ORIGINAL ARTICLE

# The Role and the Risk of Serum Vitronectin Level in patients with Diabetic and Non- Diabetic Acute Myocardial Infarction

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## ABSTRACT

**Background:** Acute myocardial infarction (AMI) is an atherosclerotic disorder of myocardial necrosis caused by constriction of blood supply to the heart, leading to myocardial dysfunction and death of the heart cells. Vitronectin (VN) is a regulatory plasma glycoprotein, which adjusts the adhesion processes of platelets, accumulation and coagulation.
**Aim**: To investigate the correlation between serum VN level and acute myocardial infarction (MI) in the presence and absence of diabetes.
**Method**: This study includes 30 patients with acute myocardial infarction which were selected from Iraqi hospitalized patients in the intensive care unit. Those patients were subdivided into two groups: group 1 involved 6 (53.3) % patients with diabetic complications; group 2 involved 14 (46.6) % patients as a non-diabetic group and 30 as control group. After an overnight fasting, 10ml of venous blood from all patients and healthy subjects was drawn to investigate the biomarkers (vitronectin, lipid profile, blood urea) in addition to having the body mass index (BMI) of all the groups.
**Results**: The results displayed significant difference in the level of vitronectin, blood urea, TC, LDL-C and HDL-C between patients with AMI (diabetic and non-diabetic) compared to control group, while there was non-significant difference in the level of TG and VLDL-C in diabetic patients with AMI compared to control group. At the same time, there was a positive correlation between vitronectin, BMI and TC.
**Conclusion**: The results of the present study were based on a small population of patients suffering from acute myocardial infarction. Some of them were complicated with diabetes. All of them presented a high level of vitronectin which may have a significant role in the induction of AMI, thus represent as a pathogenic factor for atherosclerosis. Hence, we recommend the use of this biomarker as a diagnostic test for AMI, however, more studies are needed to confirm these findings.
**Key words:** acute myocardial infarction, vitronectin, diabetes.

## INTRODUCTION

Acute myocardial infarction (AMI) is described as an atherosclerotic disorder of myocardial necrosis caused by decreased blood supply to the heart. This in turn, will lead to myocardial dysfunction and death of the cardiac cells causing obstruction to coronary artery followed by rupture of vulnerable atherosclerotic plaque. This process leads to accumulation of lipids in the arterial walls and then to disrupted blood circulation [1,2]. It is well known that the diagnosis of AMI depends on fundamental clinical assessment, electrocardiogram (ECG), invasive and non-invasive imaging, biochemical markers, and pathological assessment at the same time[3,4].

Vitronectin (VN) is a regulatory plasma glycoprotein that adjusts the adhesion processes of platelets, accumulation and coagulation. Moreover, it has been found that VN is existing and observed in atherosclerotic plaques[5]. VN is a serum glycoprotein and has 459 amino acids; the main source of these amino acids is the liver hepatocytes .VN concentration in the serum is about 4 µM, but can be precipitated in the extracellular fluid of many tissues[6,7,8].

In addition, it is found that VN regulates various physiological processes, such as fibrinolysis, pericellular proteolysis, complement-dependent immune response, cellular attachment and migration of immune cells. It also plays a major role in thrombosis, wound healing, angiogenesis, ECM modulation, signalling of growth factors in tumors and local remodelling of the tissues[9,10].

VN level in tissues is elevated at sites of sclerosis and necrosis encountered in tumors, and in vascular diseases, e.g. acute myocardial infarction (MI) in addition to renal infarction. Moreover, high levels of VN have been reported in the intimal thickening of the vascular sites and in the lesions of atherosclerotic fibrous plaques[11-14].

It is noteworthy that level of blood urea may be increased in some cases such as decreased cardiac output especially in case of heart failure. On the other hand blood urea is considered as the major nitrogen-containing metabolic product of the protein catabolism in humans, and more than 90% of it is eliminated through the renal system[15].

Regarding the dyslipidemia, it is considered as the most common risk factor for coronary heart disease (CHD). Many previous studies showed that high levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and low levels of high density lipoprotein cholesterol (HDL-C) associated with CHD incidence and mortality[16]. At the same time, studies revealed that patients with AMI receiving antihyperlipidemic therapy showed lower mortality and morbidity[17].

Diabetes was shown as an independent risk factor for coronary disease. The correlation between diabetes and coronary disease has been reported more than 70 years

ago. The risk of suffering from coronary diseases in diabetes is 2-4 times higher compared to non-diabetics[10,18].

## MATERIALS AND METHODS

This study includes 30 patients with acute myocardial infarction. They were selected randomly from Iraqi patients admitted to the department of internal medicine-diabetes unit and in intensive care unit. Those patients were subdivided into two groups: group 1 involved 6(53.3)% patients with diabetic complications; group 2 involved 14(46.6)% patients as a non-diabetic group. All patients and control subjects gave a verbal consent for their participation in this study. This study was approved by scientific jury and ethical committee. A full history was been undertaken for all patients regarding disease duration, current pharmacotherapy, smoking. Any patient with end stage or severe complications was excluded.

**Biochemical measurements:** 10ml of venous blood from all patients and healthy subjects was drawn after an overnight fasting. After centrifugation the sera were stored at -20°C for analysis. Lipid profile was estimated by specific kit method according to the kit instructions; VLDL and LDL were estimated according to specific formula[(19)]. Blood urea and vitronectin were determined according to the specific method[20].

**Statistical analysis:** The data were expressed as mean ± SD, percentages and numbers. Unpaired *t* test was used for the determination of significance of differences compared with control. *P* value is significant when *P*<0.05, and highly significant when *P*<0.01. SPSS version 21 was used for analysis the data of the present study.

## RESULTS

Patient's characteristics are given in Table 1. The results of this study showed that vitronectin was higher in the diabetic AMI patients and in non-diabetic group when compared with healthy control individuals, (*P*<0.01) table-2. Furthermore, highly significant differences were found (*P*<0.01) in BMI of diabetic AMI patients when compared with control group. Concerning the lipid profile in this study, there were highly significant differences (*P*<0.01) in non-diabetic AMI when compared to control group, while the diabetic AMI group presented highly significant differences (*P*<0.01) in total cholesterol, HDL-cholesterol and LDL-cholesterol. However, there were no significant differences in triglyceride levels and VLDL-cholesterol. The results of blood urea in this study were significantly different in the diabetic and non-diabetic AMI (*P*<0.01).

The results showed a positive correlation between BMI and vitronectin (figure 1) and there was a positive correlation between total cholesterol and vitronectin (figure 2), while there was a weak correlation between blood urea and vitronectin (figure 3).

Vitronectin seems to be highly sensitive but less specific with high positive predicative values (table 3).

Table-1: Profile of study population.

| Characteristics | Healthy | AMI |
|---|---|---|
| Number | 30 | 30 |
| **Age** | | |
| m±SD | 57.8±5.14 | 58.7±5.27 |
| Range | 50-69 | 50-67 |
| **Gender** | | |
| Male | 14 (46.66)* | 16 (53.33)* |
| Female | 16 (53.33)* | 14 (46.66)* |
| Diabetes | - | 16 (53.33)* |
| **Smoker** | | |
| | 14 (46.66)* | 15(50)* |

Table-2: Biochemical parameters of the patients

| Study group | Diabetic Group (A) | Non diabetic Group (B) | Control | *P*-value | *P*-value |
|---|---|---|---|---|---|
| Vitronectin | 2.91±0.87 | 2.45±0.65 | 1.04±0.66 | 0.001** a | 0.001**b |
| BMI | 28.86±1.75 | 29.29±3.53 | 27.57±1.61 | 0.02* a | 0.1 b |
| Blood urea | 41.5±8.2 | 43.46±9.54 | 34.5±3.82 | 0.005** a | 0.004** b |
| Total cholesterol M±SD | 194.±31.17 | 202.57±41.65 | 164.71±25.24 | 0.01** a | 0.019** b |
| Triglycerides M±SD | 60.36±15.9 | 68.92±15.1 | 57.7±13.66 | 0.19>0.05 | 0.012** b |
| HDL-C M±SD | 91.75±47.57 | 71.57±38.03 | 46.23±12.78 | 0.002<0.01**a | 0.029** b |
| LDL-C M±SD | 74.46±43.2 | 44.72±41.52 | 28.60±54 | 0.003** a | 0.03** b |
| VLDL-C M±SD | 15.07±3.98 | 17.23±3.79 | 14.42±3.41 | 0.56>0.05 | 0.027** b |

* *P*<0.05 , ** *P*<0.01

(A) Diabetic group.' (B) Non-diabetic group, (a) Represent comparison of group A with control, (b) Represent comparison of group B with control.

Figure-1: Correlation between BMI and Vitronectin in patients with myocardial infarction. P-Value 0.028 r=0.48.

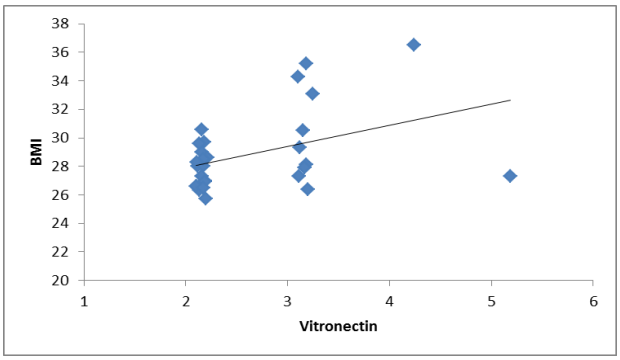


Figure-2: Correlation between total cholesterol and Vitronectin in patients with myocardial infarction. P-Value 0.015 r=0.44.

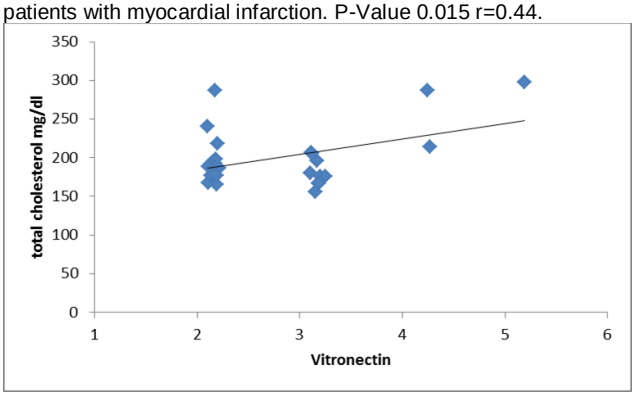

Figure-3: Correlation between blood urea and Vitronectin in patients with myocardial infarction. P-value 0.2 r=0.288.

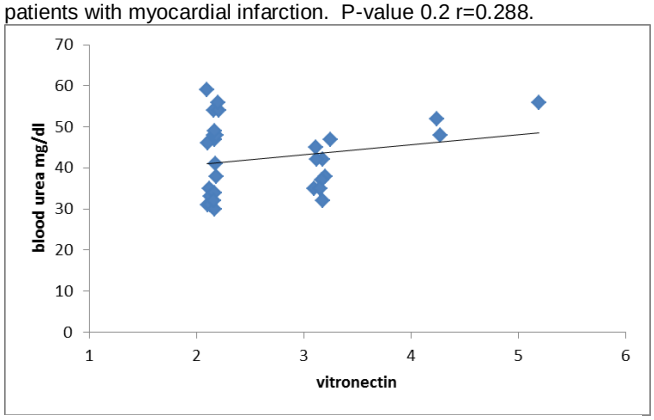


Table-3: Sensitivity and specificity of vitronectin test in patients with AMI.

| Vitronectin | Value + 95% |
|---|---|
| Sensitivity | 88% |
| Specificity | 84% |
| Positive likelihood ratio | 5.5 |
| Negative likelihood ratio | 0.14 |
| Positive predictive value | 71.7% |
| Negative predictive value | 32.3% |

## DISCUSSION

The results of this study showed that vitronectin is significantly higher in the diabetic AMI patients and in non-diabetic group when compared with healthy control individuals. These results are in line with Aslan *et al. 2015* [21], who showed that plasma level of VN was higher in diabetic patients with AMI when compared with healthy controls. Moreover, these findings were confirmed with a previous study by Yaghoubi *et al. 2015*[22] who showed that serum VN in patients with CAD was elevated and correlated with the severity of disease. This may be explained by the fact that VN has been implicated to have a regulatory function in haemostatic response to vascular injury and can be expressed in atherosclerotic lesions[23]. Moreover, VN may play an important role in controlling the response of thrombosis to vascular injury by regulating thrombin function leading to increase the possibility of acute vascular events[24]. In addition, a recent study revealed that VN can connect to platelet glycoproteins and enhances the adhesion and aggregation of platelets at the sites of endothelial damages[22]With regard to comparison of BMI in this study, it was found that there is a highly significant difference (*P*<0.01) in diabetic AMI when compared to the BMI with control group, and non-significant differences in non-diabetic group when compared to control group (table-2). On the other hand this study presented a positive correlation between BMI and vitronectin (fig.1). Some researches demonstrated that there is no significant difference when compared to BMI in non-diabetic AMI with control group, which needs further investigation[25]. Another study pointed that obesity clearly leads to Type 2 diabetes, and proved that the cardiovascular risk correlated with other metabolic syndrome, like hypertension and dyslipidemia in diabetes and acute myocardial infarction[26].

Concerning the lipid profile in this study, there were highly significant difference (*P*<0.01) in non-diabetic AMI when compared with control group, while the diabetic AMI group presented highly significant differences (*P*<0.01) in total cholesterol, HDL-cholesterol and LDL-cholesterol. There were no significant differences in triglycerides levels and VLDL-cholesterol (table-2). These findings were compatible with a study done by Sowers R. James, *1988* [27] in hospitalized AMI illustrated statistically significant differences in total cholesterol and HDL-C in non-diabetic group, though the triglycerides in diabetic group was not significantly different compared with control group.Also, in this study it was found that there was a positive correlation between total cholesterol and vitronectin (fig. 2).

Other authors like Ali F, *et al. 2016* [28] reported that there was high level of lipids profile in diabetic AMI when compared with non- diabetic AMI and they suggested that Type 2 diabetes enhancing alteration in lipids and lipoproteins utilization and induce atherogenic-dyslipidemia. This suggests an important role of atherogenic-dyslipidemia in the development of AMI in diabetic subjects. Moreover, it was described earlier that AMI is initiated by myocardial ischemia due to enhancing many factors including activation of inflammatory reactions, impaired function of antioxidants, dyslipidemia, diabetes, smoking, and obesity. All these events elicit the activation of plaque, coronary blockage and ultimately heart attack[29,30].

The results of blood urea in this study showed highly significant differences in the two groups diabetic and non-diabetic AMI (*P*<0.01), (table-2). Moreover, this study reported that there was a weak correlation between blood urea and vitronectin r=0.288 (Fig. 3)

Regarding blood urea and its correlation with vitronectin, it seems that there is a controversy in the results, and this relationship has not been fully investigated in patients with acute myocardial infarction (AMI)[31]. Other study investigated that in diabetic acute myocardial infarction; the dysfunction of the kidney is better predicted by the combined evaluation of glucose level and blood urea values rather than by assessment of it by glycemia alone[32].

## CONCLUSION

In this study, we demonstrated that vitronectin seems to be highly sensitive but it requires further investigation to prove its correlation with other biomarkers.

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