Iraqi Journal of Science, 2026, Vol. 67, No. 8, pp: 4272-4282
DOI: 10.24996/ijs.2026.67.8.10

ISSN: 0067-2904

Alteration in Growth Hormone, Insulin-Like Growth Factor- 1, and Vitamin D Levels in Patients with Diabetic Retinopathy

Maha R. Ghreeb[1] , Mohammed Q. Al-Ani[1] , Huda M. Mahmood[2*]
[1]*Department of Biology, College of Science, University of Anbar, Iraq.*
[2] *Department of Biotechnology, College of Science, University of Anbar, Iraq*

Received: 16/11/2024 Accepted: 7/ 9/2025 Published: 30/ 8/2026

Abstract

The current study was designed to explore the association between growth hormone (GH), insulin-like growth factor-1 (IGF-1), and vitamin D with the cause and development of diabetic retinopathy (DR) in Iraqi patients. The study included ninety males, separated into two categories.: Thirty controls and sixty patients (30 DR with 30 NDR). The outcomes showed that DR and NDR had higher mean HbA1c levels of 9.583 ± 0.35% and 8.713 ± 0.32%, respectively. While the vitamin D levels showed no significant difference between the three groups, IGF-1 also revealed quite notable variations. At ($p<0.001$) between the 2 groups. There was less IGF-1 present in Type 2 Diabetes mellitus (T2DM) and greater within the control group. GH showed the highest level of GH in the DR compared with the control and NDR. Additionally, the results indicated that BMI did not impact HbA1c ($p < 0.2620$). And GH ($p < 0.884$), respectively, while it did influence vitamin D ($p < 0.009$) and IGF-1 ($p < 0.016$), respectively. Age had a significant impact on both IGF-1 ($p < 0.016$) and HbA1c ($p < 0.006$), respectively, while it showed no impact on vitamin D at $p < 0.262$ and GH at $p < 0.61$

Key Words: T2DM, IGF-1, Human Growth Hormone, Diabetic Retinopathy, Vitamin D

التغيرات في هرمون النمو وعامل النمو الشبيه بالأنسولين 1 ومستويات فيتامين د لدى المرضى الذين يعانون من اعتلال الشبكية السكري

مها رباح غريب[1]، محمد قيس العاني[1]، هدى مصلح محمود[2*]
[1] قسم علوم الحياة، كلية العلوم، جامعة الانبار، الانبار، العراق
[2] قسم التقنيات الاحيائية، كلية العلوم، جامعة الانبار، الانبار، العراق

الخلاصة

تم تصميم الدراسة الحالية لاستكشاف العلاقة بين هرمون النمو وعامل النمو الشبيه بالأنسولين 1 وفيتامين د كسبب وتطور اعتلال الشبكية السكري لدى المرضى العراقيين في الفترة من نوفمبر 2023 إلى أبريل 2024 في مركز النهرين التخصصي للعيون في مدينة الرمادي غرب العراق. شملت الدراسة 90 ذكرًا،

* Email:huda.mahmood@uoanbar.edu.iq

مقسمين إلى مجموعتين: 30 من الضوابط و60 مريضًا (30 DR و30 NDR). أظهرت النتائج أن DR وNDR) لديهما متوسط مستويات HbA1c أعلى من 9.583 ± 0.35٪ و8.713 ± 0.32٪ على التوالي. في حين أن مستويات فيتامين د لا يوجد فرق كبير بين المجموعات الثلاث، فإن IGF−1 لديه أيضًا اختلافات كبيرة للغاية عند (p <0.001) بين المجموعتين. كان مستوى IGF−1 منخفضًا في مرض السكري من النوع 2 وأكبر في المجموعة الضابطة. أظهر هرمون النمو أعلى مستوى من هرمون النمو في DR مقارنةً بالمجموعة الضابطة وNDR. أظهرت النتائج أيضًا عدم وجود تأثير لمؤشر كتلة الجسم على الهيموغلوبين السكري التراكمي (HbA1c) عند قيمة p < 0.262 وهرمون النمو (GH) عند قيمة p < 0.884 على التوالي، بينما أثر على فيتامين د (D) عند قيمة p < 0.009 وهرمون النمو الشبيه بالأنسولين (IGF−1) عند قيمة p < 0.016 على التوالي. كان هناك تأثير كبير للعمر على الهيموغلوبين السكري التراكمي (HbA1c) عند قيمة p < 0.006 وهرمون النمو الشبيه بالأنسولين (IGF−1) عند قيمة p < 0.016 على التوالي، بينما لم يظهر أي تأثير على فيتامين د (P < 0.262 وهرمون النمو) عند قيمة p < 61,0

1. Introduction

The long-term, chronic metabolic condition known as diabetes mellitus (DM) is primarily caused by either an absolute deficiency in insulin, as seen in T1DM, or a relative deficiency. Insulin deficiency is the cause of type 2 diabetes mellitus (T2DM). It is among the top ten global causes of death, and its incidence is expected to double by the year 2025[1]. Chronic hyperglycemia associated with diabetes damages and impairs the function of the heart, blood vessels, kidneys, eyes, nerves, and other organs. Diabetes mellitus type 2 is a disorder of carbohydrate metabolism caused by either a primary issue with insulin production, with or without insulin resistance, or by a primary problem of insulin resistance accompanied by a relative insulin deficiency [2].

Diabetic retinopathy is among the main long-term microvascular consequences of diabetes and results in regressive changes to the inner retina's capillaries. The inner blood-retinal barrier (IBRB) is an extremely selective endothelial barrier that controls molecular transport and permeability between the neural retina and blood circulation to preserve tissue homeostasis. In patients with DR, disruption of the IBRB results in progressive retinal neurodegeneration and visual loss. The inner blood-retinal barrier (IBRB), a protective barrier in the eye, is damaged in DR patients, which exacerbates damage to the retina's nerve cells. This results in a progressive deterioration of vision over time [3]. The most prevalent and dangerous microvascular complication associated with T2DM is DR, which affects adults over 50 and is a major cause of severe vision impairment in diabetic patients [2]. DR patients are 25 times more likely to lose their vision than people of the same age and gender without diabetes. Growth Factor-Binding Protein-1 (GH-IGF-1-IGFBP) is dysregulated in both of the main types of diabetes mellitus in DR. People with type 1 diabetes have a total lack of the insulin hormone in the portal vein. [1]. The upregulation of GH levels was accompanied by the downregulation of hepatic GH receptors. Hepatic growth hormone resistance is one term for this [3].

There is also a decrease in IGF-1 and GH-IGF-1-IGFBP. Even while blood levels of IGF-I are either high or low in diabetics, there is evidence that local tissue levels of the protein may be more relevant to diabetic retinal disease. The retina's glial, neuronal, and vascular cells express (GH-IGF-1IGFBP), which are changed in response to hypoxia and hyperglycemia [4]. Vitamin D3 is a class of fat-soluble secosteroids that have a variety of biological effects in addition to improving intestinal absorption of calcium, phosphate, and magnesium. Vitamin D treatment significantly enhanced HbA1C hemoglobin (HbA1C), FBG fasting blood glucose, and glycemic control (Homeostatic Model Assessment-Insulin Resistance

(HOMAIR)) in patients with T2DM [5]. The purpose of this study is to look into how growth hormone (GH), insulin-like growth factor-1 (IGF-1), and vitamin D3 (VD3) relate to the progression of DR in Iraqi patients.

2. Materials and Methods

2.1: Subjects

A case-control study, with 90 males (to exclude the influence of female hormones that affect and interfere with the effect of type 2 diabetes), was split up into two groups: Thirty controls with sixty patients with T2DM. Two groupings of patients were created: thirty with DR and thirty without. Before collecting blood samples, subjects provided written informed consent. The samples were acquired according to scientific research ethics standards. The mean age of the control group was 45 years, while the average age of the patients was 51.7 years. All ninety patients underwent a comprehensive ophthalmic examination, which included a visual acuity test, corrected visual acuity, and intraocular pressure measurement. Additionally, a medical history focusing on eye illnesses was collected from all ninety patients, covering anterior and posterior segment examinations, prior laser therapy, previous intravitreal injections, and past intravitreal surgeries. The examination was conducted by an ophthalmologist. Patients with secondary T2DM were excluded, such as Microvascular complications (Diabetic neuropathy and nephropathy) as well as other macrovascular problems (cerebrovascular disease, peripheral artery disease, and cardiovascular disease. Blood samples were collected from Ramadi City, western Iraq, in the mornings between November 2023 and April 2024.

2.2 Quantitative measurements

The Fit Mao 280 is a device used to measure weight and height using ultrasonography quickly and with high accuracy. It provides a special report on physical fitness, which includes the following: measuring the percentage of fat and muscle mass, measuring the percentage of fluids, and measuring the percentage of minerals and protein in the body. HbA1c levels were evaluated by using the detection kit Fincare HbA1c Rapid Quantitative Test with Fincare FIA™ Meters (Model No. FS-112, FS-113, FS-114.FS-205), which is based on fluorescence immunoassay technology [6]. Serum GH was measured using a sensitive immunofluorometric assay. The IDS-ISYS Human Growth Hormone (HGH) detection kit uses chemiluminescence technology and has a normal range of 0.05-3 ng/ml. [7]

The Fincare Vitamin D Rapid Quantitative Test, which uses fluorescence immunoassay technology to quantify the total 25(OH)D2\D3 level in human serum or plasma specimens, was utilized in conjunction with Fincare FIA™ Meters (Model No. FS-112, FS-113, FS-114.FS-205)[8].

2.3. Statistical analysis

Analysis of the data was done using LSD, and a correlation test of association was performed to compare the DR, NDR, and control groups. Risk factors of DR were identified by Confidence Intervals 95% (CI). Confidence in a statistical study, a 95% CI is a range of values that, with a 95% degree of confidence, are likely to include the true population parameter (such as a mean or proportion). P-values ($P > 0.05, 0.01$) and intervals were regarded as significant differences. SPSS (version 23) was used to assess the statistical study.

3. Results and Discussion

According to the IDF's 2021 prediction, one in every six people in the Middle East and North Africa has diabetes; this proportion is expected to increase by 86% by 2045.

Furthermore, 30% of diabetics are diagnosed only after their ailment is discovered unintentionally. In 2021, the United States spent more than $32.6 billion on diabetes control [9]. DR is well documented to be one of the most typical reasons for avoidable vision loss in working-age individuals, as well as a common source of visual impairment. Over 60% of T2D patients experienced retinopathy within 20 years of diagnosis, and up to 21% already had it when they were first diagnosed with diabetes, according to a review report. A global review article comprising 20,000 patients found that the prevalence of any diabetes retinopathy was 35% overall, with an estimated 25% occurring in people with T2DM [10]. Fluorescein angiography resulted in splitting them into 2 groups. Sixty T2DM patients were split into two subgroups, whereas 30 individuals were healthy controls. A mean age of 51.7 years was observed.

Table 1 lists the biochemical markers and demographic data of the research participants. The mean values of HbA1c in T2DM patients (DR and NDR) were higher, at 9.583 ± 0.35% and 8.713 ± 0.32%, respectively. While the control group had a value of 4.463 ± 0.4175%, which was highly significant ($p < 0.001$), indicating that diabetes (DR and NDR) can influence HbA1c. Chen et al. showed that HbA1c increased significantly in T2DM patients (DR and NDR). It is an indicator of the IGF-1 factor and a helpful biomarker for long-term glucose control. [10]. The outcome is consistent with Mohammed et al., who further stated that T2DM patients showed a significant increase in HbA1c concentrations. Higher HbA1c levels are associated with microvascular injury, which causes the blood vessel walls to become glycosylated non-enzymatically, resulting in the extravasation of intravascular content, with lipids and products generated from cholesterol [11]. Consequently, increased HbA1c levels are associated with a higher possibility of DR [10].

Table.1: The comparison between the three studied groups regarding laboratory data.

Traits	Status	Mean ± S.E	CI 95%	
			Lower Bound	Upper Bound
HbA1c %	Healthy control	4.46 ± 0.417 ^{A**}	3.63	5.29
	Diabetic without RT	9.58 ± 0.35^{B*}	8.86	10.29
	Diabetic with RT	8.71 ± 0.32^{C*}	8.05	9.36
Vitamin D_3 ng\ml	Healthy control	15.70 ± 1.92	11.88	19.52
	Diabetic without RT	15.94 ± 1.65	12.65	19.23
	Diabetic with RT	15.56 ± 1.51	12.55	18.58
IGF-1 ng\ml	Healthy control	179.53 ± 10.20 ^{A**}	159.25	199.81
	Diabetic without RT	123.78 ± 8.79 ^{B}	106.30	141.26
	Diabetic with RT	144.60 ± 8.04 ^{BC}	128.60	160.59
Growth Hormone ng\ml	Healthy control	.37 ± 0.28^{A}	-.19	.94
	Diabetic without RT	.14 ± 0.24 ^{AB**}	-.34	.63
	Diabetic with RT	1.09 ± 0.22^{AC}	.64	1.54

***=Significant at p≤0.05 **=Significant p≤ 0.01**
Same letters= non-significant differences, different letters= significant differences

The vitamin D levels of the control, DM, and NDR groups were 15.70±1.92ng/ml, 15.56±1.515 ng/ml, and 15.945±1.656 ng/ml, respectively. This may be because the study showed low levels of vitamin D among study groups. These groups did not differ significantly from one another. A serious health concern that is far more common in T2DM patients is

related to vitamin D deficiency [12]. This could contribute to type 2 diabetes's T2DM) as well as the consequences of the disease, and the development of microvascular problems. Although our findings disagree with Navaei *et al.* [13].

The current findings can be explained because there are no significant differences between these groups, and they all have severe vitamin D deficiency. This is perhaps due to the nature of the environment, junk food, sedentary lifestyles, fewer outdoor activities, and reduced exposure to sunlight. Strong evidence suggests that adequate glucose homeostasis and insulin sensitivity are more related to vitamin D3 levels [14]. A clinical trial demonstrated that six months of vitamin D3 therapy significantly improved glucose homeostasis and metabolic outcomes in patients with T2DM. Moreover, vitamin D3 deficiency has a higher prevalence in people with DM. Additionally, it has been established that calcitriol synthesis gene polymorphism raises the risk of DM and IR [13]. The evidence that is now available suggests that vitamin D3 plays a role in the progression of insulin resistance and diabetes mellitus [14].

IGF-1 varies significantly ($P<0.001$) between the three groups being studied. IGF-1 was low in the T2DM and higher in the control group, with a mean ± S.E. of 123.78 ± 8.79 ng/ml and 144.60 ± 8.04 ng/ml in the T2DM groups (NDR and DR), respectively. Whereas, the mean ±S. E. for the control is 179.53 ± 10.20 ng/ml (Table 1). This study demonstrated the influence of IGF-1 on the diabetic group at $p < 0.001$. IGF-1 stimulates insulin sensitivity and has hypoglycemic properties in both human and animal subjects. According to Sesti *et al*., type 1 and hybrid insulin/IGF-1 receptors are thought to mediate the organic performance of IGF-1. According to Sesti et al., type 1 receptors and hybrid insulin/IGF-1 receptors are thought to mediate the organic performance of IGF-1; patients with type 1 or type 2 diabetes and those with severe insulin resistance have demonstrated the effectiveness of recombinant human IGF-1 in improving insulin sensitivity and metabolic mechanisms [15].

Numerous investigations have confirmed an association between IGF-1 levels and T2D [15]. This study's findings, which align with another study conducted in various groups, revealed lower IGF-1 serum levels in patients with or without DR [16]. The outcomes concur with those of Khan *et al*. IGF-1 levels were seen to be lower in DR and NDR compared to the control ($p=1.54E{-}7$ and $9.14E{-}9$, respectively) [17]. Furthermore, in line with the findings of Abdullah et al., the IGF-1 concentrations in diabetes patients were significantly lower ($P = 0.0001$) than those in both the control group and diabetic patients [18]. A negative correlation between blood IGF-1 levels and insulin sensitivity was also found in the Danish population by other studies with a slightly larger cohort (n=303 twin pairs, 125 monozygotic and 178 dizygotic), with $p<0.0001$ (OR=0.88, SE=0.03), even though those studies only included 30 T2D and 30 control samples [19]. The result of growth hormone revealed a notable distinction between the two groups, control and (DR and NDR), this result found the highest level of GH in the DR group compared with control and NDR at a mean of 1.09 ± 0.22 ng/ml, 0 .14 ± 0.24 ng/ml and .37 ± 0.28 ng/ml respectively, which indicates DR influence IGF-1 ($p<0.001$). Overproduction of GH can result in microvascular problems such as retinopathy and has been linked to diabetes for almost a century [20]. A study that linked pituitary ablation to the remission of DR established the first relationship between GH and the condition. For example, Merimee observed that athletic dwarfs deficient in growth hormone did not develop retinopathy while showing signs of carbohydrate intolerance [20]. DR is around three times more common in Type I diabetic individuals with enough GH than in those with insufficient GH, as demonstrated by Alzaid and colleagues. Additionally, it has been observed that patients with GH deficiency receiving GH replacement medication would

develop retinopathy, like that of diabetes, a condition that would subside upon stopping GH treatment [21].

Our result agrees with Wilkinson *et al.* that the abnormal neovascularization and aberrant cell proliferation that define proliferative DR are associated with GH and IGF-1 [22]. It has long been known that GH/IGF-1 signaling plays a part in DR.19 GH mediates insulin sensitivity and glucose metabolism, two well-documented diabetogenic activities [20]. GH directly stimulates the development of human retinal microvascular endothelial cells, according to research. These results suggest that GH may contribute to DR by regulating the angiogenic process, leading to the development of blood vessels [23]. Also, the result was similar to Wu and Chen, who indicated that the patients suffering from DR and acromegaly showed high levels of GH serum compared to controls and acromegaly without retinopathy [23].
However, the findings indicated that BMI has an impact on (HbA1c, Vit.D3, IGF-1, and GH), are shown in Table 2.

Table 2: The influence of BMI on HbA1c, Vit.D3, IGF-1, and GH.

Source	Dependent Variable	Type III Sum of Squares	Df	Mean Square	F	Sig.
BMI	HbA1c%	3.665	1	3.665	1.275	.262
	Vit.D3 ng/ml	422.703	1	422.703	7.213	.009
	IGF-1 ng/ml	1022.032	1	1022.032	.538	.465
	Growth ng/ml	.034	1	.034	.021	.884
Age	HbA1c%	23.173	1	23.173	8.065	.006
	Vit.D3 ng/ml	19.303	1	19.303	.329	.568
	IGF-1 ng/ml	11394.963	1	11394.963	5.998	.016
	Growth ng/ml	.405	1	.405	.251	.618

Our findings showed that BMI did not affect HbA1c ($p < 0.262$), which is contrary to Sharahili et al., who demonstrated a relationship between HbA1c and BMI [24]. Perhaps the difference in our results is due to therapies aimed at lowering BMI and HbA1c, which may have a substantial effect on the management of T2D, considering the rise in BMI and decline in the proportion of persons attaining glycemic control over the research period. Additionally, the increases in hemoglobin A1C that occur simultaneously are not taken into consideration by BMI. BMI may consequently not be very useful in identifying prediabetic people who are most likely to acquire diabetes. Fat is primarily responsible for the pathophysiology of type 2 diabetes and the macrovascular problems that accompany it. The proportional contribution of obesity to cardiovascular risk in persons who already have a higher risk of cardiovascular difficulties owing to diabetes should be better understood by performing empirical research on cardiovascular risk factors among T2D patients and varying BMI ranges [25].

Table 2 shows the influence of BMI on the distribution of vitamin D. The findings revealed a strong relationship between BMI and vitamin D ($p < 0.009$). This finding supports that of Elhadi et al., who found that obesity is impacted by a VD3 deficit [26]. Vitamin D metabolism in adipose tissues is frequently regulated by the sequencing of vitamin D metabolism, and vitamin D deficiency in obese people [27].

Regarding obesity, vitamin D storage makes it inaccessible in adipose tissues, leading to decreased calcitriol levels and an increase in the hormone parathyroid hormone (PTH). This ultimately raises intracellular calcium levels in adipocytes and promotes lipogenesis, resulting in glucose intolerance [26]. The lack of a clear relationship between BMI and IGF-1 ($p < 0.465$) explains our findings. This supports the results of Mohammed et al., who found a significant negative association between BMI and IGF-1 and a strong positive correlation between BMI and HbA1c [27]. Some theories suggest that persistently high levels of IGF-1 may be linked to obesity and various aspects of carcinogenesis. According to the proposed negative feedback loop, humans' increased body weight is associated with the downregulation of IGF-1 [28].

Additionally, there was no discernible impact of body mass index on growth hormone ($p < 0.884$); therefore, there was agreed to another research performed by Lee *et al.* [29] agreed. However, no statistically significant correlation was observed between peak blood GH level and BMI in the idiopathic short-stature group. Uncertainty exists over the pathophysiological pathways causing abdominal obesity's deleterious effects on DR. The impact of visceral fat on unfavorable metabolic profiles, such as inflammation and insulin resistance, which are linked to the pathophysiology of DR, may be the mechanism via which abdominal obesity occurs. Additionally, high belly fat has been linked to abnormal neovascularization in DR, which may be caused by disruptions in growth hormone secretion [29].

The prevalence of overweight (BMI > 25 kg/m2) and obesity (BMI ≥ 30 kg/m2) is increasing in both developed and developing countries, posing a global public health risk. Even though obesity plays a major role in the development of diabetes and insulin resistance, the molecular mechanism underlying this association is yet unknown. Over 1 billion people worldwide—650 million adults, 340 million adolescents, and 39 million children—are obese, according to the World Health Organization (WHO), which hurts people's health [30]. The findings demonstrated a favorable relationship between BMI and T2D (DR and NDR). Numerous risk factors shared by T2D and obesity are linked to diseases, including genetic predisposition, gut microbiota, and modifiable environmental factors (such as sedentary lifestyle and insufficient exercise [30].

Furthermore, research revealed an association between T2D and elevated weight gain. Our findings concur with those of Nasser *et al.,* who examined the metabolic effects of two putative polymorphisms in the fat mass and obesity-linked gene (FTO) on insulin sensitivity and hyperglycemia, about their possible predictive value for type 2 diabetes in the obese Iraqi population. [31].

Table 2 indicates that age has a significant impact on HbA1c ($p < 0.006$). The findings are consistent with those of Gülsen *et al.,* who examined individuals and discovered that when participants were divided into different age groups, HbA1c levels were higher in all groups. Age and gender effects must be taken into account when using HbA1c measurements, screening, and treatment, especially in young and middle-aged people. Implementing this situation in routine medical care could potentially lower the rate of incorrect diabetes diagnoses in senior citizens, excessive diabetic treatment, and related complications [32].

Additionally, the results indicated that age had no discernible impact on vitamin D levels ($p < 0.262$). Our findings concur with Qahwaji's [32]. The current study highlights the strong negative linear relationship between age and blood vitamin D levels in both MetS and non-MetS individuals. Moreover, age and body weight have an impact on the vitamin endocrine system. Secondary hyperparathyroidism has been linked to both obesity and advanced age, as

evidenced by elevated PTH and decreased 25-D levels. The interaction of these elements within the vitamin D endocrine system is poorly understood, despite being known for many years [33].

Results also showed that age has a significant impact on IGF-1. ($p < 0.016$). The results of IGF-1 in our research align with those of AbdlWhab *et al.,* who observed a high influence of advancing age on IGF-1 [34]. IGF-1 serum levels rise with age in children, peaking during puberty and then declining with maturity, according to studies that seek to define reference values for the protein. People with diabetes have been shown to exhibit a similar tendency as they age. IGF-1 levels, however, are often found to be lower in people with T1D and T2D, at least in those under the age of 65, than in the general population [34].

Lastly, this data demonstrated that aging had no discernible impact on GH. ($p < 0.618$. Other findings on the effect of age on growth hormone are not consistent with our results. A study by Muggeo *et al.* noted a significant decrease in the response of growth hormone to insulin with age [35]. Our results, which differ from those of Muggeo *et al.* [35], can be explained by the following: As a result of the gender difference, our research was limited to men and excluded women; the explanation for the difference is that women secrete more growth hormone than men. According to Van Den Berg *et al.*, women produce three times as much GH daily as men do. Usually, an amplitude-specific divergence in the pulsatile manner of GH secretion causes this discrepancy. This sex difference is mostly caused by estrogen secretion, while serum testosterone levels may also be involved [33].

Age has a variety of effects on the retina. Male albino rats' overall retinal thickness decreased with age, particularly in the INL, according to Mohamed et al. Furthermore, aging is linked to slower retinal microglia motility and damage response, larger dendritic spindles, slower cell density, decreased retinal macular blood flow, and a greater susceptibility of Müller cells to oxidative stress. Aging and the onset of DR interact in several ways. Senescent cells accumulate in the retina in DR, a condition exacerbated by inflammatory processes, DM, and accelerated aging. The age-related rise in the risk of developing DR may possibly be explained by immune response impairments and retinal pigment epithelial cell damage [36, 37].

Conclusion

This study showed that HbA1c and the duration of diabetes were strongly correlated with the risk of DR. Furthermore, we initially put up a unique notion to forecast the occurrence of the disease in men: blood IGF-1 and the prevalence of DR in men are significantly correlated. In contrast, a higher BMI—especially one of ≥25 kg/m²—is strongly related to the degree of insulin resistance, which can lead to prediabetes. Furthermore, increasing the GH concentration promotes the growth of DR. Large-scale, long-term follow-up studies are still needed to support a more exciting inference in the population.

Ethical Approval Permission

Local ethics committee of the University of Anbar's Faculty of College of Science accepted the study (ref: CSE/721/0070).

Conflict of Interest

There were no conflicts of interest.

References

[1] A. H. Khudair and A. M. Radhi, "Diabetes Diagnosis Using Deep Learning," *Iraqi Journal of Science*, vol. 65, no. 1, pp. 443-454, 2024.

[2] M.R. Ghreeb, M.Q. Al-Ani, and H.M. Mahmood, "Association of lipid profile, calcium, and phosphorus with development of diabetic retinopathy in Iraqi patients," *International Journal of Diabetes in Developing Countries*, vol. 45, no.1, pp.1-8,2025.

[3] A. T. Haneen, A. Zeina, and A. A. Louay, "Genetic study of ITGA2 polymorphisms and impact on diabetic retinopathy risk in Al-Anbar population," *Archivos Venezolanos de Farmacología y Terapéutica,* vol. 40, no. 5, pp. 469-476, 2021**.**

[4] T. Truong and R. Z. Silkss, "Growth factor-1 and its receptor in the eye: a review and implications for IGF-1R inhibition," *Ophthalmic Plastic and Reconstructive Surgery*, vol. 39, no. 1, pp. 4-12, 2023.

[5] J. H. Abu-Shana, N. G. Abdulkareem, A. O. Jasim, and Y. H Abbood, "Effect of Diabetes Mellitus Type 2 on the Correlation of Vitamin D with Lipid Profile in Iraqi Patients," *Iraqi Journal of Science*, vol. 65, no. 9, pp. 4881-4889, 2024.

[6] N. Younes, M. M. Al Ghwairi, S. I. Da'As, E. A. Zaabi, A. F. Majdalawieh, N. Al-Dewik, and G. K. Nasrallah, "Performance Evaluation of a New Fluorescent-Based Lateral Flow Immunoassay for Quantification of Hemoglobin A1c (HBA1c) in Diabetic Patients," *Frontiers in Bioscience (Landmark edition),* vol. 28, no. 3, pp. 60, 2023.

[7] R. Huang, J. Shi, R. Wei, and J. Li, "Challenges of insulin-like growth factor-1 testing," *Critical Reviews in Clinical Laboratory Sciences*, vol. 61, no. 15, pp. 388-405, 2024.

[8] M. H. Ragab, E. M. Sherif, N. B. Abd-El Gawad, S. M. Elserougy, E. E. Shaban, and E. M. Mostafa, "Influence of supplementary vitamin D on the prognostic pathway of type 1 diabetes among children," *Biomedical and Pharmacology Journal*, vol. 14, no. 1, pp. 303-309, 2021.

[9] K. Andersson, A. Halling, and B. Agvall, "Factors associated with development of retinopathy in patients with type 2 diabetes mellitus at onset and within three years after diagnosis," *Scandinavian Journal of Primary Health Care*, vol. 42, no. 3, pp. 408–414, 2024.

[10] H. S. Chen, T. E. Wu, L. C. Hsiao, and S. H. Lin, "Interaction between glycaemic control and serum insulin-like growth factor 1 on the risk of retinopathy in type 2 diabetes," *European Journal of Clinical Investigation*, vol. 42, no. 4, pp. 447-454, 2012.

[11] A. A. Mohammed, D. M. Abo El-Matty, E. A. Abd ElSalam, M. A. Hussein, W. Hafez, S. A. Ibrahim, and A. S. Wahba, "Evaluating the Feasibility of Pro-Neurotensin and 25-Hydroxyvitamin D3 as Possible Indicators for Type 2 Diabetes Mellitus and Its Complications," *Healthcare*, vol. 11, no. 8, pp. 1088, 2023.

[12] K. Dobrzeniecki, N. Hopej, K. Muc, K. Turek, K. Błaszczyszyn, M. Bolek, and M. Pachla, "The Association between Vitamin D Deficiency and the Prognosis of Type 2 Diabetes Mellitus," *Quality in Sport*, vol. 14, no. 2, pp. e22221, 2022.

[13] S. Navaei, S. Nazemi, M. H. Emamian, H. Hashemi, and A. Fotouhi, "Vitamin D deficiency and diabetic retinopathy risk," *Journal Français d'Ophtalmologie*, vol. 46, no. 7, pp. 737-741, 2023.

[14] M. Cojic, R. Kocic, A. Klisic, and G. Kocic, "The effects of vitamin D supplementation on metabolic and oxidative stress markers in patients with type 2 diabetes: A 6-month follow-up randomized controlled study," *Frontiers in endocrinology*, vol. 12, no. 610893, 2021.

[15] M. Federici, O. Porzio, D. Lauro, P. Borboni, B. Giovannone, L. Zucaro, and G. Sesti, "Increased abundance of insulin/insulin-like growth factor-I hybrid receptors in skeletal muscle of obese subjects is correlated with in vivo insulin sensitivity," *The Journal of Clinical Endocrinology and Metabolism*, vol.83, no 8, PP.2911-2915, 1998.

[16] N. Khan, A. D. Paterson, D. Roshandel, A. Raza, M. Ajmal, N. K. Waheed, and R. Qamar, "Association of IGF-1 and VEGFA polymorphisms with diabetic retinopathy in Pakistani population," *Acta Diabetologica,* vol. 57, no. 2, pp. 237-245,2020.

[17] **A**. R. Mahmood, "Association of serum insulin-like growth factor-1 with obesity in type 2 diabetic Iraqi patients and acute renal failure," *Biochemical and Cellular Archives*, 2019.

[18] F. Liu, Y. Wang, Q. Zhao, M. Zhang, and B. Ban, "Association between uric acid and insulin-like growth factor-1 in type 2 diabetes mellitus," *International Journal of General Medicine,* vol. 14, no. 27, pp. 4017-4023, 2021.

[19] M. A. Sperling, "Traditional and novel aspects of the metabolic actions of growth hormone," *Growth Hormone and IGF Research*, vol. 28, pp. 69-75, 2015**.**

[20] S. Munjral, M. Maindarkar, P. Ahluwalia, A. Puvvula, A. Jamthikar, and T. Jujaray, " Cardiovascular risk stratification in diabetic retinopathy via atherosclerotic pathway in COVID-19/non-COVID-19 frameworks using artificial intelligence paradigm: a narrative review, " *Diagnostics*, vol. 12, no. 5, pp.1234, 2022**.**

[21] T. Truong and R. Z. Silkiss, "The role of insulin-like growth factor-1 and its receptor in the eye: a review and implications for IGF-1R inhibition," *Ophthalmic Plastic and Reconstructive Surgery,* vol. 39, no. 1, pp. 4-12,2023.

[22] Y. J. Qin, S. O. Chan, H. L. Lin, Y. Q. Zhang, B. T. He, L. Zhang, and H. Y. Zhang, "Increased expression of growth hormone–releasing hormone in fibrinous inflammation of proliferative diabetic retinopathy," *American Journal of Ophthalmology*, no. 215, pp. 81-90,2020.

[23] T. E. Wu and H. S. Chen, "The role of growth hormone and IGF-1 in retinopathy: a prospective study of retinopathy in patients with acromegaly and impaired fasting glucose," *Diabetology and Metabolic Syndrome*, vol. 14, no. 1, pp. 38, 2022.

[24] A. Y. Sharahili, S. A. Mir, S. ALDosari, M. D. Manzar, B. Alshehri, A. Al Othaim, and J. S. Alotaibi, "Correlation of HbA1c level with lipid profile in type 2 diabetes mellitus patients visiting a primary healthcare center in Jeddah City, Saudi Arabia: a retrospective cross-sectional study," *Diseases*, vol. 11, no. 4, pp. 154, 2023.

[25] T. M. Powell-Wiley, P. Poirier, J. P. Burke, P. Després, C. J. Gordon-Larsen, and American Heart Association Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Epidemiology and Prevention; and Stroke Council, "Obesity and cardiovascular disease: a scientific statement from the American Heart Association," *Circulation*, vol. 143, no. 21, pp. e984-e1010, 2021.

[26] A. A. Elhadi and A. A. Ahmed, "Correlation of vitamin D with glycemic control and body mass index in patients with type II diabetes mellitus," *Mediterranean Journal of Pharmacy and Pharmaceutical Sciences*, vol. 2, no. 1, pp. 29-37,2022.

[27] A. H. Mohammed, A. Al-Saffar, and K. Allehibi, "The relation between insulin resistance and both growth hormone and insulin-like growth factor (IGF-1) levels in a sample of Iraqi patients with type 2 diabetes," In *Endocrine Abstracts*, vol. 81, pp. 107,2022.

[28] I. Lingvay, P. Sumithran, R. V. Cohen, and C. W. LeRoux, "Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation," *The Lancet*, vol. 399, no. 10-322, pp. 394-405, 2022**.**

[29] **N**. Y., Lee, S. E., Kim, S., Kim, M. B., Ahn, S. H., Kim, W. K., Cho, and B. K. Suh, " Effect of body mass index on peak growth hormone level after growth hormone stimulation test in children with short stature*," Annals of pediatric endocrinology and metabolism*, vol.26, no. 3, pp.192-198,)2021.

[30] A. L. Liu, H. J. Xie, H. Y. M. Xie, J. Liu, J. Yin, J. S. Hu, and C. Y. Peng, "Association between fat mass and obesity-associated (FTO) gene rs9939609 A/T polymorphism and polycystic ovary syndrome: a systematic review and meta-analysis," *BMC Medical Genetics*, vo.18, no.1, pp 89,2017.

[31] S. Gülsen, K. E. Deniz, C Başak, G. Alper, B. S. Yesil, and E. Betül, "The effect of age and gender on HbA1c levels in *adults* without diabetes mellitus," *Journal of Medical Biochemistry*, vol. 42, no.4, pp 714–721, 2023.

[32] D. M. Qahwaji, "Association of Age and Serum Vitamin D Levels in Men with Metabolic Syndrome," *Journal of the College of Physicians and Surgeons Pakistan*, vol. 32, no.3, pp 298-303, 2022.

[33] G. Van Den Berg, J. D. Veldhuis, M. Frölich, and F. Roelfsema, "An amplitude-specific divergence in the pulsatile mode of growth hormone (GH) secretion underlies the gender difference in mean GH concentrations in men and premenopausal women," *The Journal of Clinical Endocrinology and Metabolism*, vol. 81, no.7, pp 2460-2467, 1996.

[34] H. M. AbdlWhab, A. Al-Saffar, O. A. Mahdi, and R. B. Alameri, "The impact of insulin resistance and glycaemic control on insulin-like growth factor-1 in patients with type 2 diabetes: a cross-sectional study," *Clinical Diabetes and Endocrinology*, vol. 10, no.1, pp 36, 2024.

[35] M. Muggeo, P. Moghetti, M. Querena, S. Girotto, E. Bonora, and G. Crepaldi, "Effect of aging on growth hormone, ACTH and cortisol response to insulin-induced hypoglycemia in type I diabetes," *Acta Diabetol Lat.*vol.22,no.2, pp 159-68, 1985. doi: 10.1007/BF02590790. PMID: 3000117

[36] M. E. I. Mohamed, E. A. A. El-Shaarawy, M. F. Youakim, D. M. A. Shuaib, and M. M. Ahmed, "Aging changes in the retina of the male albino rat: a histological, ultrastructural and immunohistochemical study," *Folia morphologica*, vol. 78, no.2, pp 237-258, 2019.

[37] L.M. Al-Ani, H.M. Mahmood, and N.A. Abdulhaleem, " Genetically determined ABO and (Rh) rhesus blood groups and their associations with diabetes mellitus," *Systematic Reviews in Pharmacy,* vol.11, no.4, pp. 604–608, 2020.