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Galectin-3: A Predictor Marker for Cardiopathy Complication Caused by Type 2 Diabetes in. A Biochemical Study in the Sample of Iraqi People

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Abstract

Background and Aims: Galectin-3(Gal-3) is receiving growing attention due to its potential role in heart failure(HF), is an independent predictor of poor outcomes and mortality in patients with HF from risk evaluation to diagnosis, prognosis and therapy. Therefore, it is recommended as a reliable prognostic biomarker in HF that due to epicardial atherosclerosis is the presence of atherosclerotic plaques in diabetic arteries. Cultured cardiomyocytes secrete Gal-3 in response to hypoxia and proinflammatory cytokines. The goal of this study is to assess galectin-3 levels in patients undergoing percutaneous coronary intervention (PCI) following myocardial infarction to know the extent of the possibility of predicting myocardial infarction, this enabled management of the risk factors to prevent the development of thrombosis. **Subjects:** The current study included 100 samples that divided into two groups the first involved 70 individuals who were patient with myocardial infarction who undergoing elective percutaneous coronary intervention while the second group included 30 samples as a healthy individuals. Using sandwich ELISA method to determine galectin-3 levels for both groups. **Results:** galectin-3 was measured in sera samples of the study both groups it shows statistically high significant differences(p=0.000) between myocardial infarction patient group with healthy individuals.

Key Words:CVDs,PCI,Gal-3,HF,MI,AF,SCA,T2D,MMPs

Introduction

Cardiovascular diseases (CVDs) constitute the leading cause of global mortality and are a major contributor to reduced quality of life. In 2017, CVD caused an estimated 17.8 million deaths world- wide [1], an estimated 7.4 of deaths million were due to coronary heart disease [2] such as many types of disease: stable angina, unstable angina, myocardial Infarction (MI) is commonly called heart attack when there is an interruption in the blood supply resulting in heart failure because of lack of oxygen. Occlusion of a coronary artery is the most common causes. Atherosclerotic plaque ruptured due to the unstable collection of lipids (cholesterol and fatty acids) and white blood cells in artery walls. The resulting ischemia restriction in blood supply and ensuing oxygen shortage, if the condition left untreated can cause damage or death (infarction) of myocardium [3]. Risk factors adversely affecting myocardial infarction including: Physical inactivities, Smoking, Obesity, Hypertension, dyslipidemia and Diabetes which is one of the most long-term factors negatively affecting heart disease, especially coronary artery disease which is a metabolic disorder coinciding with hyperglycemia due to lack of synthesis or resistance to insulin or failure of its function thus the inability to maintain normal glucose levels in the blood [1,2,4,5].Despite the fact that diabetes does not directly cause death, the seriousness of diabetes is due to the secondary pathophysiological complications which could be divided into short-term complication which is hyperglycemia, that leads to diabetic keto acidosis and long-term complications such as nephropathy, retinopathy, neuropathy and cardiopathy [6,7].Coronary heart disease and peripheral arterial disease are considered of the most serious disorders associated with diabetes, Globally chronic diseases are the leading cause of death; they develop unnoticed over a period and are often discovered in later [8]. Type 2 diabetes (T2D) or insulin-independent diabetes is the most common and clinically significant metabolic disorder in the world today and T2D is a widespread chronic inflammatory disease in adults [9,10].There is a strong association between atherosclerotic disease and myocardial infarction in T2D patients in the long term, T2D impairs the structure of the blood vessels, and most long-term blockages with T2D occur in the coronary arteries that feed the heart muscle, leading to heart failure [6,11].

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Gal-3 belongs to the family of lectins [12], and is a structurally unique glycoprotein that has been extensively studied in many diseases. Gal-3 gene contains also a special regulatory element called galig (gal-3 internal gene)[13], located in the second intron of the *LGALS3* gene, which located in 14q22.3, and made up of 6 exons and 5 introns. Numerous single nucleotides in *LGALS-3* are found in exon 3 of chromosome 14 and influence its gene expression, such as; rs2274273, rs4644, and rs4652 [14].Gal-3 expression is regulated by promoter methylation status of LGALS3, and such elements as: carbohydrate response element CRE motifs, region similar to nuclear factor kappa B (NF-κB) [15]. Gal-3 has been studied extensively in different disease, basing on the fact of this its participating in numerous biological processes [12,16,17].Monomeric Gal-3 undergoes physicochemical modifications, which increase the range of its biological functionality, particularly extracellular activity [13]. It is a potent inflammatory protein at the onset of the inflammatory response and it associated to many diseases, including organ cirrhosis, infections, cancers, atherosclerosis and cardiovascular disease (CVDS) [16]. This led to the use of GAL-3 as a predictive marker for heart failure, in addition, there is an association between GAL-3 and future heart failure [12,13].

Materials and Methods

During the extended period from August 2021 to February 2022, 100 participants were enrolled in the current work. These cases were divided into two groups, the first included 70 Arabic Iraqi T2 diabetic patients suffered MI (30-65 years old) who underwent to elective coronary Percutaneous Intervention (PCI) in Najaf Center for Cardiac Surgery and Interventional Catheterization, Al-Saddar Medical City, Iraq. Specialist physicians made the initial diagnosis based on clinical and laboratory examinations of MI patients. The second group included 30 healthy individuals (55-30 years). Sandwich ELISA method was applied to assess Gal-3 in the serum samples of patients and control groups.Through oral interviews with patients and collaboration with the supervising physician, all the information about the current study patients has been collected. The questionnaire, which was prepared in advance based on the opinion of cardiovascular disease specialists, which included information about: age, gender, place of residence, profession, period of onset of symptoms, medical history, investigation of diabetes, type of treatments used by patients, and number of PCI times.

Results and Discussion

Normally, gal-3 is expressed at low levels in the cytoplasm, serum, and tissue fluids in healthy subjects, but is abnormally expressed in the presence of lesions *in vivo*. In recent years, serum gal-3 levels have been confirmed to be elevated in CDV, such as ,atrial fibrillation (AF), myocardial fibrosis, acute coronary syndrome (SCA) and heart failure (HF). Activated macrophages and pathologically damaged cardiomyocytes are the major sources of serum gal-3, which has been implicated as a positive contributor to cardiac remodeling, including cardiac remodeling. myocardial fiber formation and development of HF[13],as shown in **Table1**gal-3 levels were estimated in the sera samples of the participants in the current studywas noted an increase of Gal-3 levels in PCI patient(≥9.935ng/mL) compared to those in control group as it is considered as a strong inflammatory protein that increases its response to inflammation.,the results recorded a significant (p=0.000) increase in Gal-3 levelsin the patients group compared to those in the healthy group, illustrates in **Table 1**.

Table1: Levels (Mean±S.D.) of Galectin-3 (pg/mL) in The Sera of The StudyIndividuals

Parameters	Subjects (N)		*p-value*
	Patients (70) **Mean ± S.D.** **Min.-Max.** **Range**	**Controls (30)** **Mean ± S.D.** **Min.-Max.** **Range**	
Gal-3	**9.935±2.051** **4.3-13.9** **9.5**	**3.283±1.809** **1.0-7.8** **6.8**	**0.000**

The Mean Difference is Significant at 0.001 Level

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The study examined data by ANOVA.By measuring serum Gal-3 levels as an indicator of gender after categorizing the study samples into 4 groups, current study present a statistically significant deference (p=0.033) among male and female patients who undergoing elective PCI; as well as, same results were noted when comparing the PCI patient with healthy males and females in both groups.In contrast **Table 2** illustrates absence of significant variation between males and females in the same control (p=0.538) group.

Table 2: Levels (Mean±S.D.) of Galectin-3 (pg/mL) in Sera of The Different Study Groups

Subjects (n)	Sex (n)	Gal-3 (pg/ml) Mean ± S.D.	Gal-3(pg/ml) Min.-Max. Range	*p-value*
Patients (70)	Male (44)	9.543±2.018	4.34-13.79 9.45	1vs2 0.033
	Female (26)	10.597±1.967	6.21-13.86 7.65	2vs4 0.000
Controls (30)	Male (16)	3.603±1.901	1.02-5.55 4.53	1vs3 0.000
	Female (14)	3.025±1.790	1.32-7.80 6.48	3vs4 0.538

1: Elective PCI Male Patients, 2: Elective PCI Female Patients, 3:Healthy Male Control, and 4:Healthy Female Control. The Mean Difference is Significant at 0.001 Level

Gal-3 widespread and present in various organs including: the lungs, heart, stomach, colon, adrenals, uterus and ovaries [19]. Gal-3 consists of 251 amino acid residues of relative molecular mass 29–35 kDa and it has been identified for the first time in murine peritoneal macrophages [20]. Gal-3 has been used as a possible clinical biomarker in the early detection of MI [17]. In previous studies it was observed Gal-3 levels were obviously increased in atherosclerotic vessels and were shown to be a significant and independent predictor for coronary atherosclerosis Gal-3 promotes the formation of atherosclerotic plaques by exacerbating the formation of oxidized LDL-C and activating vascular smooth muscle cells Therefore, increase Gal-3 levels may facilitate the occurrence of MI [12,17].

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