The role of Galectin-3 as biochemical markers for cardiac fibrosis in patients with Myocardial Infarction

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Abstract

Ischemic heart disease is the first cause of the top ten causes of death in Iraq with a rate of 11.2% and the fourth reason is among the top ten reasons for inpatient in Iraq with a rate of 5.35% in the year 2020. A myocardial infarction (MI) occurs when blood flow decreases or stops to the coronary artery of the heart, causing damage to the heart muscle. This condition occurs most often during exertion or excitement, when the heart requires greater blood flow. Is common in the Iraq and is a leading cause of death worldwide. Galectin-3 is a lectin that binds beta-galactosides. It is involved in cardiac remodeling and fibrosis through the activation of macrophages and fibroblasts. **Objective:** - Study the association between galectin-3 and myocardial infarction. And Study the role of galectin-3 in progression of ischemic heart disease. **Subjects and Method:** - A case-control study involved 90, 30 of them were diagnosed with myocardial infarction, while another 60 were healthy controls. The samples were collected in the morning fasting state from November 2021 to May 2022, and Galectin-3 levels were analyzed using ELISA technique from Sun Long Biotech Co /China. Biochemical variables BMI calculated weight divided by square height in meter (Kg/m2) lipid profile had been measured by spectrophotometer (UV-1800 Shimadzu /Japan). **Result:** - The mean galectin-3 levels (ng/ml) in the patients group were significantly higher than in the controls group (P<0.001). In addition In comparison to healthy groups, lipid profile, atherogenic index, Non-HDL cholesterol and BMI were shown to be significantly higher in patients. Also found positive significant correlation between galectin-3 and cholesterol, triglyceride, VLDL-C, LDL-C, AIP and non-HDL-C levels. However, significant negative correlations with HDL-C levels p value<0.05. **Conclusion:** - Galectin-3 level is increase in IHD patient and had positive correlation with cholesterol, triglyceride, VLDL-C, LDL-C, AIP and non-HDL-C level. And a significant high level of cholesterol, triglyceride, VLDL-C, LDL-C, AIP and non-HDL-C were found in patients group with myocardial infarction as compared with the control, except the HDL-C values was decrease.

Keyword: - Galectin-3, myocardial infarction.

1. Introduction

A myocardial infarction (MI), commonly known as a heart attack occurs when blood flow decreases or stops to the coronary artery of the heart, causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck or jaw. Often it occurs in the center or left side of the chest and lasts for more than a few minutes. The discomfort may occasionally feel like heartburn. Other symptoms may include shortness of breath, nausea, feeling faint, a cold sweat or feeling tired(Groot, 2021). About 30% of people have atypical symptoms. Women more often present without chest pain and instead have neck pain, arm pain or feel tired(Khandelwal et al., 2021). Among those over 75 years old, about 5% have had an MI with little or no history of symptoms. An MI may cause heart failure, an irregular heartbeat, cardiogenic shock or cardiac arrest (Groot, 2021).

A number of tests are useful to help with diagnosis, including electrocardiograms (ECGs), blood tests and coronary angiography. An ECG, which is a recording of the heart's electrical activity, may confirm an ST elevation MI (STEMI), if ST elevation is present. Commonly used blood tests include troponin and less often creatine kinase MB**(Falk, 2019)**.

One of the markers of inflammation and tissue fibrosis is Galectin-3 which is Galectin-3 is a protein that in humans is encoded by the LGALS3 gene **(Barondes *et al.*, 1994)** . Galectin-3 is a member of the lectin family, of which 14 mammalian galectins have been identified.Galectin-3 is approximately 30 kDa and, like all galectins, contains a carbohydrate-recognition-binding domain (CRD) of about 130 amino acids that enable the specific binding of β-galactosides (Heit et al., 2002) .Galectin-3 (Gal-3) is also a member of the beta-galactoside-binding protein family that plays an important role in cell-cell adhesion, cell-matrix interactions, macrophage activation, angiogenesis, metastasis and apoptosis.Galectin-3 is encoded by a single gene, LGALS3, located on chromosome 14, locus q21–q22.Galectin-3 is expressed in the nucleus, cytoplasm, mitochondrion, cell surface, and extracellular space (Heit et al., 2002).

Elevated levels of galectin-3 have been found to be significantly associated with higher risk of death in both acute decompensated heart failure and chronic heart failure populations. In normal human, murine, and rat cells galectin-3 levels are low. However, as heart disease progresses, significant upregulation of galectin-3 occurs in the myocardium (Lok & Van Der Meer, 2010) .

Subject and material:-

This study was carried out in chemical and Biochemistry department, College of Medicine, University of Karbala and the cases samples were collected from Karbala Centre for Cardiac Diseases and Surgery /Karbala Health Directorate. study included 30 males of myocardial infarction (patients) and another 60 apparently healthy males (controls) with age range (35 - 68) years. Exclusion criteria were included participants who suffered from Acute Kidney Injury (AKI), Cancer, Hepatitis, Idiopathic

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pulmonary fibrosis and Athletes. Patients with MI were diagnosed by the clinical history, presentation confirmed by ECG and various investigations of cardiac biomarker.
Blood samples are collected in the morning at fasting state from vein puncture. The samples were transferred into gel tube and left for 15 minutes at room temperature to clotting then separated by centrifuge at 3000 rpm for 10 min, and then measurement of serum galectin-3 was tested by using ELISA method test based on the quantitative sandwich principle by (Sun Long Biotech Co /China) and lipid profile had been measured by spectrophotometer (UV-1800 Shimadzu /Japan).
The Statistical Package for the Social Sciences (SPSS) model 23 statistic program was used to examine the data of study. It was designed to make comparisons and use significant differences. It was considered to be significant when p≤0.05 presented as mean ±SD (standard deviation). Independent T-test statistics were applied for parameters to compare between patients and controls groups.

2. Results

Table 1: Associations of biochemical parameters between MI Patients and healthy control

Parameters	Control group Mean ± SD N = 60	Myocardial Infarction Patients group Mean ± SD N = 30	p.value
SBP (mmHg)	119.16 ± 2.46	125.63 ± 24.21	NS
DBP (mmHg)	79.17 ± 2.78	78.8 ± 15.22	NS
TC (mg/dl)	93.43 ± 10.92	176.63 ± 54.27	S
TG(mg/dl)	89.49 ± 9.96	128.15 ± 44.56	S
LDL-C (mg/dl)	22.87 ± 10.87	82.88 ± 40.51	S
VLDL-C (mg/dl)	17.88 ± 1.99	25.63 ± 8.93	S
HDL-C (mg/dl)	52.67 ± 3.38	45.57 ± 7.47	S
AIP(log TG/HDL-C)	0.23 ± 0.05	0.43 ± 0.21	S
Non-HDL(TC-HDL)	40.75 ± 11.29	131.06 ± 60.47	S
Galectin-3 (ng/ml)	8.75 ± 0.9	12.31 ± 2.40	S

BMI: Body mass index, DBP: Diastolic blood pressure, N: Number of subject, SBP: Systolic blood pressure, SD: Stander deviation, AIP: (log TG/HDL) atherogenic index of plasma, HDL-C: High density lipoprotein-cholesterol, TG: Triglyceride, TC: Total cholesterol, LDL-C: Low density lipoprotein-cholesterol, Non-HDL-C :(TC-HDL), VLDL.C: Very Low-Density Lipoprotein- Cholesterol, NS: t-test p- value ≥ 0.05, S: p- value ≤0.05.

According to the presented data there was a significant increase in the serum levels of Galectin-3 in Myocardial Infarction patients when compared with the healthy group p<0.05. results were also showed that serum total cholesterol, triglyceride, VLDL-C and LDL-C were a significantly increased (P < 0.05) in myocardial infarction patients in comparison with controls. In addition Serum HDL-C recorded a significant decreases in myocardial infarction patients in comparison with controls (P <0.05). On the other hand, atherogenic index and Non-HDL showed a significant increase (P < 0.05) in myocardial infarction patients in comparison with healthy control groups.
In figure: 1, the mean levels of Galectin-3 (ng /ml) increased in MI patient than controls group.

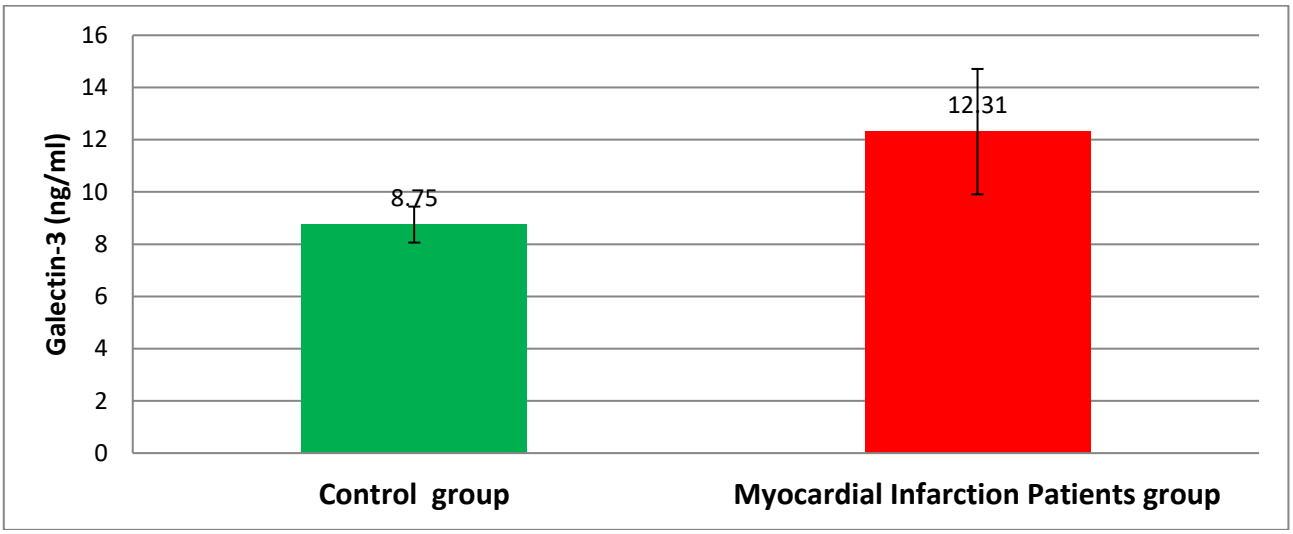

Figure 1: Mean levels of Galectin-3 (ng/ml) in patients group of Myocardial Infarction versus controls subject.

different in SBP, Galectin-3 and HDL-C between smoker patients and non-smoker patients as shown in table (2) p.value<0.05 figure (

A comparison between smoker and non-smoker of MI patients group in the measured parameters using T test showed that there was a significant

Table 2: Comparison between smoker and non-smoker patients of MI group in the measured parameters using T test.			
Parameters	patient smoker mean ± SD N:33	patient non-smoker mean ± SD N:27	p.value
Galectin-3 (ng/ml)	13.89±5.33	11.57±1.83	0.002
sST2 (pg/ml)	223.72±62.46	201.96±44.99	0.034
Age (years)	55.21±11.32	60.81±7.78	NS
BMI (Kg/m^2)	29.49±5.09	27.61±3.38	NS
SBP (mmHg)	122.91±21.01	133.52±26.12	0.016
DBP (mmHg)	76.55±13.21	81.04±14.80	NS
TC (mg/dl)	185.10±53.83	171.95±47.41	NS
TG (mg/dl)	134.03±39.25	127.85±40.42	NS
HDL-C (mg/dl)	45.22±7.57	48.46±7.63	0.036
VLDL-C (mg/dl)	26.81±7.85	25.57±8.08	NS
LDL-C (mg/dl)	84.28±41.58	80.54±39.33	NS
AIP (log TG/HDL-C)	0.45±0.19	0.41±0.20	NS
Non HDL-C (TC-HDL)	139.87±60.10	123.49±54.35	NS

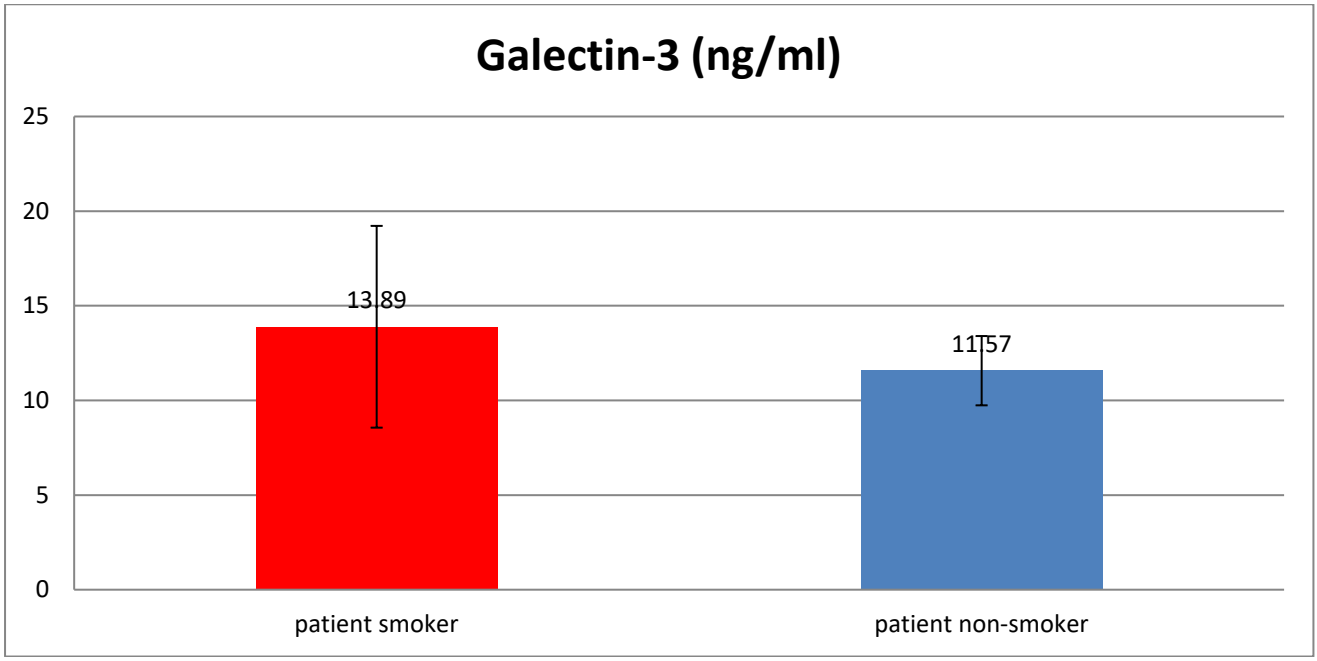

Figure (2): Mean levels of Galectin-3 (ng/ml) in patient smoker versus patient non-smoker.

Galectin-3 in patients group with MI. The correlation of Galectin-3 level showed a significant positive correlation with age, Systolic blood pressure, cholesterol, triglyceride, VLDL-C, LDL-C, AIP and Non HDL-C levels. And significant negative correlations with HDL-C levels p value<0.05.

Correlation Study

Correlations study between marker galectin-3 with all of the studied variables were estimated, by using Pearson's correlation coefficient (r) for the evaluation of data,

In table (3) data analysis was used to verify the relationship of the biochemical with the levels of

Table 3: the correlations between serum galectin-3 levels with other clinical parameters in MI patients group.		
Parameters	Galectin-3	
	r	p.value
Age (years)	0.277	0.002
BMI (Kg/m^2)	0.033	0.722
SBP (mmHg)	0.232	0.011
DBP(mmHg)	0.056	0.543
T-C (mg/dl)	0.392	0.000
TG (mg/dl)	0.281	0.002
HDL-C (mg/dl)	-0.193	0.035
VLDL-C (mg/dl)	0.281	0.002
LDL-C (mg/dl)	0.369	0.000
AIP (log TG/HDL-C)	0.267	0.003
Non HDL-C (TC-HDL)	0.379	0.000

3. Discussion

There are many diverse and recent studies that confirmed high levels of Galectin-3 in patients with cardiovascular disease compared to healthy people, and this is consistent with the results of this study **(Mitić et al., 2022)(Redondo et al., 2021)(Zhang et al., 2022)**.

Galectin-3 is a pro-inflammatory, pro-fibrotic molecule implicated in the pathogenesis of heart failure, and associated with poor prognostic outcome. When measured following ST-elevation myocardial infarction (STEMI), a high plasma galectin-3 predicts greater 30-day morbidity and mortality, and increased heart failure incidence at a median of 2 years **(Mitić et al., 2022)**.

Galectin-3 expression was increased in cancer, inflammation and fibrosis, heart disease, and stroke. Studies have also shown that the expression of galectin-3 is implicated in a variety of processes associated with heart failure, including myofibroblast proliferation, fibrogenesis, tissue repair, inflammation, and ventricular remodeling **(Winter et al., 2016)**.

Gal3 was constitutively expressed in macrophages and was localized in atrial but not ventricular cardiomyocytes. It is postulated that it may be a marker in the initial phase of the fibrosis and remodeling process **(Frunza et al., 2016)**.

Gal3 has been previously correlated with a large number of cardiovascular risk factors and has the ability to bind to the von Willebrand factor, thus being implicated in the modulation of thrombus formation in its early phase **(Janus et al., 2020)**.

Galectin-3 positive cells are located close to a lipid core or to the areas with fibrosis, hemorrhage, or thrombosis in the atherosclerotic lesions. Moreover, galectin-3 was strongly expressed in the foam cells of the atheromatous plaques, while in the absence of its expression, the occurrence of atheromatous plaques was lower **(Mitić et al., 2022)**.

Gal3 has been shown to be useful in predicting the development of HF in the general population. In a Framingham Offspring study that included 3353 patients, Gal3 was associated with an increased risk of developing HF and all-cause mortality **(Merino-Merino et al., 2021)**. In another study that included 5958 patients, an increase in the serum levels of Gal3 was independently associated with an increased risk of developing HF **(van der Velde et al., 2013)**.

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