify their dependability and investigate their potential for synergistic usage with existing biomarkers. The search for new biomarkers to enhance diagnostic methods and improve patient outcomes in acute myocardial infarction is furthered by this work.

CONCLUSION

The study demonstrates that blood MG53 levels are significantly increased in STEMI patients compared to healthy control. MG53 reveals excellent diagnostic performance, with high sensitivity and specificity. The findings of this research indicate that MG53 is a highly sensitive and specific novel biomarker for the diagnosis of STEMI, supporting its potential as a novel tool for early detection and risk stratification in acute myocardial infarction.

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