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## Evaluation of the role of prolactin to prevent diabetic retinopathy

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## Evaluation of the role of prolactin to prevent diabetic retinopathy

### Abstract

Abstract:

**Introduction:** Diabetic retinopathy (DR) is a one of the long-term complications of DM and constitutes the leading cause of blindness in working-age individuals and affects a majority of diabetic patients by 20 years after disease onset.

**Objective:** The aim of this study is investigation of the potential role of prolactin in the prevention of Diabetic retinopathy.

**Methods:** The study was conducted on 90 diabetic patients who were divided into a group that included 37 patients without retinopathy and a group that included 27 patients with non-proliferative retinopathy and 26 patients with proliferative retinopathy who attended the Endocrinology clinic and Division at Tishreen University Hospital in Lattakia during the period from 2023 to 2024.

**Results:** Independent samples T-test analysis showed Significant decreased in prolactin level in diabetic patients with DR in comparison to diabetic patients without DR ( $p=0.0001$ ). Person correlation showed a statistically significant inverse relationship between prolactin levels and Glycosylated hemoglobin levels between patient groups.

**Conclusions:** From this study it can be concluded that diabetic patients with retinopathy had lower level of prolactin and serum prolactin does seem to have protective role in diabetic retinopathy.

### Keywords

Diabetic retinopathy, Prolactin, Glycosylated Haemoglobin

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## Introduction

**Diabetic Retinopathy:** It is one of the complications affects small blood vessels common in diabetic patients leading to vision loss through diabetic macular oedema (DMO) and proliferative diabetic retinopathy (PDR) (1-2) where it mainly affects the arteries before the capillaries, the capillaries, and the veins after the capillaries. Large vessels may be affected also. (3)

Although early diagnosis and treatment can reduce the risk of vision loss in some patients, diabetic retinopathy remains a serious threat to vision.

**Epidemiology:** Diabetic retinopathy is considered the number one cause of vision loss in the western world between the ages of 20-65 years. 80% of patients develop diabetic retinopathy after the first two decades of developing diabetes. (4) Diabetic retinopathy is also the main cause of blindness and visual impairment in adults of working age, which is associated with poor quality of life, low psychological and social level and increased risk of other diabetic complications and mortality. (5) Globally, about 95 million (35.4%) of patients with diabetes suffer from diabetic retinopathy and about 7.6% from macular oedema. (6) It was found that some degree of diabetic retinopathy develops in 99% of patients with type 1 diabetes and in 60% of patients with type 2 diabetes after 20 years of diabetes. It has been noted that the development of developmental diabetic retinopathy is more common in patients with type 1 diabetes, while macular oedema develops. It is considered the main reason for the decline in visual ability in these patients. (7)

PRL (pituitary hormone prolactin) has several functions in immune response, reproduction, growth, osmoregulation, brain function energy metabolism, and behaviour. PRL is likely to have a preventive role against DR as well (8). Studies have revealed that vasoinhibin produced by the proteolysis of PRL, is a multi-function peptide and has a vasoconstrictive, anti-vasopermeable and anti-angiogenic action. This gives Vasoinhibin a role in protection from the complications of diabetes on the eye (9). Proteolysis cleavage of PRL is caused by several endogenous proteolytic enzymes, namely bone morphogenetic protein-1 (BMP1), Cathepsin D and matrix metalloproteinase (MMP) (10). The retinal Vasoinhibin is likely derived from PRL synthesized in the retina and from systemic PRL.

## **Study Design and Patient Population**

This study was designed as an analytic case control study (cross sectional). The research sample included 90 patients with type 1 and 2 diabetes attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period of 2023-2024 and who met the inclusion criteria of the research.

The research aimed to verify the role of prolactin in preventing the occurrence of diabetic retinopathy in these patients.

The ages of the patients of the studied research sample ranged between 13 to 82 years with an average of  $53.30 \pm 15.7$  years.

### **Exclusion criteria included:**

Patients with previous thyroid disorders

Patients with previous pituitary disorders

Medicines that may cause high prolactin, such as estrogen, haloperidol, metoclopramide, methyl dopa and ranitidine

Renal and liver failure patients

Pregnant women

Alcoholics

Diabetic retinopathy patients treated with laser or inhibitors VEGF

### **Laboratory Analysis:**

Serum PRL was measured by Enzyme-linked immunosorbent Assay (ELISA). HbA1c was measured by Fluorescence Immunoassay.

### **Ethical Consideration:**

All patients were provided complete and clear informed consent after discussing the study. This study was performed by the Declaration of Helsinki.

## **Discussion**

Our study included 90 male and female patients with type 1 and type 2 diabetes of ages 13-82 years. The percentage of males were 45.6% (41) and females 54.4% (49). The proportion of type 1 was 16.7% (16) and type 2 was 83.3% (75).

The number with duration of the disease less than 10 years is 53.3 % (48), more than or equal to 10 years is 46.7% (42). Patients with oral hypoglycaemic agents treatment is 67.8 % (61), insulin therapy is 28.9% (26) and without treatment is 3.3%(3) patients.

Patients with proliferative disorder were 28.9% (26), non-proliferative disorder 30 % (27) and without illness 41.1% (37). The percentage of females was higher in the non-proliferative morbidity group (74.1%) with  $P=0.04$ . The mean values of prolactin were lower in the presence of morbidity, especially proliferative morbidity with  $P=0.0001$ .

The mean values of HbA1c were higher in the morbidity group, especially the proliferative morbidity group with  $P=0.002$ . We noticed a statistically significant difference in terms of age between the patient groups, as it was higher in the proliferative disease group with  $P=0.001$ .

We noticed a statistically significant difference in terms of the duration of disease, which was more than or equal to 10 years in the proliferative disorder group with  $P=0.0001$ .

We did not notice any statistical difference between the groups in terms of the type of disease, type of treatment or blood sugar values.

The relationship of prolactin with variables -

Presence of morbidity: The mean values were lower within the morbidity group, especially proliferative morbidity with  $P=0.0001$

Regarding gender: Values were lower in males, especially in the morbidity group  $P=0.0001$

For type of injury: Values were low only in type 2 in the morbidity group  $P=0.04$ .

Duration of disease: Significant difference was not noticed, but it was lower within the morbidity group.

Type of treatment: A statistically significant difference was not noticed.

Glycosylated haemoglobin: An inverse correlation was noticed with statistically significant differences with  $p=0.001$  in the morbidity group and  $P=0.02$  in the non-morbidity group.

Age and blood sugar values: No relationship or statistical differences were noted.

## Results

**Table) 1 (Distribute a sample 90 Patients by gender attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.**

Sex	the number	The ratio
Male	41	45.6%
Females	49	54.4%
the total	90	100%

We note from the previous table that 45.6% The studied research sample was male and female 54.4% Females.

**Table 2 (Distribute a sample 90 Patients according to the type of Diabetes who visited the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.**

Pattern of injury	the number	The ratio
First Type	15	16.7%
Second Type	75	83.3%
the total	90	100%

We note from the previous table that The majority of the studied research sample was of the second type 83.3%.

**Table 3 (Distribute a sample 90 Patients according to the duration of the infection visited the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.**

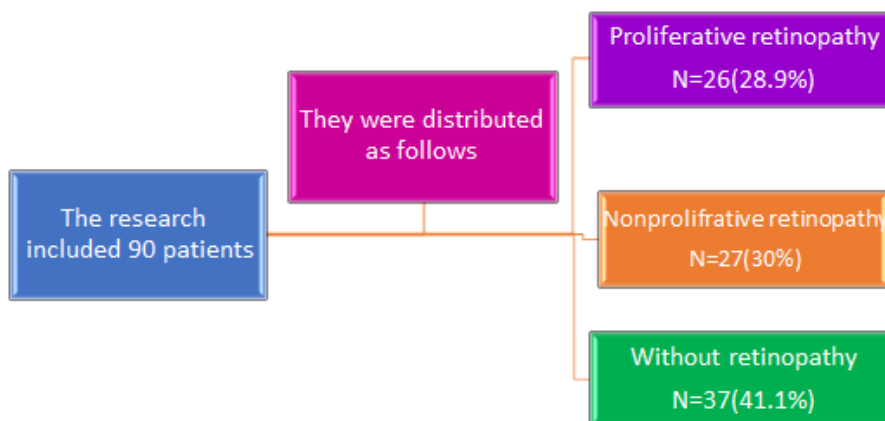
Duration of injury (year{	the number	The ratio
<10	48	53.3%
10≥	42	46.7%
the total	90	100%

We note from the previous table that 53.3% Of the research sample studied, the duration of diabetes was less than 10 years and 46.7% With a duration of more than 10 years, and the duration of diabetes ranged between 6 months and 35 An average year  $9.15 \pm 7.7$  year.

Table 4 (Distribute a sample 90 Patients according to the type of treatment who visited the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.

Type of treatment	the number	The ratio
Oral depressants	61	67.8%
Insulin	26	28.9%
There is no cure	3	3.3%
the total	90	100%

We note from the previous table that 67.8% Of the research sample studied, the treatment used was oral depressants. 28.9% Insulin and 3.3% They had no cure.



the shape) 5 (Distribute a sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.

Table 5 (the distribution By gender in a sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period 2023-2024.

Sex	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Male	15(57.7%)	7(25.9%)	19(51.4%)	0.04
Females	11(42.3%)	20(74.1%)	18(48.6%)	

We note from the previous table that there are statistically significant differences between the research groups with regard to gender, as we find that the highest percentage in the non-proliferative morbidity group was among females, where they represented 74.1% Of which with p-value=0.04.



Table) 6(Mean values for age ina sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

the age	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Mean±SD	60.34±12.2	55.96±14.9	46.40±15.9	0.001
Min - Max	40 - 82	16 - 74	13 - 72	

We note from the previous table that there are statistically significant differences between the research groups with regard to the average values for age, which were higher in patients with diabetic retinopathy compared to a group without the disease, and within the same disease group, the average values for age were higher in the group of proliferative diabetic retinopathy withp-value=0.001.

Table) 7(the distribution Depending on the pattern of infectiona sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Pattern of injury	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
First style	1(3.8%)	4(14.8%)	10(27%)	0.05
Second style	25(96.2%)	23(85.2%)	27(73%)	

We note from the previous table that there are no statistically significant differences between the research groups regarding the pattern of infection withp-value=0.05.

Table) 8(the distribution Depending on the duration of the infectiona sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Duration of injury	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
<10	9(34.6%)	10(37%)	29(78.4%)	0.0001
10≥	17(65.4%)	17(63%)	8(21.6%)	
Mean±SD	13.19±9.4	10.88±6.02	5.04±5.4	0.0001

We notice from the previous table that there are statistically significant differences between the research groups with regard to the duration of the infection, which was higher in diabetic retinopathy patients and higher in the proliferative retinopathy group.

Table) 9(the distribution Depending on the type of treatment ina sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Type of treatment	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Oral depressants	16(61.5%)	18(66.7%)	27(73%)	0.5
Insulin	9(34.6%)	7(25.9%)	10(27%)	
There is no cure	1(3.8%)	2(7.4%)	0(0%)	

We note from the previous table that there are no statistically significant differences between the research groups with regard to the type of treatment used, and the highest percentage of treatment in all groups was for oral depressants withp-value=0.5.

Table) 10(Mean values of prolactin ina sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Prolactin	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Mean±SD	5.62±2.1	7.12±1.3	11.36±2.1	0.0001
Min - Max	2.36 – 10.80	4.06 – 9.80	8.03 - 16	

We notice from the previous table that there are statistically significant differences between the research groups with regard to the mean values of prolactin, which were lower in patients with diabetic retinopathy compared to a group without the disorder, and within the same group of diseases, the mean values of prolactin were lower in the group of proliferative diabetic retinopathy withp-value=0.0001.

Table) 11(Average values of glycosylated hemoglobin ina sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Glycosylated hemoglobin	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Mean±SD	9.78±1.6	8.39±1.9	7.45±1.5	0.002
Min - Max	7.90 – 14.50	5.50 – 14	5.80 - 14.30	

We notice from the previous table that there are statistically significant differences between the research groups with regard to the average values of glycohemoglobin, which were higher in patients with diabetic retinopathy compared to a group without the disease. Within the same morbidity group, the average values of glycosylated hemoglobin were higher in the group of proliferative diabetic retinopathy withp-value=0.002.

Table 12(Average blood sugar values ina sample 90 Patients attending the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Blood sugar	Proliferative disorder	Non-proliferative disorder	Without impairment	P-value
Mean±SD	261.80±130.8	303.88±124.6	263.54±121.6	0.3
Min - Max	104 – 600	124 – 620	123 – 600	

We note from the previous table that there are no statistically significant differences between the research groups regarding the average values of blood sugar withp-value=0.3.

Table) 13(Mean values of prolactin according to sex ina sample90 patients and according to the presence of diabetic retinopathy, visitors to the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Sex	With impairment	Without impairment
Male	5.21±1.5	10.19±1.6
Females	7.42±1.6	12.62±1.5
P-value	0.0001	0.0001

We notice from the previous table that there are statistically significant differences regarding the average values of prolactin according to gender, whether in the diabetic retinopathy group or without the disorder. The values were lower in males compared to females, and the values were lower in the retinopathy group.

Table) 14(Average values of prolactin according to the type of infectiona sample 90 patients and according to the presence of diabetic retinopathy, visitors to the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Pattern of injury	With impairment	Without impairment
First style	8.11±1.3	11.55±1.4
Second style	6.32±1.7	11.24±2.1
P-value	0.04	0.8

We notice from the previous table that there are statistically significant differences with regard to the average values of prolactin depending on the type of infection in the diabetic retinopathy group only, where the values were lower with the second type, and the values were lower in the diabetic retinopathy group.

Table) 15(Average values of prolactin depending on the duration of infectiona sample90 patients and according to the presence of diabetic retinopathy, visitors to the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Duration of injury (year)	With impairment	Without impairment
<10	6.32±1.9	11.64±2.1
10≥	6.58±1.6	10.19±1.6
P-value	0.2	0.07

We note from the previous table that there are no statistically significant differences with regard to the average values of prolactin depending on the duration of the disease in both the diabetic retinopathy group as well as the group without the disease, except that the values were lower in the retinopathy group.

Table 16(Average values of prolactin according to the type of treatment ina sample 90 patients and according to the presence of diabetic retinopathy, visitors to the Endocrinology Department at Tishreen University Hospital in Lattakia during the time period2023-2024.

Treatment style	With impairment	Without impairment
Insulin	7.19±2.2	11.58±1.8
Oral depressants	6.30±1.8	11.23±2.2
There is no cure	5.69±1.2	- - - -
P-value	0.7	0.4

We note from the previous table that there are no statistically significant differences with regard to the average values of prolactin depending on the type of treatment in both the diabetic retinopathy group as well as the group without retinopathy, except that the values were lower in the retinopathy group.

Table)18(The relationship between prolactin and (age, hemoglobin, blood sugar) ina sample 90Patients and according to the presence of diabetic retinopathy referred to the Endocrinology Department at Tishreen University Hospital2023-2024.

Variables	With impairment	Without impairment
the age	Pearson Correlation= - 0.12 P-value=0.4	Pearson Correlation= - 0.15 P-value=0.3
Glycosylated hemoglobin	Pearson Correlation= - 0.36 P-value=0.001	Pearson Correlation= - 0.29 P-value=0.02
Blood sugar	Pearson Correlation=0.10 P-value=0.1	Pearson Correlation=0.04 P-value=0.9

We note from the previous table that there is an inverse correlation between both prolactin and glycohemoglobin in both research groups, as in the diabetic retinopathy group with high glycohemoglobin, prolactin values decrease, while in the group without morbidity with low glycohemoglobin values, prolactin values increase. There are differences. Statistically significant.

## Conclusion

We found a decrease in prolactin values with the presence of retinopathy and with increased degree of severity, especially in males.

There is an inverse correlation between the values of prolactin and glucose, consistent with the presence and severity of the disorder.

We did not notice any significance in the relationship between prolactin values and disease groups in terms of age, blood sugar values or type of treatment.

## **Recommendations**

Good control of diabetes and risk factors, and early diagnosis are the most important steps to avoid the occurrence of retinopathy or reduce its severity. It is necessary to search for treatment options that achieve good results before reaching severe degrees of illness, especially in light of the determinants of current treatment options (cost, availability, extent of effectiveness)

Conducting subsequent studies that include a larger sample of diabetes patients with the possibility of calibration PRL, Vasoinhibin is necessary. Conducting a future experimental study on the effectiveness of the drug group Levosulpiride in improving the degree of morbidity could prove useful.

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