

# The Role of Omentin-1, Vaspin and Asprosin in Sera of Patients with Diabetic Foot Ulcer in Babylon Province

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#### **ABSTRACT**

Diabetic foot ulcer (DFU) represent the unsafe complication of diabetes mellitus. Omentin-1 has several functions like, anti-inflammatory, vasodilating, anti-hyperglycemia and modulating insulin sensitivity, which affects the brain, liver, muscle, fat as well as many other tissues, while in fasting Asprosin induced glycogenic protein hormone. Vaspin have a local and endocrine role in the progression of vascular damage in diabetic foot ulcer patients. For the assessment of Omentin-1, Asprosin, Vaspin ,glycated hemoglobin (HbA1c) and body mass index level and to observe the correlation between parameters and study the probable relation of them with DFU in Babylon province. Omentin-1, Asprosin, Vaspin and HbA1c were estimated in ninety subjects; 45 patients with DFU and 45 healthy persons were involved in this study. Patients and control groups with an age ranged between (35-65) years. The level of Omentin-1, Asprosin and Vaspin were assessed in serum by sandwich-ELIZA kit as the method. Serum levels of Omentin-1 displayed a significant decrease, serum Asprosin and HbA1c were significantly elevated (p<0.001) in DFU patients, while Vaspin level decreased no significantly. On the other hand, Omentin-1 and Asprosin linked significantly with glycated hemoglobin but Asprosin don't linked. Among diabetic foot ulcer patients in Babylon province the variability in Omentin-1, Asprosin and Vaspin indicate the significant relationship with diabetic foot ulcer.

# **OPEN ACCESS**

## **Key Words**

Omentin-1, asprosin, vaspin, diabetic foot ulcer and glycated hemoglobin

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#### **INTRODUCTION**

Diabetic foot ulcer represent the unsafe complication of diabetes mellitus. The lower extremities were affect, lead to a complex condition<sup>[1]</sup>. Most cases of diabetic foot ulcer occurs due to neuroischemic abnormalities or neuropathy represent the risk factors for diabetes and the complications that lead to ulcers in the lower extremities<sup>[2]</sup>. The major source of morbidity is diabetic foot ulcer disease, about 20% of diabetes patients are hospitalized due to DFU<sup>[3]</sup>.

Several studies talk about the function of two specific adipokines (omentin and vaspi) in vascular inflammation and atherosclerosis of diabetic patients. Omentin-1 or (intelectin-1) have the molecular weight about (34 kDa) is a new deposition of fat. The protein (Omentin-1) consists of 313 aminoacids. Omentin-1 is produced by adipocytes of visceral and subcutaneous fat and by endothelial cells. It expressed highly in visceral omental adipose tissue (AT). Also, heart, lungs, ovaries and placenta<sup>[4]</sup>. Firstly Omentin was observed in intestinal Paneth cells and related to the mechanisms of defensive in gut in contradiction of bacterial pathogenesis. The main circulating form of omentin is Omentin-1 with several function like, anti-inflammatory, anti-hyperglycemia, vasodilating and modulating insulin sensitivity that affects the brain, liver, muscle, fat and many other tissues<sup>[5]</sup>.

Patients with impaired glucose regulation and T2DM diabetes have low levels of omentin-1. Also the effect of omentin-1 on many chronic diseases like rheumatoid arthritis and T1DM diabetes were shown by several studies<sup>[6]</sup>. Vaspin is one of the most newly learned adipokines, serine protease inhibitor with insulin-sensitizing effects derived from visceral adipose tissue, Vaspin is a member of serpin superfamily, clade A (Serpina12)<sup>[7,8]</sup>. Visceral adipose tissue derived an adipocytokines, vaspin. It have an endocrine function in the progression of initial and advanced atherosclerosis in obese subjects by disturbing the endothelium, smooth muscle cells in vessel and macrophages, thus disturbing homeostasis of vascular [9]. Therefore, Vaspin and Omentin serum levels may might be an applicant linkage between diabetic inflammatory-complication and vascular damage in diabetic foot ulcer patients.

In fasting Asprosin induced glycogenic protein hormone, Asprosin firstly was discovered by Romere *et al.*<sup>[10]</sup>. This hormone circulated in the Nano molar levels. The name of "asprosin", derived from the Greek word "aspros" meaning white <sup>[11]</sup>. Asprosin is produced primarily by white adipocytes, which have large amount of fibrillin 1 (FBN1) mRNA expression across all tissues. So, asprosin might be produced by the skin, pancreatic cells, human saliva samples and several organs such us lung and heart<sup>[12]</sup>.

After a meal and in response to insulin, the liver stores excess amount of glucose as glycogen. In fasting, the liver is stimulated to break down this glycogen and release glucose. Also, synthesizes new glucose<sup>[13]</sup> this glucose is released into the circulation to maintaining the normal function of the brain and other organs that use glucose as a source for energy. The breakdown of glycogen and the synthesizes of new glucose are stimulated by hormones such as glucagon which activated the cyclic AMP pathway in liver hepatocytes, this cAMP stimulates the activation of metabolic enzymes leading to produce and release glucose, asprosin utilized by the same system of control, as in Fig. 1<sup>[14]</sup>.

Several studies institute the reduction of the levels of Omentin-1 in serum and elevated the level of Asprosin in DFU patients. This study directed to evaluate the association and fluctuation of Omentin-1 level ,Asprosin, Vaspin and HbA1c in patients with DFU.

#### **MATERIALS AND METHODS**

**Study design:** The study designated as Case-control.

Patients and control: Daniel sample size formula equation were used for the designated of sample size. Ninety Iraqi subjects were participated in this revision, fifty four of the members have Diabetic foot ulcer, clinical history was taken from all patients, that involve residence, age, smoking habits, family history and treatment that may affect with the measured factors. Fifty four subjects appear healthy were contributed as control group. The age of studied groups between 35-65 years. Patients with type 1 diabetic mellitus, concomitant acute or chronic inflammatory disorders and patients with malignancy, were excluded from the revision. SPSS version 20 was conducted for the statistical analysis. Mean±SD were used for the expression of results and p-values considered significant when it is less than 0.05.

#### Chemicals and methods:

- Determination of serum Omentin-1, Asprosin and Vaspin concentration by the sandwich-ELIZA kit as the method. In this kit, an antibody specific to Omentin-1 and Asprosin was pre-coated to the micro-ELIZA plate (Bioassay Technology Laboratory, ELIZA kit)
- Glycated hemoglobin A1c (HbA1c) determined by cobas integr (Roche) fully automated analyser<sup>[15]</sup>
- Determination of creatinine concentration by the improved Jaffe's method<sup>[16]</sup> and urea was determineded by Urease-Berthelot's method<sup>[17]</sup> by using cobas integra (Roche) fully automated analyser

 Body Mass Index (BMI) was intended by weight (in kilograms) divided by the square of height (in meters)<sup>[18]</sup> BMI = Weight (kg) Square Height (m 2)

**Ethical approval:** Before sample was taken the study was approved with verbal and analytical approval of patients. The study procedure and the information and agreement form subjects were studied and accepted by a local ethics committee.

#### **RESULTS**

The studied individuals consist of 90 adults designated on two groups:

- Adults have Diabetic foot ulcer (n = 45)
- Adults as control group (n = 45)

**Age:** Regarding age there was non-significant variable amongst control and DFU patients (p = 0.641), as in Table 1. The similarity in age benefits in the elimination of differences in the results of studied parameters that might originated as a result of significant variation in age $^{[19]}$ .

**Gender:** The group of healthy subjects comprised of (19) (42%) females and (21) (58%) males whereas DFU group included of (18) (40%) females and (22) (60%)males, as shown in (Fig. 2).

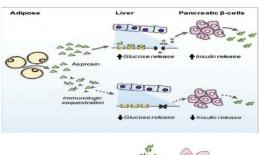
**Body mass index (BMI):** The difference of BMI between control group and DFU was non-significant (p = 0.51), as shown in (Table 1).

The biochemical parameters measured in diabetic foot ulcer patients and control group: Table 1 shows decrease concentration of Omentin-1 and Vaspin while increase concentration of Asprosin in DFU patients compared with the control with significant (p<0.05) mean differences between them.

Correlation between omentin-1, asprosin and HBA1C concentration in DFU patients. A significant negative relationship was detected between Omentin-1 with HbA1c (r = -0.62, p = 0.05) concentration. On the other hand, Vaspin has non-significant correlation with HbA1c in DFU patients, R = 0.52, p = 0.06). While, Asprosin, urea and creatinine have significant positive correlation with HbA1c in DFU patients, R = 0.725, p = 0.01) R = 0.67, p = 0.03) and R = 0.49, p = 0.05) respectivly, (Table 2).

#### **DISCUSSIONS**

The common complication of T2DM is diabetic foot ulcer the human with age range from 40 years to older are more affected by T2DM and increased age is



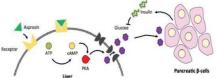


Fig. 1: The Asprosin-Induced Hepatic Glucose Release Cascade<sup>[14]</sup>

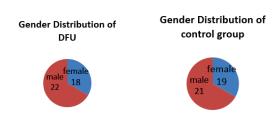


Fig. 2: Gender distribution in control and DFU group

a main risk factor for impaired wound healing<sup>[20]</sup>. In diabetic patients education, Age, sex, smoking and history of foot ulcer have two fold risk for mortality than subject of Non-diabetics<sup>[21]</sup> This fact was in harmony with the measurements of these revision the mean age of subjects who were established as DFU patients and control were 55 and 50 years, respectively. Furthermore, this review found a slight male predominance 60%, this outcome is in agreement with previous study, found that the number of male had DFU more than female due to contact of male to environmental factor with uncontrolled blood glucose level, stress and education<sup>[22]</sup>.

Patient with poor glycaemic control (was measured by HbA1c, urea, creatinine) might be a strong predictive of subsequent ulceration and amputation. The present study reveals high significance of HbA1c, urea and creatinine in the DFU group, this finding conducted by Kadhim, 2021<sup>[23]</sup>The anti-inflammatory adipokine is Omentin-1, it have a role in control the secretion of insulin by endocrine and paracrine dynamic that controls the breakdown of glucose and the secretion of insulin by maintaining omentin-1 level in adipose tissue, similarly to elevating of the transduction of insulin by stimulating of protein

Table 1: Demographic and biochemical data of study and control groups

Variable	DFU Group (N = 45) Mean±SD	Control groups (N = 45) Mean±SD	p-value
p = 0.641	55±9.87	50±14.32	Age (years)
p = 0.51	27.74±3.63	26.13±2.91	BMI (kg $m^{-2}$ )
p<0.05	7.9±0.514	5.9±0.2	HbA1c
p<0.05	39.7±5.98	28.5±6.94	Urea (mg $dL^{-1}$ )
p<0.05	1.3±0.581	0.785±0.126	Creatinine (mg dL <sup>-1</sup> )
p<0.05	127.39±57.95	487.5±83.50	Omentin-1 $(ng mL^{-1})$
p = 0.428	34.9±12.1	36.5±11.2	Vaspin (Pg $mL^{-1}$ )
p<0.05	80.5±3.55	19.43±12.93	Asprosin (ng mL <sup>-1</sup> )

SD = standard deviation, p<0.05: significant

Table 2: Correlation coefficient between Omentin-1 and Asprosin with HbA1c in DELL groups

	DFU group	
Variables	r	Р
Omentin-1 v HbA1c	-0.62	0.05
Asprosin vs HbA1c	0.725	0.01
Vaspin vs HbA1c	0.52	0.06
Urea vs HbA1c	0.67	0.03
Creatinine vs HbA1c	0.49	0.05

Correlation is significant at p<0.05

kinase. Then, enhanced the spreading of fat across the body regarding the visceral and in subcutaneous<sup>[24]</sup>. Omentin-1enhanced insulin to device the transport and metabolism of glucose in muscle, liver and subcutaneous fat. In human the secretion of omentin-1 in blood causes an acceleration of insulin sensitivity<sup>[25]</sup>The present study demonstrated significant decrease in omentin-1 level in patients with DFU when compared with control groups. Our results are agreed with previous study, reported that omentin-1 concentration decrease in impaired glucose tolerance, obesity and T2DM<sup>[26]</sup>.

Another study shown a links among omentin-1 concentrations and the progression of ischemic and neuropathic complications<sup>[27]</sup>. Vaspin is submitted to control immune responses and inflammation and it was correlated with numerous metabolic parameters. Yet, vaspin has been displayed to improve glucose tolerance and the sensitivity of insulin significantly in mice and to be linked positively with complication of obesity in humans<sup>[28]</sup>. Previous study found that serum vaspin levels might be change with the development of diabetes<sup>[29]</sup>. Vaspin might be elevated at the beginning of diabetes and then decrease with deteriorating of diabetes in humans.

This study suggested that serum values of vaspin and decrease serum values of omentin, may be included in pathological mechanisms of endothelium vessels inflammation and may be associated with a high degree of arterial stiffness, endothelial dysfunction and microvascular brain damage in DFS patients. Asprosin might be one of the important hormones in the etiopathology of all types of diabetes<sup>[30]</sup>.

In skeletal muscle, Asprosin can decrease insulin signal and stimulate insulin resistance by promoting inflammation and stress of endoplasmic reticulum<sup>[31]</sup>. The present study revealed significant increase in

asprosin level in patients with DFU when compared with control groups, these results are in consistence with other previous study<sup>[32]</sup>. Current study showed serum omentin-1 and asprosin associated significantly with glycosylated hemoglobin (HbA1c) in diabetic foot ulcer. Likewise, study the level of plasma asprosin by Naiemian *et al.*<sup>[32]</sup> they were establish a significant association of plasma asprosin and HbA1C level. After the special effects, could display a significant negative relationship amongst Omentin-1 with HbA1c and a significant positive relation of Asprosin with HbA1c in DFU patients.

#### **CONCLUSION**

Among diabetic foot ulcer patients in Babylon province, alteration in the level of omentin-1, Vaspin and Asprosin with glycated hemoglobin, may indicate the significant linked to diabetic foot ulcer.

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