



RESEARCH ARTICLE

Novel Chemomarkers as Predictors of Left Ventricular Remodeling in Patients with Myocardial Infarction

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ARTICLE INFO	ABSTRACT
Received: Apr 24, 2024	<p>The aim of this study to evaluate Serum Levels of brain natriuretic peptide, galectin-3, Ischemia modified albumin and IL-1-RA as Predictors of Left Ventricular Remodeling in patients with acute ST Elevation myocardial infarction (ST elevation of myocardial fraction). A total of 110 (62 patients and 48 control) enrolled in the present study. Forty-eight of apparently healthy sex and age matched control were included in this study. The data were collected from the control group (G1) composed of (48) individuals who were apparently healthy, the cases group as (G2) means: From the moment the patient arrives to internal resuscitation and up to 48 hours and at the baseline of the STEMI, and (G3) means: After 4-6 months follow up. serum levels of brain natriuretic peptide, galectin-3, Ischemia modified albumin, brain natriuretic peptide (BNP), and IL-1RA levels were quantified. The results of the study showed that the serum concentration of H Gal-3, IMA, and BNP were significantly higher in group G2 (patients group) in comparison to those of the G1(control group) $P < 0.01$. However, the study also found that G3 group showed a significant reduction in serum H Gal-3 levels compared to G2 group at $P < 0.01$. Regarding the IL-1RA mean concentration levels, the highest mean level (248.4 ± 49) was seen among the G2 in matching to (222.9 ± 43.5) for the control group at $p < 0.05$. The current study concluded that there are significantly increasing of H Galectin 3, BNP and IMA levels in patients in matching to control groups. our study demonstrated that the concentration mean levels of IL-1RA was greater in patients in matching to control group. The current study showed highly significant ($P < 0.01$) changes of Gal-3 levels in regards to LVR and Non LVR in G2 and G3. The levels of Gal-3 were higher of LVR patients than Non LVR. Our study showed highly significant results ($P < 0.01$) between LVR and Non-LVR in regards to IL-1RA levels at G2.</p>
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INTRODUCTION

Myocardial Infarction (MI) or Acute Myocardial Infarction (AMI), commonly known as a heart attack, is the interruption of blood supply to part of the heart, causing some heart cells to die. This is most commonly due to occlusion (blockage) of a coronary artery following the rupture of a vulnerable atherosclerotic plaque, which is an unstable collection of lipids (fatty acids) and white blood cells (especially macrophages) in the wall of an artery. The resulting ischemia (restriction in blood supply) and oxygen shortage, if left untreated for a sufficient period of time, can cause damage or death (infarction) of heart muscle tissue (Wu et al., 2021; Jam et al., 2018). Important risk factors are previous cardiovascular disease (such as angina, a previous heart attack or stroke), old age (especially men over

65 and women over 50), tobacco smoking, high blood levels of certain lipids (triglycerides, low-density lipoprotein or "bad cholesterol") and low levels of high density lipoprotein (HDL, "good cholesterol"), diabetes, high blood pressure, obesity, chronic kidney disease, heart failure, excessive alcohol consumption, the abuse of certain drugs (such as cocaine and methamphetamine), and chronic high stress levels (Nascimento et al., 2019; Jam et al., 2014).

In cardiology, ventricular remodeling (or cardiac remodeling) refers to changes in the size, shape, structure, and function of the heart. This can happen as a result of exercise (physiological remodeling) or after injury to the heart muscle (pathological remodeling). The injury is typically due to acute myocardial infarction (usually transmural or ST segment elevation infarction), but may be from a number of causes that result in increased pressure or volume, causing pressure overload or volume overload (forms of strain) on the heart (Zhao et al., 2022a; Alneyadi et al., 2023b).

Adipokines play a role in cardiac diseases due to their involvement in lipid metabolism and endothelial functions (Merkhan et al., 2021; Mohammad et al., 2023; Wardat et al., 2024; Kanval et al., 2024). Galectin-3 (Figure 1) levels were found to be significantly higher in patients with LVR compared to those without LVR, suggesting that Galectin-3 could be used as part of a screening strategy to identify patients at higher risk of developing heart failure after STEMI (Tsutsui et al., 2023; Zakariya et al., 2023). Natriuretic peptides, specifically brain (B-type) natriuretic peptide (BNP) (Figure 1) and N-terminal prohormone of brain natriuretic peptide (NT-pro BNP), are widely used for the diagnosis of HF and have important complementary roles in risk stratification and prevention. Natriuretic peptides have universal applicability globally and high diagnostic, therapeutic, and prognostic validity (Shevtsova et al., 2021; Jarrah et al., 2022).

IL1-RA (Figure 1) has a promising role as prognostic biomarkers both as independent markers and also as a group in patients with STEMI. They hold potential for future use in clinical practice for risk stratification, guidance of clinical care and as therapeutic targets. (Scărlătescu et al., 2022; Tashtoush et al., 2023b). IMA has been proposed as an early biomarker for various diseases associated with ischemia and oxidative stress, including myocardial infarction and cerebrovascular accidents, diabetes mellitus and renal failure, and hypothyroidism and hyperthyroidism (Turkyilmaz et al., 2022; Tashtoush et al., 2023a) (Figure 2). Aim of this study to identify some biochemical parameters that help in prediction of LV remodelling after STEMI By determining serum levels of brain natriuretic peptide, galectin-3, Ischemia modified albumin, and IL-1RA in patients with ST-segment elevation MI (STEMI) and apparently healthy controls.

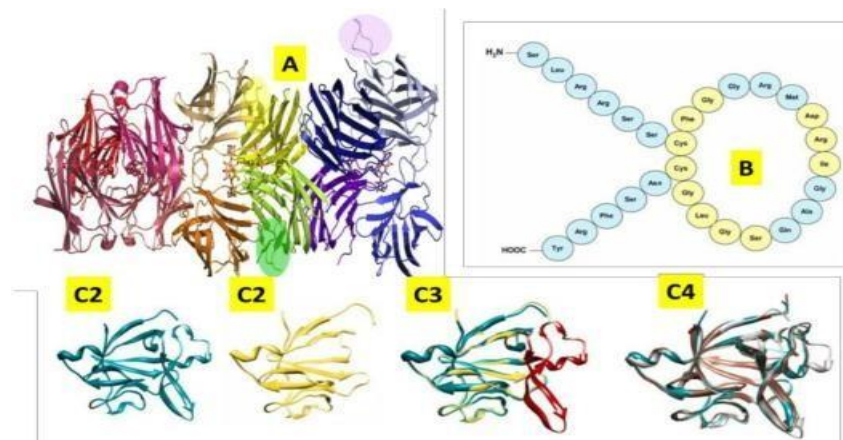


Figure 1. Structure of (A) Galectin 3 (Flores-Ibarra et al., 2018), (B) brain natriuretic peptide (Piechota et al., 2009), and (C) IL-1RA (Nouri Barkestani et al., 2022).

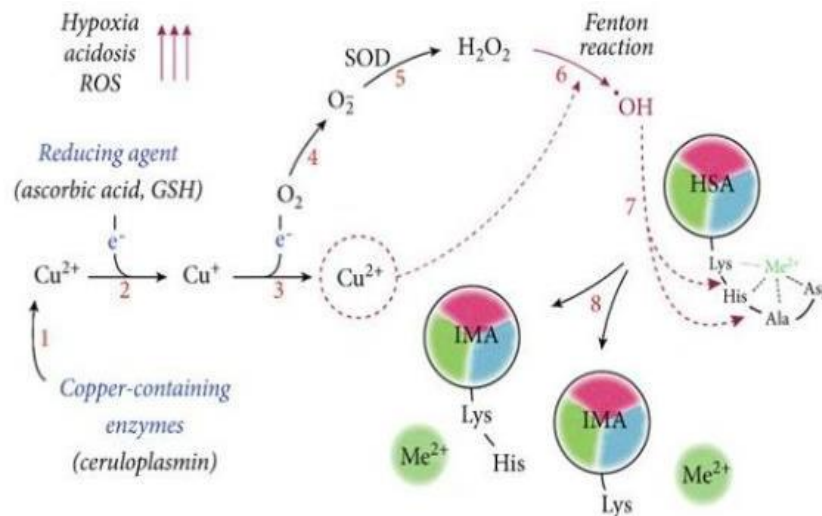


Figure 2. Pathological role of IMA in hypoxic situation and diseases (Shevtsova et al., 2021).

PATIENTS AND METHODS

This prospective case-controlled study was conducted from beginning May 2023 to end of October 2023. This study was conducted on sixty-two patients who had undergone a STEMI. After 4 to 6 months these patient's follow-up after STEMI and Forty-eight healthy control subjects. The information about patients in this study was retrieved from patient's hospital records. The samples were collected from Azadi teaching Hospital/ Kirkuk on patients with STEMI. Fortyeight of apparently healthy sex and age matched control were included in this study. Apparently healthy sex and age matched control with any autoimmune, inflammatory disease or infection were excluded from this study. The data was collected from the study participants directly and filled in prepared questionnaire. The questionnaire was designed by support of supervisor on previous literatures.

Routine baseline laboratory investigations, in addition to galectin-3, Ischemia modified albumin (IMA), Brain natriuretic peptide (BNP), and Interleukin 1RA (IL-1RA).

Follow-up after STEMI will include a clinical visit and blood sampling for Gal-3, Ischemia modified albumin (IMA), Brain natriuretic peptide (BNP) and Interleukin 1RA (IL-1RA) at 4 to 6 months, when a two dimensional echocardiogram will be again obtained.

A total number of sixty-two patients (males & females) who have STEMI, (Females 19% - Males 81%) were included in the study. Their ages were between (40-75) years and BMI range (24-35). The criteria of exclusion include the following: malignant disease, infectious disease, and liver disease.

The results of the patient groups were compared with forty-eight comparable age and sex-matched healthy subjects, with the age ranged between (18-53) years old used as control group, with exclusion criteria that include a history of infection, inflammation, cancer, and liver disease. Control group were clinically diagnosed to be free from symptoms and signs of any diseases including renal disease, liver disease, diabetes, hypertension and malignancy which affect STEMI. Control subjects did not receive any treatment.

About five milliliters of blood were collected from the antecubital vein of the patients and health control have been kept in gel tubes without any anticoagulant at room temperature for 10-15 minutes then allowed to clot. The samples in gel tubes then were centrifuged (3000 rpm) for 15min. The clear serum was pipetted into clear dry Eppendorf's tubes then stored at (-20Co) until used for the various investigations.

The serum was thawed at (20-25Co) temperature for two hours then submitted to the centrifuged for five minutes at 3000 rpm.

Full history taking was collected from all patients including time of ischemic symptom, Killip classification during admission. End Systolic Volume (ESV), End Diastolic Volume (EDV) and Ejection fraction (by Simpson's biplane method) as measured at baseline by conventional echocardiography

)36-48 after pPCI (and at 4 to 6 months follow up when a two dimensional echocardiogram will be again obtained and through it was determined while the patient is LVR or Non-LVR. and through the EF% measuring, it was determined the severity of LVR (normal, mild or severe).

RESULTS AND DISCUSSION

The current study offers a comprehensive demographic and clinical profile of the patient cohort, illuminating significant trends pertinent to age, BMI, left ventricular ejection fraction (LVEF), and comorbid conditions. The mean age of patients was established at 57.87 years, while the mean BMI was recorded at 28.77, indicating that this group largely consisted of older adults who are generally overweight. Notably, the mean LVEF was documented at 48.22%, suggesting compromised cardiac function among participants. A detailed examination reveals that out of 62 patients, a substantial majority—38 individuals or 61.29%—had diabetes mellitus, compared to 24 non-diabetic patients (38.7%). Similarly, hypertension prevalence was high, with 34 patients (54.8%) affected versus 28 (45.16%) who were normotensive. Gender distribution indicated a male predominance with 50 males (83.33%) compared to only 12 females (19.35%). Family history seemed less common in this group; only 18 patients (29.03%) reported such a background against the larger subset of 44 patients (70.96%) without familial ties to the disease condition in question. Lastly, smoking status showed that a vast majority were smokers—44 patients or 70.69%—compared to just 18 non-smokers (29.03%), reflecting potential lifestyle risk factors contributing to their health issues as presented in Table 1. (Table 1).

Table 1. Sociodemographic variables of the patients

Variables	Means
Age mean	57.87
BMI mean	28.77
EF mean	48.22
Variables	No.(%)
Diabetes/non-diabetes	38/24(61.29/38.7)
Hypertensive/non-hypertensive	34/28(54.8/45.16)
Male/Female	50/12(83.33/19.35)
Family history/no-family history	18/44(29.03/70.96)
Smokers/non-smokers	44/18(70.96/29.03)

Our results align closely with several studies, for instance, Mohammad et al. (2022), found that a majority of the patients were older than 50 and predominantly male, which echoes our demographic observations. Similarly, Alwan and Zangana (2021), detected an average patient age of 59.3 years with a higher number of male patients compared to females; they also noted a significant prevalence of

hypertension and diabetes among their cohort. Our study diverged from theirs regarding family history prevalence but agreed on the high number of smokers among patients. Additionally, Khaznadar and Wahid Salh (2020), corroborated our conclusions by identifying old age, hypertension, diabetes mellitus, and smoking as critical risk factors for myocardial infarction. In terms of biochemical

markers, we observed the highest mean H Gal-3 levels in group G2 compared to group G1 at $P < 0.01$ and a significant reduction in serum H Gal-3 levels between groups G3 and G2 at $P < 0.01$. The elevated IMA concentration levels we recorded align with Majid et al. (2014), on acute myocardial infarction patients' albumin levels while noting that BNP levels significantly increased in our patient group compared to controls. Moreover, the IL-1RA mean concentration levels were higher among group G2 compared to controls at $P < 0.05$, consistent with Orrem et al., (2018). Finally, variations in Gal-3 levels between diabetic subgroups reveal significant differences within non-diabetic cohorts but nonsignificant differences within diabetic ones between groups G2 and G3—highlighting intricate interplays between metabolic states and cardiac biomarkers consistent with previous regional studies such as those by Al-Salam et al (2020).

Table 2. Levels of measured parameters in diabetes and non-diabetes patients.

Parameters	Group	Non-diabetic (n=36)	Diabetic patient (n=26)
Human Galactin 3	G2	237.7±59.3	286.4±46.1*
	G3	159.9±42.5	143.1±19.4
Ischemia modified albumin	G2	77.2±3.6	77.4±7.5
	G3	76±5.29	77±5.33
BNP	G2	176.1±73.9*	68.3±15.6
	G3	165.1±72.7*	61±15.5
IL-1RA	G2	253±61.5	279.1±60.9
	G3	161.9±40.9	152.2±37.0

Data expressed as mean±SD, * indicates significant differences as compared to comparative group at P value less than 0.05 using t-test

The present study elucidates a complex relationship between various biomarkers and their levels in diabetic versus non-diabetic patients, particularly in the context of acute myocardial infarction (AMI) and left ventricular remodeling (LVR). The findings revealed that Gal-3 levels were significantly elevated in diabetes patients, aligning with previous research by Tyminska et al. (2019) which underscored a strong association between diabetes mellitus and heightened Gal-3 levels. Furthermore, this study corroborates earlier observations by researchers who documented significant elevations of Gal-3 in patients with AMI. Interestingly, Ischemia Modified Albumin (IMA) levels showed insignificant differences between diabetic and non-diabetic groups post-myocardial infarction, echoing the results reported by (Mahmoud et al., 2024; Alneyadi et al., 2023b). In contrast to BNP, where non-diabetic patients exhibited higher mean levels compared to diabetic counterparts, diverging from Jawad et al. (2024) findings potentially due to sample size discrepancies. IL-1RA concentrations also peaked notably among diabetic individuals during G2 but not in G3 phases of LVR; these results are congruent with studies conducted by Scărlătescu et al., (2022). Significant variations were observed concerning Gal-3 levels across different LVR timeframes, emphasizing increased levels during extended remodeling periods as noted by Berezin and Berezin (2020). Contrarily, IMA presented no substantial fluctuation relative to remodeling times. Nonetheless, the combination of biomarkers including albumin demonstrated superior predictive value for acute coronary syndromes than individual metrics

alone—a finding consistent with multiple prior studies but limited by its specificity due to overlapping high values seen in other severe health conditions such as neoplasms or kidney disease. Ultimately, significant distinctions were marked for BNP and IL-1RA during various remodeling stages reaffirming existing literature while shedding new light on biochemical dynamics amid cardiac events in diabetic populations.

Table 3. Levels of measured parameters in LVR and Non LVR patients

Parameters		Group	LVR(10-14hr)(n=36)	Non LVR(4-9hr)(n=26)
Data	Human Galactin 3	G2	252.5±52.8*	224.2±62.3
		G3	154.5±34.4*	136.8±37.1
	Ischemia modified albumin	G2	76.9±3.5	78.4±7.2
		G3	76.78±5.49	77.96±7.2
	BNP	G2	78.6±17.6	108.9±58.3*
		G3	77.6±17.5	58±1.7*
IL-1RA	G2	250.1±57.7	284.9±87.3	
	G3	133.8±35.0*	130.8±74.9	

expressed as mean±SD, * indicates significant differences as compared to comparative group at P value less than 0.05 using test

The current study elucidated notable variances in Gal-3 levels between groups H1 and H2 within the G2 phase, with highly significant differences observed ($P < 0.01$), while G3 exhibited non-significant results. Specifically, higher levels of Gal-3 were recorded in group H1 compared to H2, corroborating findings by Luo et al. (2020) who identified a positive correlation between left ventricular ejection fraction (LVEF) and Gal-3 levels. This outcome aligns with previous research by Lax et al. (2015). Furthermore, the study echoed Yasin et al. (2022), findings which demonstrated a positive relationship between LVEF and BNP levels. Additionally, Celebi et al. (2022), discovered that patients experiencing acute myocardial infarction (MI) who developed left ventricular aneurysm had significantly elevated baseline N-terminal pro-B-type natriuretic peptide levels. In line with these findings, our study reported the highest mean BNP level in group H1 at 79.8 ± 15.1 compared to 74.6 ± 21.9 in group H2, with these differences being highly significant, echoing partial agreement with Tiller et al. (2022) and Mohammad et al. (2020). Regarding IL-1RA levels, there were highly significant differences between groups H1 and H2 during the G2 stage ($P < 0.01$), whereas no significant differences were noted at the G3 stage—findings consistent with Pugliese et al. (2023) and Scărlătescu et al. (2022) both of whom also found a positive correlation between IL-1RA levels and LVEF (32;17). Conversely, our results diverged from those by Mitsis et al. (2022), who reported a substantial increase in Resistin among more severe patient cases as opposed to our cohort's observations. Although an insignificant rise in IMA levels was documented for group H2 versus group H1, this finding contradicts Turkyilmaz et al. (2022), Othman (2022), and Acet et al. (2021), potentially due to their focus on more severe cases compared to ours.

Table 4. Levels of measured parameters in H1 and H2 patients

Parameters	Group	H1(31-49%) n=30 (Mild / Moderate)	H2(50-62%)n=32(Normal)
Human Galactin 3	G2	274.1±35*	227.4±60.4
	G3	155.5±35.5*	141.5±32.9
Ischemia modified albumin	G2	77.1±3.5	78.1±7.0
	G3	77±4	77.2±6
BNP	G2	79.8±15.1*	74.6±21.9
	G3	78±15*	73.5±21.8
IL-1RA	G2	238.9±58.1*	230.8±93.8
	G3	132.5±38.4	125.5±43.3

Data expressed as mean±SD, * indicates significant differences as compared to comparative group at P value less than 0.05 using t-test

CONCLUSION

High levels of H Galactin 3 in patients in matching to control groups However, the study also found that G3 group showed a significant reduction in serum H Gal-3 levels. Our study revealed significant increasing in the IMA concentration levels in patients in comparison to control. The BNP was increased significantly in patients in comparison to control group. It was also noted that the concentration mean levels of IL-1RA was greater in patients in matching to control group. The current study showed highly significant ($P<0.01$) changes of Gal-3 levels in regards to LVR and Non LVR in G2 and G3. The levels of Gal-3 were higher of LVR patients than Non LVR. Our study showed highly significant results ($P<0.01$) between LVR and Non-LVR in regards to IL-1RA levels at G2

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