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Effect of Diabetes Mellitus Type 2 on the Correlation of Vitamin D with Lipid Profile in Iraqi Patients

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Abstract

Vitamin D deficiency has been linked to several conditions, including type 2 diabetes. The purpose of this study is to determine if there is an effect of type 2 diabetes on the association between vitamin D level, glycemic indices, and lipid profiles. The study was conducted at Al-Noamman Hospital, included 257 patients with type 2 diabetes and 40 healthy participants of both sexes with matching ages ranging from 26 to 80 years. The lipid profile, postprandial glucose (PPG), HbA1C, and serum vitamin D were measured. The results showed that 89 (34.6%) of diabetics have vitamin D insufficiency (less than 30 ng/mL). 155 diabetic patients (uncontrolled glycemic) with elevated HbA1C (9.07% ± 2.5), and from those, about 33.5% have vitamin D insufficiency; they are of age ≥ 55 years, 58.1% female, and 41.9% male, and they have a significant correlation ($r = 0.17$, $P < 0.05$) between HbA1C and vitamin D. All diabetic patients who are classified according to HbA1C subgroups have highly significant correlations ($P < 0.01$) among age and vitamin D; cholesterol with VLDL and LDL; and TG with VLDL. In controlled diabetes patients (HbA1C < 5.7%), a highly significant correlation was found between HDL and vitamin D ($r = 0.50$, $P < 0.01$). We conclude that vitamin D level is highly significantly related to age and sex in diabetic patients who displayed highly significant dyslipidemia and were associated with 34.6% vitamin D insufficiency (significantly with uncontrolled diabetes mellitus patients).

Keywords: HbA1C, Lipid profile, Type II diabetes mellitus, Vitamin D.

تأثير داء السكري من النوع الثاني على ارتباط فيتامين د مع الدهون في المرضى العراقيين

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الخلاصة

تم ربط نقص فيتامين (د) بالعديد من الحالات، بما في ذلك مرض السكري من النوع الثاني. الغرض من هذه الدراسة هو تحديد ما إذا كان هناك تأثير لمرض السكري من النوع الثاني على الارتباط بين مستويات فيتامين د، ومؤشرات نسبة السكر في الدم، وانواع مختلفة من الدهون. أجريت الدراسة في مستشفى النعمان، وشملت 257 مريضاً يعانون من مرض السكري من النوع الثاني و40 مشاركاً يتمتعون بصحة جيدة من كلا الجنسين وأعمارهم متطابقة تتراوح بين 26 الى80 عاماً. تم قياس نسب الدهون المختلفة، الجلوكوز بعد الأكل (PPG)، HbA1C وفيتامين د في مصل الدم. أظهرت النتائج أن 89 (34.6٪) من مرضى السكر لديهم

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نقص فيتامين د (أقل من 30 نانوغرام / مل). 155 مريضًا غير مسيطرين على نسبة السكر في الدم مع ارتفاع HbA1C (9.07٪ ± 2.5)، ومن هؤلاء (33.5٪) لديهم قصور بمستوى فيتامين د، هم من سن ≤ 55 سنة، 58.1٪ إناث و41.9٪ ذكور، ولديهم ارتباط معنوي (r = 0.17، P <0.05) بين HbA1C وفيتامين د. جميع مرضى السكري الذين تم تصنيفهم وفقًا لمجموعات فرعية من HbA1C لديهم ارتباطات ذات دلالة معنوية (P <0.01) بين العمر وفيتامين د؛ الكولسترول معLDL & VLDL، والدهون الثلاثية مع VLDL. في مرضى السكري المسيطر على سكرهم في الدم (HbA1C <5.7%) وجدوا ارتباطًا ذا دلالة إحصائية معنوية عالية بين HDL وفيتامين د (r = 0.50, P < 0.01) . نستنتج أن مستوى فيتامين د يرتبط ارتباطًا وثيقًا بعمر وجنس مرضى السكري الذين أظهروا اضطرابات معنوية عالية في شحميات الدم، وكانت مرتبطة بنقص فيتامين (د) بنسبة 34.6٪؛ (ارتباط معنوي مع مرضى السكري غير المسيطرين على سكرهم في الدم).

1. Introduction

Elevated glucose levels due to insufficient insulin production or activity characterize diabetes mellitus, a chronic pancreatic ailment. Insulin resistance and impaired pancreatic beta cell function are caused by type 2 diabetes. Alterations in insulin function cause lipid, amino acid, and carbohydrate imbalances [1-4]. Vitamin D major role is to increase plasma calcium and phosphate concentrations for bone health. Nevertheless, vitamin D receptors (VDR) are also found in the nucleus of different tissues, where they regulate up to 5% of the human genome (or several hundred genes) [5]. Vitamin D insufficiency may have an effect on cellular metabolism, especially in beta-pancreatic cells and in illnesses characterized by insulin resistance [6]. Vitamin D biological relevance is shown by the correlation between insulin action, glucose homeostasis, and serum vitamin D concentrations. Direct stimulation of $1,25(OH)_2D_3$ production in pancreatic cells or indirect stimulation of calcium balance and calcium flow across membranes are also possible [5,7]. Researchers have shown that vitamin D may prevent diabetics' brains from shrinking [8]. It has been established that a lipoprotein profile that raises cardiovascular risk, blood pressure, or obesity is associated with low vitamin D levels [5,9,10]. Previous research concluded that total vitamin D levels do not play a role in the detection of type 2 diabetes. Altering the glycemic status may, however, be essential [11]. Fasting insulin, HOMA-IR, and hemoglobin A1C levels were not affected by vitamin D status, as reported by Raheem, Ali, and Shareef [12]. The determination of vitamin D status is based on the measurement of the circulating concentration of 25-hydroxyvitamin D (25(OH)D) rather than the fully active form of vitamin D, 1,25-dihydroxyvitamin D ($1,25(OH)_2D$). Although somewhat counterintuitive, 25(OH)D is measured because it is the most abundant circulating form of vitamin D and has a longer serum half-life than $1,25(OH)_2D$. Despite progress in developing sensitive and accurate assays for 25(OH) D, there remains a lack of consensus on the 25(OH)D concentration that is necessary for optimal health [13]. Half of the world's population has healthy levels of vitamin D. Direct exposure to sunlight, physical and health issues, gender, age, lifestyle, environment, and skin color are all factors in the development of vitamin D deficiencies, in addition to sociodemographic factors. The risk of developing type 2 diabetes is associated with low levels of vitamin D [2,14]. Systemic cytokine inflammation causes beta pancreatic cells to undergo apoptosis. Vitamin D may extend the longevity of beta cells by regulating cytokines and decreasing insulin resistance [2]. In this work, we aim to ascertain if type 2 diabetes affects the relationship between vitamin D, glycemic indices, and lipid profiles.

2. Subjects, materials and methods

2.1. Subjects and methods

Two hundred and fifty-seven patients with type 2 diabetes (male and female) and forty apparently healthy people (aged 26 to 80) participated in a prospective study at Al-Noaman Hospital and Private Clinic. The sample collection period is from December 2022 to March

2023. Serum was taken for vitamin D, lipid profile, and postprandial glucose (PPG) analyses from 5 mL of blood obtained from each participant. Gel tubes were used to estimate vitamin D, lipid profile, and PPG, then centrifuged at room temperature for 10 minutes at 3500 r.p.m. to get the serum, while the EDTA tube was for the management of HbA1C. According to the Endocrine Society, the 25(OH)D levels are classified as follows: Adequate concentrations (≥ 30 ng/mL), insufficient concentrations (<30 ng/mL) [15]. The PPG and HbA1C glycemic indicators were used. The levels of HbA1C may be placed in one of three groups [16]:

1) Diabetic are under control if HbA1C is less than 5.7%.
2) Control impairment (5.7-6.4%).
3) Un-control (≥6.4%).

A blood glucose level of 140 mg/dL or less is regarded as normal, whereas levels over that signify abnormality [17]. The Faculty of Medicine at Al-Iraqia University granted ethical approval for this research *via* its Ethical Approval Committee in the Division of Scientific Affairs.

2.2. Materials

Vitamin D and HbA1C levels were measured using the Afias kit of Korean origin, while other biochemical tests were evaluated using biosystem kits of Spanish origin.

2.3. Statistical analysis

We utilized the latest version of the SAS (Statistical Analysis System) software (2018) to analyze the impact of explanatory variables on our measures of interest. The t-test was employed to statistically compare the two means. In order to determine the probabilities of 0.05 and 0.01, as well as to compute the correlation coefficient and its r-degree, the chi-square test was heavily used in this work.

3. Results and discussion

Diabetes mellitus has a major effect on lipid profiles, as shown in Table 1. Very significant increase ($P < 0.01$) in cholesterol, TG, VLDL, HbA1C, and PPG levels across the evaluated groups. Patients who had higher levels of HbA1C and PPG are in line with the research of Abudawood *et al.* [18].

Table 1 : Comparison of measured parameters between studied groups

Parameters	Control (N = 40) Mean ± SE	Patients (N = 257) Mean ± SE	t-test	P-value
Cholesterol (mg/dL)	183.42 ±5.03	207.58 ±2.71	14.08 **	0.001
Triglyceride (mg/dL)	148.72 ±4.20	241.43 ±6.84	34.34 **	0.001
HDL (mg/dL)	43.25 ±2.23	40.31 ±0.74	4.07	0.156
LDL (mg/dL)	110.17 ±4.01	118.82 ±2.46	12.71	0.181
VLDL (mg/dL)	29.90 ±0.86	48.35 ±1.37	6.89 **	0.001
HbA1C (%)	5.12 ±0.08	7.71 ±0.16	0.82 **	0.001
PPG (mg/dL)	99.10 ±3.60	167.5 ±4.28	22.25 **	0.001
Vit. D (ng/mL)	36.12 ±2.13	35.37 ±0.83	4.49	0.741
** (P< 0.01): Highly significant				

In Table 2, it was found that there were extremely significant differences ($P < 0.01$) between the number of male and female diabetic patients in the patient group. These findings corroborate those of the research by Abudawood *et al.* on Saudi patients with type 2 diabetes [18].

Table 2: Distribution of studied samples according to gender

Factor		Control (No = 40)	Patients (No = 257)
Gender No (%)	**Male**	16 (40.00%)	111 (43.19%)
	Female	24 (60.00%)	146 (56.81%)
	P-value	0.188 NS	0.0027**
** (P< 0.01): Highly significant			

The correlation between sexes and the clinical indicators was assessed in diabetic individuals, as shown in Table 3. Females may have clinically greater HDL-C levels than males, even though they are not clinically deemed to be below normal, and vitamin D levels vary tremendously widely. The lipid profiles of women with diabetes showed elevated levels of LDL, total cholesterol, and HDL. HbA1C and VLDL values did not significantly differ between males and females.

Table 3: Effect of gender on measured parameters in the patient group

Parameters	Mean ± SE		P-value
	Male	Female	
Cholesterol (mg/dL)	200.36 ± 3.97	213.07 ± 3.63	0.02*
Triglyceride (mg/dL)	239.99 ± 11.54	242.52 ± 8.28	0.85
HDL (mg/dL)	37.96 ± 0.85	42.09 ± 1.10	0.003**
LDL (mg/dL)	114.05 ± 3.54	122.44 ± 3.38	0.092
VLDL (mg/dL)	48.35 ± 2.31	48.36 ± 1.66	0.99
HbA1C (%)	7.69 ± 0.22	7.71 ± 0.23	0.95
PPG (mg/dL)	171.02 ± 6.69	164.82 ± 5.58	0.47
Vitamin D (ng/mL)	30.29 ±1.04	39.2336 ± 1.14	0.001**
*(P<0.05): Significant **(P< 0.01): Highly significant (P>0.05): Non-Significant			

Women with diabetes are more likely to be adversely affected than men by changes in coagulation, vascular function, and cardiovascular risk factors. Also, lipoproteins in women with hyperlipidemia are affected by both body fat distribution and the influence of sex hormones [18,19]. The non-significant changeable values of HbA1C, VLDL, and LDL in our study agreed with Khan's *et al*. results [20]. In Table 4, the prevalence of diabetes appeared to be significantly higher in the age group ≥ 55 years. This may be related to obesity, increased insulin resistance, and insufficient physical activity [2].

Table 4 : Distribution of patients according to age

Age groups	Number and patients' frequency (Total No. = 257)
<55 yr.	111 (43.19%)
≥55 yr.	146 (56.81%)
P-value	0.0027 **
**(P< 0.01): Highly significant	

Table 5 shows age-related differences in vitamin D levels, which are significantly (P < 0.01) lower in individuals less than 55 years old than in those over 55 years old.

Table 5: Effect of age on measured parameters in the patient group

Parameters	Mean ± SE		P-value
	<55 years old (No. = 111)	≥55 years old (No. = 146)	
Cholesterol (mg/dL)	209.18 ±2.93	206.37 ±4.22	0.610
Triglyceride (mg/dL)	252.69 ±11.28	232.86 ±8.42	0.151
HDL (mg/dL)	39.83 ±0.94	40.67 ±1.08	0.569
LDL (mg/dL)	118.72 ±3.44	118.88 ±3.47	0.975
VLDL (mg/dL)	50.54 ±2.25	46.69 ±1.69	0.166
HbA1C (%)	7.52 ±0.22	7.84 ±0.23	0.325
PPG (mg/dL)	166.35 ±7.05	165.56 ±5.66	0.929
Vitamin D (ng/mL)	29.42 ±1.18	39.90 ±1.02	0.001 **
**(P < 0.01): Highly significant			

The results of Mehta, Patel, and Shah's research [21] support our findings. This may be brought on by a sedentary lifestyle, little exposure to sunlight, and a poor diet [21,22]. Table 6 displays the percentage of individuals with diabetes with varying concentrations of HbA1C, PPG, and vitamin D. Results demonstrate that vitamin D insufficiency is 34.6% common in diabetic patients. Aberrant HbA1C levels are present in 60.3% of diabetic patients, and high PPG levels are present in 53.3% of diabetic patients. Seventeen of forty-seven patients with pre-diabetic HbA1C levels (5.7-6.4%) had vitamin D insufficiency.

Table 6: Demography of some parameters in the patient group

Parameters	Sub-groups	Frequency (%)	Vitamin D < 30 ng/mL	Vitamin D ≥ 30 ng/mL
HBA1C (%)	< 5.7	55 (21.4%)	20 (36.36%)	35 (63.64%)
	5.7- 6.4	47 (18.3%)	17 (36.17%)	30 (63.83%)
	≥ 6.5	155 (60.3%)	52 (33.5%)	103 (66.5%)
PPG (mg/dL)	< 140	120 (46.7%)	47 (39.16%)	73 (60.84%)
	≥ 140	137 (53.3%)	42 (30.66%)	95 (69.24%)
Vitamin D (ng/mL)	< 30	89 (34.6%)	-	-
	≥ 30	168 (65.4%)	-	-

In T2DM, a previous study elucidated the link between blood vitamin D levels and beta-cell activity in the pancreas [23]. However, our findings did not line up with a study that discovered a significant rise in blood glucose in people with low vitamin D levels [24]. In contrast to the results found by Tran *et al*. [25], our investigation found that 65.4% of patients had sufficient vitamin D levels. The disparity is likely attributable to cultural and culinary differences across the countries in question. As a result, supplementing with vitamin D is given to high-risk individuals such those with prediabetes as a prophylactic approach [26]. Another study discovered that T2DM patients with NAFLD had a significant prevalence of vitamin D insufficiency [27]. Table 7 represents Pearson correlations among the measured parameters in the patient group, which was divided into three subgroups according to HbA1C levels: controlled diabetes (<5.7%), impaired (5.7-6.4%) and uncontrolled (≥6.5%). The three subgroups shared the same type of highly significant ($P < 0.01$) correlations between age and vitamin D, cholesterol and LDL, TG and VLDL, as well as cholesterol and VLDL. In addition to other significant relationships mentioned in the table, the most important of which is the significant correlation ($r = 0.17$, $P < 0.05$) between HbA1C and vitamin D in the uncontrolled

diabetic subgroup and the highly significant relationship ($r = 0.50$, $P < 0.01$) between HDL and Vitamin D in the controlled diabetic group.

Table 7: Pearson correlations between different parameters in the patient group

Parameters	HbA1C < 5.7% No. of patients = 55	HbA1C 5.7-6.4% No. of patients = 47	HbA1C ≥ 6.5% No. of patients = 155
	Pearson correlations	Pearson correlations	Pearson correlations
Age and TG	-0.28*	-	-
Age and VLDL	-0.28*	-	-
Age and PPG	-0.27*	-	-
Age and vitamin D	0.52**	0.60**	0.49**
Cholesterol and LDL	0.88**	0.89**	0.82**
TG and LDL	-0.31*	-	-0.23**
TG and VLDL	1.00**	1.00**	0.99**
TG and PPG	0.46**	-	-
HDL and Vitamin D	0.50**	-	-
Cholesterol and VLDL	0.88**	0.46**	0.32**
LDL and VLDL	-0.31*	-	-0.22**
VLDL and PPG	0.46**	-	-
Cholesterol and TG	-	0.41**	0.30**
Cholesterol and HDL	-	0.56**	0.31**
HDL and LDL	-	0.38**	-
HbA1C and PPG	-	0.35*	0.47**
HbA1C and Vitamin D	-	-	0.17*

*Correlation is significant at the 0.05 level.
**Correlation is significant at the 0.01 level.

A meta-study by Forouhi *et al*. [28], discovered a significant negative relationship between baseline vitamin D and the incidence of type 2 diabetes. Additionally, Lips *et al*. [29] observed a link between inadequate vitamin D intake and glycemic control, while, among diabetics, the amount of HbA1C did not significantly correlate with blood vitamin D levels [2]. A study in 2017 focusing on the relationship between vitamin D status and glycemic indices and the prevalent diabetes consequence of peripheral neuropathy in persons with T2DM was reviewed [30]. Santos *et al*. [31] discovered that individuals with T2DM who had better glycemic control also had higher vitamin D levels. Clinical studies on individuals with and without diabetes reveal that taking more vitamin D did not lower blood glucose levels, insulin resistance, or HbA1C levels. Accordingly, taking vitamin D supplements does not generally prevent people with prediabetes from getting diabetes [32]. Pittas *et al*. [33], claim that the existence of Vitamin D Dedicated Receptors (VDRs) on pancreatic cells is evidence of vitamin D's influence on glucose regulation. Muscle cells have VDR, and 1,25-hydroxyvitamin D has a direct influence on insulin receptor gene transcription. Vitamin D supplementation has been shown to improve beta cell activity and decrease insulin resistance in people with type 2 diabetes. Insulin sensitivity is also affected by vitamin D deficiency [2]. Inconsistent results on the correlation between hemoglobin A1C and vitamin D status have been reported and may be attributed to the diverse racial and ethnic compositions of the study populations as well as the use of a wide variety of experimental method [34]. While Abudawood *et al*. [18] believe that high levels of HbA1C are associated with low levels of vitamin D, raising a signal for early diagnosis of type 2 diabetes. The significant positive

correlation between vitamin D and HbA1C in uncontrolled DM patients that was shown in our investigation is not consistent with Al-Fayyadh's results [35], who reported a negative correlation between vitamin D and HbA1C. This research shows dyslipidemia in the diabetic group, which comes in line with Balaky and Kakey [36], although vitamin D levels did not correlate significantly and favorably (unless with HDL in the control diabetic patients) with the altered lipid abnormalities in T2DM patients.

4. **Conclusion**

Diabetic individuals, whether controlled or uncontrolled, displayed dyslipidemia (highly significant elevated levels of cholesterol, TG, and VLDL) and were associated with 34.6% vitamin D insufficiency. Uncontrolled diabetes mellitus patients with HbA1C $\geq$ 6.5 are significantly more likely to be vitamin D insufficient than impaired and well-managed diabetes patients. Vitamin D levels were significantly related to the age and sex of diabetic patients.

Conflict of Interests

The authors declare that they have no conflicts of interest.

Ethics clearance

The research ethical committee at scientific research has the ethical approval of environmental, health, higher education, and scientific research ministries in Iraq.

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