

# Serum Levels of Irisin and Vaspin in Diabetic Retinopathy Patients and Their Relation to Patient's Obesity

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## Abstract

The study was carried out in Kirkuk city, from 20<sup>th</sup> January to September to November 2019 included 40 Diabetic patients with retinopathy and 40 healthy persons within the range of age: 45-75 years of old. The information about patients in this study was retrieved from patient's itself. The diabetic patients with retinopathy were diagnosed by analysis RBS and HbA1c and fundoscopic examination by the ophthalmologist. The criteria of exclusion include non-diabetic and malignant disease. The results of the patients groups were compared with healthy individuals nearly comparable age and BMI. Four ml of blood were collected from patients and for determination of irisin, vaspin and HbA1c. The study showed that the mean serum level of irisin was significantly elevated in DR patients compared to control group ( $27.57 \pm 4.22$  and  $17.57 \pm 5.9$  pg/ml) respectively at a P value  $< 0.01$ . This study showed that the mean serum level vaspin was higher in DR patients especially in persons with high BMI and decreased in lower BMI persons (75.1, 59.3 and 48.3 ng/ml) respectively but still higher than healthy ones ( $P < 0.01$ ), as compared with the control group (32.17ng/ml). The study showed that, HbA1c was elevated significantly ( $P < 0.01$ ) in diabetic retinopathy patients (10.17%) compared with healthy control (5.17%). The study concluded that, vaspin and irisin levels were highly elevated in diabetic patients with retinopathy.

**Keywords:** Malondialdehyde; Diabetic retinopathy; Oxidative stress; HbA1c.

## Introduction

Diabetes mellitus (DM) is expected to affect around 550 million people all over the world according to global estimates of the prevalence of diabetes<sup>(1)</sup>. DM is characterized by constant hyperglycemia that damages various organs and manifests in macro vascular complications like premature atherosclerosis resulting in strokes, peripheral vascular disease, and myocardial infarctions and micro vascular complications such as nephropathy, neuropathy, and retinopathy<sup>(2)</sup>. Diabetic retinopathy (DR) is the number one cause of blindness in people between 27 and 75 years of age. Prevalence of DR is around 25% and 90% at 5 and 20 years, respectively, from diagnosis; it is calculated that 191 million people will be diagnosed with this micro-vascular complication by the year 2030<sup>(3)</sup>. Through the last three decades, extensive scientific reports have shown ROS to play an important role in DM complications such as diabetic neuropathy, nephropathy, and retinopathy due to alterations on

the biomechanisms involved in the instauration and progression of micro-vascular complications<sup>(4)</sup>. These three micro-vascular complications share high glucose levels as a starting point; such condition is necessary, but may not be enough to initiate the damage present in the peripheral nervous system (neuropathy), kidneys (nephropathy), and retinas (retinopathy) of diabetic patients<sup>(5,6)</sup>. Hyperglycemic states favor the activation of alternative pathways leading to reactive oxygen species (ROS) formation and augmented concentrations locally and in the rest of the body even at the point of surpassing the antioxidant capacity, a state known as oxidative stress affecting retinal integrity<sup>(7,8)</sup>. The study aim of this work was to evaluate the level of Malondialdehyde (MDA) in diabetic patients with and without retinopathy and healthy controls.

## Patients and Method

The study was carried out in Kirkuk city, from 20<sup>th</sup> January to September to November 2019 included

40 Diabetic patients with retinopathy and 40 healthy persons within the range of age: 45-75 years of old. The information about patients in this study was retrieved from patient's itself. The diabetic patients with retinopathy were diagnosed by analysis RBS and HbA1c and fundoscopic examination by the ophthalmologist. The criteria of exclusion include non-diabetic and malignant disease. The results of the patients groups were compared with healthy individuals nearly comparable age and

BMI. Four ml of blood were collected from patients and controls in plain tubes without any anticoagulant at room temperature for 10-15 minutes and allowed to clot. The tube then were centrifuged (3000 rpm) for 15min. The clear serum was pipetted into clear dry Eppendorf's and stored at (-20°C) until used for the various investigations. The levels of malondialdehyde, HbA1c were measured by using immunofluorescence technique.

### Results

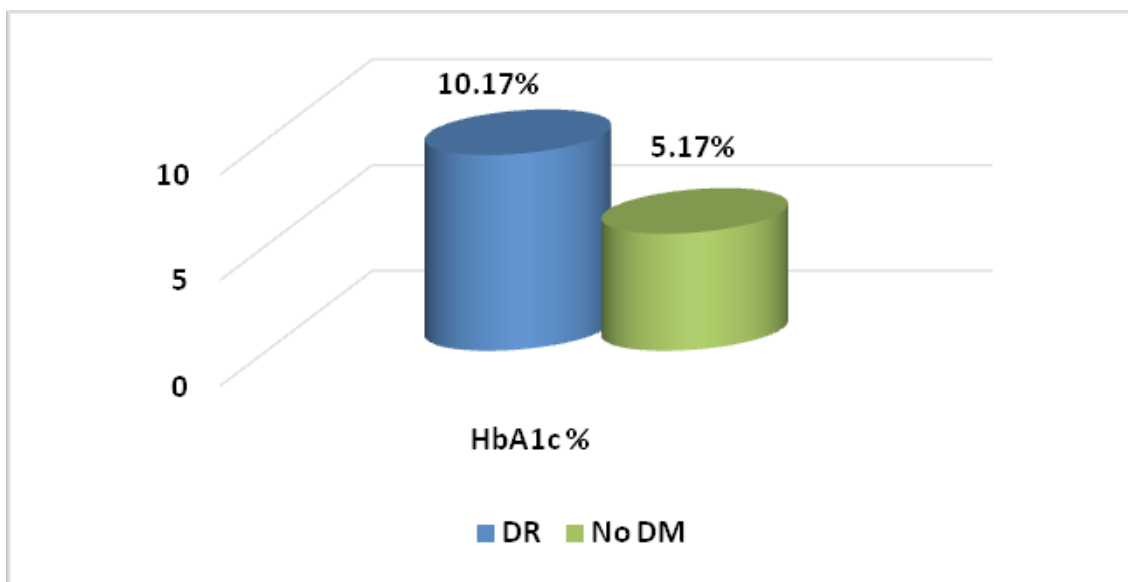


Figure 1: Means of HbA1c levels in the studied groups

In the following Table 1, general characteristics of DR patients:

Table 1: Distribution of the general characteristics Diabetes patients

Parameters	n(%)	
BMI (kg/m <sup>2</sup> )	Non-Obese (18.5-24.9)	30
	Overweight (25-29.9)	30
	Obese ≥ 30	40
Age (years)	17-26	12
	27-36	14
	37-46	24
	47-56	25
	57-66	17
	67-76	8
	Mean: 45.01±4.5	

Parameters	n(%)	
Sex	Males	36
	Females	64

As shown in Table 2, the mean serum level of irisin was significantly elevated in DR patients compared to control group (27.57 ± 4.22 and 17.57 ± 5.9 pg/ml) respectively at a P value < 0.01.

Table 2: The mean and standard deviation (SD) of irisin level in studied groups

Irisin level (pg/ml)	DR patients	Control group
No.	40	40
Mean	27.57	23.98
SD.	4.22	5.9

P<0.01

This study showed that the mean serum level vaspin was higher in DR patients especially in persons with high BMI and decreased in lower BMI persons (75.1, 59.3 and 48.3 ng/ml) respectively but still higher than healthy ones ( $P < 0.01$ ), as compared with the control group (32.17ng/ml). This result was highly significant at a P value of 0.001, Table 2.

**Table 3: Relation of vaspin with obesity of DM patients**

Vaspin level (ng/ml)	DR patients			Control group
	Obese	Overweight	Normal	
No.	10	20	10	30
Mean	75.1	59.3	48.3	32.17
SD.	6.8	5.9	5.2	4.28

$P < 0.01$

The study showed that, HbA1c was elevated significantly ( $P < 0.01$ ) in diabetic retinopathy patients (10.17%) compared with healthy control (5.17%), Figure 1.

## Discussion

In several studies, women had significantly higher rate of DR than men, as it seems that females may take care about their general health more than males, which is similar to a study in Sweden where women had a higher rate than men<sup>(1-3)</sup>. Esteghamati et al<sup>(10)</sup> also established that, there was significant relation of irisin and vasoin with occurrence and development of diabetic retinopathy. While Choiet al<sup>(11)</sup> in recent study reported that the rate of diabetic retinopathy was significantly associated with elevation of vaspin in obese DR patients. In agreement with the current results, Jeonget al<sup>(12)</sup> indicated a highly significantly increased irisin levels, in cases with respect to controls, point towards a role of free radicals in causation of diabetic complications like retinopathy. In addition, Rickhamet al<sup>(13)</sup> showed that, serum irisin has been found to be significantly associated with the severity of DR in patients with *type 2* insulin-dependent DM. Taal et al<sup>(14)</sup> reported that increased vaspin is associated with oxidative stress and poor antioxidant defense, which promotes the progression of DR to its proliferative form. Some other studies speculate that retinal microvascular complications are closely related to the severity of oxidative stress, as expressed as increased level of MDA among DR patients<sup>(7,8)</sup>. Indeed, the exact mechanism by which the oxidative stress contributes to diabetic complications remains unclear, but all biochemical

alterations due to DM lead to anatomical and functional impairment in the retinal microvascular network, such as changes in blood flow in the retina, disruption of the blood-retina-barrier and consequently capillary occlusion and ischemia<sup>(15)</sup>. Moreover, El-Mesallamy et al<sup>(16)</sup> showed that, serum vaspin was significantly higher in DR patients and the lowest mean was in the control group. Al- El-Lebedy et al<sup>(17)</sup> in their study showed that, HbA1C was elevated significantly in DR group followed by DM patients and indicating that poor glycemic control is a strong predictor for the development of DR. Our findings were also consistent with that stated by other studies in the world<sup>(17,18)</sup>. The elevated levels of HbA1c in DR patients may be due to their induction of retinal inflammation and vascular leakage due to their effect on blood vessels which may lead to retinal cell death<sup>(7)</sup>. The positive association between DR and duration of diabetes is noted in the literature. The retinopathy rate in Southern India was 7% in individuals with short duration of diabetes (less than 10 years), 26% in those with 10-14 years duration and 63% in those with 15 years and more duration of diabetes<sup>(6)</sup>. Our findings were also in agreement with the well established statement of several studies denoted that the severity of retinopathy is strongly associated with the duration of diabetes<sup>(19,20)</sup>. Navneet et al<sup>(27)</sup> showed level OF Vaspin increased as the grade of obesity increased performed a similar study and reported that the concentration of MDA increased with increasing BMI, which was found to be statistically in overweight subjects.

## Conclusions

The study concluded that, vaspin and irisin levels were highly elevated in diabetic patients with retinopathy.

**Financial Disclosure:** There is no financial disclosure.

**Conflict of Interest:** None to declare.

**Ethical Clearance:** All experimental protocols were approved under the College of Medicine and all experiments were carried out in accordance with approved guidelines.

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