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REVIEW ARTICLE

Relevance of GDF15 biomarker with left ventricular ejection fraction in coronary artery disease (CAD) Patients

Ola Muslim Alhussainy[1] , Haider Abd Jabbar ALammar[2], Aqeel Raheem Hassan[3]

1 Master science student at Medical Biochemistry , College of Medicine , University of AL – Qadisiyah

2 Assist prof. at College of Medicine , University of AL – Qadisiyah

3 Prof . at College of Medicine , University of AL – Qadisiyah

Corresponding author : 1- olamuslim23@gmail.com

Abstract:

According to cohorts studies of heart failure based on an extended period of time. Plasma GADF 15 is a highly effective independent predictor of death and morbidity. Furthermore, it seems to be a reliable indicator of a positive reaction when beta blocker is added to anti-heart failure medication. When changing therapy for heart failure based on serial measures of GDF15, as opposed to altering therapy based on independent clinical judgment, better results are expected.

Aim : the aim of present study is to find out the significant importance of GDF 15 as a new biomarkers for left ventricular ejection fraction in coronary Artery disease patients.

Methods : this case control study based on 65 patients who has been diagnosed with myocardial infarction and angina, along with 60 apparently healthy control group. 3 ml of Blood samples has been collected from each individual by using sterile syringe under aseptic condition, and collected in gel tube for serum separation, The serum levels of GDF15), were measured using sandwich ELISA method according to instruction manual. Serum urea, creatinine, and RBS are measured using colorimetric and fully automated methods.

Results

Between individuals with coronary artery disease (CAD) Patients. GADF15, serum creatinine, urea, and RBS all differ statistically significantly from the healthy group. Mean levels of Random Blood Sugar (RBS) were 158.25 ± 18.66 and 102.97 ± 9.05, in patients with coronary artery disease and healthy control subject respectively; the level was higher in the patient's group in comparison with healthy control. Regarding the mean levels of blood urea and serum creatinine , the present results show the mean levels of blood urea and serum creatinine in patients with coronary artery disease were slightly non-significant higher than the mean levels of blood urea and serum creatinine in healthy control subjects, 32.87 ± 8.25 versus 31.69 ± 3.77 respectively.

Conclusion

Individuals with significantly greater levels of coronary artery disease of(GDF15) and, which are diagnostic markers

Keyword: GDF15, Heart failure, coronary artery disease

Introduction

The relationship between newly discovered biomarkers and left ventricular ejection fraction in patients with coronary artery disease (CAD) Globally, coronary artery disease is a significant non-communicable disease issue[1]. Numerous significant risk factors, including smoking, diabetes mellitus, dyslipidemia, and hypertension, can result in coronary artery disease[2]. Despite comprehensive documentation and guidelines highlighting the prescription of medication for secondary prevention, there was a documented underutilization of these medications, resulting in many patients with coronary artery disease failing to meet the secondary prevention therapy aim[3].

Studies on epidemiology have shown that men are more likely than women to suffer from obstructive coronary artery disease[4]. Furthermore, it's thought that although obstructive coronary artery disease is less common in female patients, they have a higher rate of functional disability and a heavier weight of symptoms. Men are more likely than women to have a greater lipid core in coronary heart disease patients. Previous research on the relationship between serum total cholesterol and coronary artery disease and left ventricular ejection

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fraction discovered that greater levels of total cholesterol and high density lipoprotein are linked to increased left ventricular ejection fraction[5].

It is yet unknown how well it will categorize patients in order to adjust their course of care. It will be challenging to develop therapeutic approaches using GDF15 or anti-GDF15 medications until the mechanism of action is found. First identified from a cDNA library enriched for genes linked with macrophages derived from the U937 cell line, growth differentiation factor 15 (GDF15), also known as macrophage inhibitory cytokine 1, was separated [6]It was identified as a divergent member of the superfamily known as human transforming growth factor-β (TGF-β).There is a GDF15 gene on chromosome 19p12–13.

Consequently, managing comorbidities may not be sufficient therapy for many individuals, even though it may postpone or stop the onset of HFpEF. A significant public health risk, HFrEF is associated with high rates of morbidity and mortality[7].

Materials and Methods .

Study design :

A case control study based on 65 patients who has been diagnosed with myocardial infarction and angina, along with 60 apparently healthy control group. Blood samples has been collected from each individual. Diagnosis of coronary artery disease has been done both by clinical and lab investigation, all test that required for diagnosis confirmation was done at the Specialized Center For Surgery and Cardiac Catheterization in Diwanyah province.

Samples and other data were obtained from participants in the study, which included both healthy individuals and patient group. Other experiment test was done at biochemistry department of the College of Medicine at the University of Al-Qadisiyah. During the period between September 2023 and January 2024,

Ethical consideration

This study, conducted at The Specialized Center for Surgery and Cardiac Catheterization in Diwanyah, in accordance with University of AL-Qadisiyah, College of Medicine criteria, was approved by the Clinical Research Ethics..

Blood sample collecting

Each patient had three milliliters of blood drawn from their vein that has been placed in a gel and sodium citrate test tube for biochemistry analysis and the identification of GDF15. A serum sample was obtained by centrifuging blood specimens in gel tubes at 3000 ×g for 10 minutes. After that, the sample was kept in three separate Eppendorf tubes in the freezer at -20 C until the study was required.

Detection of serum GDF15 and, Urea, Creatinine and Random blood sugar.

With the use of the ELISA technique, GADF15 serum levels were detected. The following parameters were measured with a spectrophotometer: blood urea, creatinine, and RBS.

Results

Between individuals with coronary artery disease (CAD) Patients. GADF15, serum creatinine, urea, and RBS all differ statistically significantly from the healthy group.

Growth differentiation factor 15 (GDF-15) level in patients with coronary artery disease versus healthy control.

GDF-15 levels were compared between patients with coronary artery disease and healthy control subjects; the findings are shown in table (3-1) and picture (3-1). The mean GDF-15 levels in patients with coronary artery disease and healthy controls were 908.16 ± 150.64 and 1038.62 ± 139.45, respectively; the difference between the two groups' levels was not statistically significant.

(P= 0.074).

Table (3-1): GDF-15 level in patients with coronary artery .disease and healthy control

	Cases –control comparison		
	Patients n = 55	Healthy control n = 71	P
GDF-15 levels			
Mean± SD	908.16 ± 150.64	1038.62 ± 139.45	0.074 † NS
Range	400.16 – 2028.24	452.38-2102.00	

Evaluation of GDF-15 levels.

The GDF-15 cutoff value was evaluated, and coronary artery disease was predicted using receiver operator characteristic (ROC) curve analysis as a diagnostic or adjuvant diagnostic test. The table (3-2) and picture (3-2) show the results. Using the area under the curve, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and 58.2%, 57.7%, 51.6%, 64.1%, and 0.574 (0.474-0.675), the GDF-15 cutoff value was greater than 872.08 times. According to the current data, GDF-15 is regarded as a poor diagnostic marker.

Table (3-2): Sensitivity and specificity of GDF-15 level (> 872.08-fold) in coronary artery disease

GDF-15 levels	Patients n = 55	Healthy control n = 71
> 872.08	32 (%)	31 (%)
< 872.08	23 (%)	40 (%)

Sensitivity %	58.2 %
Specificity %	57.7%
PPV %	51.6 %
NPV %	64.1%
AUC (95% CI)	0.574 (0.474- 0.675)

Results of biochemical markers

The comparison of biochemical parameters in patients with coronary artery disease and healthy control subject has been carried out and the results were demonstrated in table (3-3). Mean levels of Random Blood Sugar (RBS) were 158.25 ± 18.66 and 102.97 ± 9.05, in patients with coronary artery disease and healthy control subject respectively; the level was higher in patients group in comparison with healthy control subject but the difference was highly significant (P < 0.001).

Regarding the mean levels of blood urea, the present results show the mean levels of blood urea in patients with coronary artery disease was slightly non-significant higher than the mean levels of blood urea in healthy control subject, 32.87 ± 8.25 versus 31.69 ± 3.77 respectively, (P= 0.284). Also the mean levels of serum Creatinine in patients with coronary artery disease was slightly non-significant higher than the mean levels of serum Creatinine in healthy control subject, 0.72 ± 0.21 versus 0.68 ± 0.13 respectively, (P= 0.229).

Table(3-3): Mean levels of biochemical parameters in patients with coronary artery disease and healthy control subject

	Cases –control comparison		P
	Patients n = 55	Healthy control n = 71	
Random Blood Sugar (RBS) mg/dl			
Mean± SD	158.25 ± 18.66	102.97 ± 9.05	< 0.001 † HS
Range	79.00 -547.00	87.00-126.00	
Blood Urea mg/dl			
Mean± SD	32.87 ± 8.25	31.69 ± 3.77	0.284 † NS
Range	15.00 -57.00	22.00-40.00	
Serum Creatinine mg/dl			
Mean ± SD	0.72 ± 0.21	0.68 ± 0.13	0.229 † NS
Range	0.30 -1.20	0.40-0.90	

n: number of cases; **SD**: standard deviation; †: independent samples t-test; HS: Highly significant at P ≤ 0.001; NS: non-significant at P 0.0° >

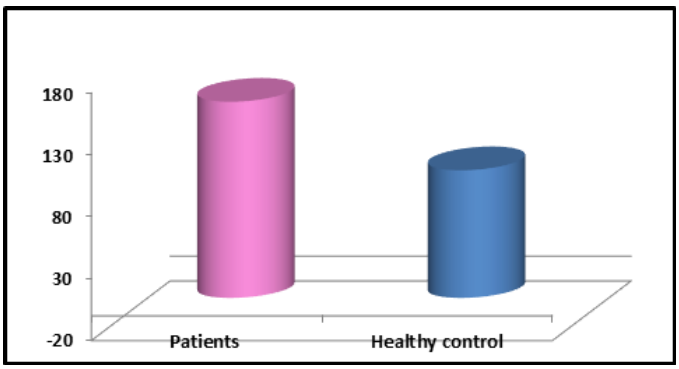

Figure (3-1): The means level of Random Blood Sugar in patients and control groups

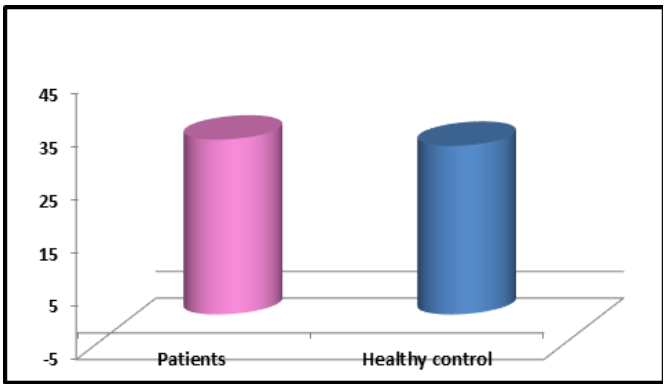

Figure (3-2): The means level of blood urea in patients and control groups

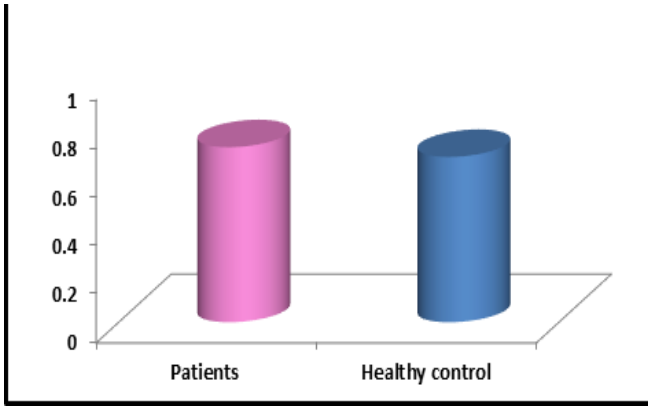

Figure (3-3): The means level of Serum Creatinine in patients and control groups

Discussions

Better biomarkers are needed, as our analysis makes clear, to help cardiologists concentrate on individuals with CAD who have intricate and distinct pathophysiological pathways. Traditional measures such as blood pressure, ejection fraction, serum urea, creatinine, and proteinuria are insensitive[1]. and depending too much on them may cause lengthy delays that prevent the application of efficient treatments. Even though several of the investigated biomarkers have demonstrated great promise,

more validation in a larger and more diverse population is required before they can be used in clinical practice. Among all the indicators examined[8], GADF15 showed the most promise as a biomarker for the comparative left ventricular ejection fraction in coronary artery disease and for the progression of CAD. Patients with either blood or other sample types are still being looked at validation[9]. However, given the near impossibility of accurately reflecting the intricacies of all the underlying pathophysiological processes involved, it is unlikely that a single marker will meet the criteria for forecasting the course of CAD[2]. For the specifically targeted CAD group, A small panel of biomarkers is more likely to produce the best outcomes]. In addition, biomarkers need to be prospectively studied in a large[10], diverse population over extended follow-up periods and validated against concrete outcome indicators like mortality and the development of end-stage renal disease [11](ESRD) before being implemented in clinical practice. While The process of finding biomarkers has become much more productive and efficient because to advances in proteomics and other domains[12]. Technology related to metabolism, sample preparation, and analytic procedures, biomarker verification and validation nevertheless remain a major, expensive, and high-risk enterprise in the commercial development biomarkers for CAD [13].

The arterial walls become damaged by high blood pressure. Damage to the arteries may increase their susceptibility to plaque accumulation, which may result in a blockage or decreased blood flow.

A heart attack or stroke may result from a blockage that happens close to the heart or brain, respectively.

In line with the CDCT8 out of 10 people who have their first stroke and 7 out of 10 people who have their first heart attack also have rusted source. An abrupt stoppage of blood supply to a portion of the heart is known as a heart attack[14], or myocardial infarction Trusted Source. Usually, this is caused by an obstruction that stops blood from flowing normally[15], but supply and demand can also play a role.Heart failuresimilarly to congestive heart failure A disorder known as inadequate cardiac pumping occurs when the heart cannot adequately pump blood throughout the body. This could be because the heart is too weak to pump blood effectively or it is not filling with enough blood[16]. It does not refer to the heart stopping, despite the name.

In the past ten years, a number of biomarkers have been found in blood and serum that allow for the early detection of chronic renal (tubular) injury and dysfunction in coronary artery disease patients, which in turn allows to find the left ventricular ejection fraction before it starts to decrease[17]. These indicators may need to meet a number of characteristics in order to be useful in therapeutic settings. They should enable early detection of coronary artery disease[18]. To maximize sensitivity and specificity for CAD, most indications for early identification include prospective, GDF15, and Pro-BNP. This could potentially lead to early preventive and therapeutic interventions. However, as of right now, there are no clinical data available about the biomarkers linked to the reversibility of coronary artery injury. Therefore, in the interim, these mediators and markers might be helpful for the noninvasive assessment of Clinical data are available on biomarkers associated with reversal of coronary artery injury. Therefore, in the meantime, these mediators and markers may be useful for non-invasive assessment of cardiac integrity in the research setting. According to the study, G1 has significantly higher serum levels of GDF15 than G2[19].

Additionally, G1's blood urea and serum creatinine levels were higher[20]. In G1, the patient's blood pressure was higher. G1's blood sugar levels had been intermittently elevated. The ejection fraction was smaller in G1.

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