Original Article

Evaluation of HbA1C and serum levels of vitamin D in diabetic patients

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Abstract

Background: Diabetes mellitus is the most common metabolic disease around the world. The present study aims at studying hemoglobin A1C (HbA1C) and vitamin D serum levels in diabetic patients. **Materials and Methods:** A descriptive study was conducted on 102 diabetic patients presenting to the diabetic clinic of a tertiary care hospital in West of Iran in 2016 (Shahid Mostafa Khomeini Hospital of Ilam city). The data collected were inserted into the SPSS-20 software, and it was then analyzed by using the relevant statistical tests. For describing the quantitative variables, mean and standard deviation were used. Moreover, for describing the qualitative variables, number and percentage were applied. The mean serum levels of HbA1C and vitamin D were compared for different variables using the Chi-square and ANOVA. **Results:** There is a positive and statistically significant relationship between the HbA1C and fasting blood sugar (FBS). Moreover, there is a statistically significant relationship between the serum level of vitamin D with smoking and body mass index (BMI). There is also an inverse linear relationship between vitamin D with HbA1C, FBS, BMI, and disease duration. The relationship between HbA1C with FBS and disease duration is a linear direct one. Their relationship between HbA1C and BMI is an inverse linear one, yet not significant. **Conclusion:** Given the role of this vitamin in secretion and the effect of insulin, it seems useful to monitor the serum level of vitamin D in a diabetic patient and prescribe its supplements if necessary.

Keywords: Diabetic patients, hemoglobin A1C, Ilam, serum levels of vitamin D

Introduction

Diabetes mellitus is the most common metabolic disease in the world. More than 150 million people suffer from this disease in the world, and it is predicted that this number will rise to 300 million in 2025.[1] Iran is facing an increasing prevalence of diabetes, and its prevalence is currently 7% in Iran.[2] Vitamin D is an indispensable part of nutrition. In comparison to the other vitamins, vitamin D has unique metabolic and physiological effects.[3–7] The shortage of vitamin D is epidemically prevalent in the world; 20–25% of the population suffers from the lack of vitamin D in USA, Canada, Europe, Mexico, Asia, and Australia.[8] Surprisingly, the lack of vitamin D in the Persian Gulf countries is highly prevalent, though there is enough sunshine. The prevalence of vitamin D (serum level of vitamin D) deficiency is higher among female adolescents and young adults in Iran and >80% in Saudi Arabia.[9]

The lack of vitamin D and type 2 diabetes have similar risk factors including race, obesity, high age, place of residence, and lack of physical activity. In a number of studies, it has been observed that 25-hydroxyvitamin D serum level is significantly lower in diabetic patients than healthy individuals.[10-12] Vitamin D

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affects the production and secretion of insulin as well as insulin sensitivity.[13] Vitamin D is also likely to affect reduced risk[14-17] and control type 2 diabetes.[11,14] Given the increasing prevalence of type 2 diabetes and shortage of vitamin D, it is important to study this relationship. For this reason, various studies have been conducted all over the world on this issue.

For the incidence of type 2 diabetes, there is an increased performance of pancreatic beta cells, resistance to insulin, and systemic inflammation. There is evidence indicating the effects of vitamin D on the abovementioned complications.[18] Vitamin D is likely to indirectly affect insulin secretion and insulin sensitivity through beta cells and environmental tissues that are the targets of insulin. The immunomodulatory features of vitamin D in relation to T cells activity is effective for some immune processes leading to type 1 diabetes.[19]

Different studies have indicated the relationship between the lack of vitamin D and concentration changes of blood glucose and insulin and the sensitivity of tissues targeted for insulin.[20,21] Moreover, the lack of vitamin D in patients suffering from type 2 diabetes is likely to cause a metabolic syndrome and the replacement of vitamin D can reduce resistance to insulin.[22] Some of the studies have confirmed that vitamin D plays a key role in insulin secretion and performance disorder.[23] A number of cross-sectional studies have indicated the coincidence of vitamin D status and the prevalence of impaired glucose tolerance (IGT) or diabetes. Two studies conducted by Kohert in America and a study conducted in Finland have reported the coincidence of vitamin D status and the risk of suffering from type 2 diabetes.[24,25] In women's health study, receiving 511 units of vitamin D, in comparison to 159 units, is likely to result in a reduced risk of suffering from type 2 diabetes. However, this analysis has not been modified for any other intervention factors other than age.[24] There is a significant statistical coincidence between high serum levels of vitamin D and low incidence of diabetes in Finnish men.[25] Another study conducted in New Zealand indicated that patients with type 2 diabetes and IGT had a lower level of vitamin D in comparison to the control group.[26] There is a hypothesis indicating that there is a positive relationship between 25-hydroxyvitamin D serum level and obesity. Given the effect of vitamin D on increased lipogenesis and lipolysis control in the *in vitro* studies conducted, some researchers have reported this relationship as positive.[27] However, other studies conducted in this regard indicated the negative effect.[28,29]

Given the contradictory findings of the existing studies, it seems necessary to conduct further studies with different statistical populations; if it is proved that lack of vitamin D has a major role in the incidence of type 2 diabetes, the compensation of this lack will constitute the main part of the treatment for diabetic patients. Thus, given the importance of the issue, variety in the research findings, difference in climatic conditions, the dietary regime of people in different areas, and the lack of conducting a similar study in Ilam, the present research was conducted to study HbA1C and vitamin D serum levels and determining the serum level of vitamin D in diabetic patients. Moreover, the patients' demographic variables [age, gender, smoking, place of residence, body mass index (BMI), diabetes duration, glycated hemoglobin, fasting glucose level, and vitamin D] were determined.

Materials and Methods

The present study is a cross-sectional descriptive one conducted on the diabetic patients being referred to the internal clinic of a tertiary care hospital in Ilam. The patient's demographic and anthropometric information were recorded by using individual questionnaires. Sampling was conducted in the fasting state from 8 to 10 in the morning and before taking glucose-lowering drugs and the serum level of vitamin D was measured by using the enzyme-linked immunosorbent assay **(**ELISA) method and applying the kit. Given the prevalence of >70%, lack of vitamin D of 81 individuals was measured in diabetic patients with the sample size error rate of 0.1. For increasing the statistical power of the research, 102 patients were studied.

Sample size was selected randomly after implementing the inclusion and exclusion criteria. Inclusion criteria are as follows: diagnosed type 2 diabetes for >1 year; lack of drinking alcohol; lack of treatment with insulin; lack of menopause or pregnancy (for female participants); lack of taking intervention drugs or vitamin D (corticosteroids, anticonvulsants, and contraceptives); lack of history of angina, myocardial infraction, stroke, kidney or liver diseases, chronic inflammatory diseases, and thyroid diseases during the recent year; lack of treatment with thiazolidinedione drugs; and lack of smoking of all kinds. The exclusion criteria are suffering from diagnosed liver or kidney diseases, having a creatinine of >2 mg/dl, malabsorption, infertility, oligomenorrhea, pregnancy, breastfeeding, diagnosed malignancy, taking drugs affecting bone metabolism, drinking alcohol, inactivity for >1 week, taking calcium supplement in the last 2 weeks, taking vitamin D pills in the last 3 months, injection of vitamin D in the last 6 month, obesity (BMI >40 kg/m^2), severe complications of diabetes in patients suffering from diabetes (nephropathy, retinopathy, and so on), and HbA1C >11%.

After recording the demographic and anthropometric characteristics, measuring the blood pressure, and after 12 h fasting, the qualified participants were referred to the laboratory, and 10 ml of blood was taken from them. The analysis of blood samples for measuring fasting blood sugar (FBS) was conducted by the Hitachi 917 auto analyzer. For measuring blood lipids profile Hitachi 917 machine was used by a photometric method. 25-hydroxyvitamin D serum level was measured by using the chemiluminescence method using LIAISON machine and it was then analyzed in the DIaSorin30 kit, and 30–100 ng/mL was determined as the natural amount. Moreover, 20 < vit D (OH) <25 ng/mL was determined as vitamin D deficiency, 25 < vit D <30 ng/mL was determined as inadequacy of vitamin D, and vit D >30 ng/mL was defined as adequacy of vitamin D.[30]

The data collected from the patients were inserted into the SPSS-20 and it was then analyzed by using relevant statistical tests. For describing the quantitative variables, mean and standard deviation were used. Moreover, for describing the qualitative variables, number and percentage were applied. The mean serum levels of HbA1C and vitamin D were compared for different variables using the Chi-square and analysis of variance (ANOVA). Glycated hemoglobin (HbA1C) was used as the gold standard of blood glucose control and a criterion for estimating the intensity of its complications.

Findings

Frequency distribution of demographic variables and the means of quantitative variables are shown in Tables 1 and 2.

The findings indicate a positive significant relationship between HbA1C and FBS [Table 3].

The findings indicate that there is a significant relationship between the serum level of vitamin D with smoking and BMI [Table 4].

Pearson correlation coefficient test indicates that there is an inverse linear relationship between vitamin D with HbA1C, FBS, BMI, and disease duration. Moreover, Pearson correlation coefficient indicates that the relationship between HbA1C with FBS and disease duration was a linear direct one. The relationship between HbA1C and BMI was an inverse linear one and it was not significant [Table 5].

Table 1: Frequency distribution of demographic variables in the patients studied

Demographic variables		Frequency	Percentage
Age	<30	11	10.8
	30-60	66	64.7
	>60	25	24.5
Gender	Male	28	27.5
	Female	74	72.5
Smoking	Yes	24	23.5
	No	78	76.5
BMI	<20	37	36.3
	20-25	48	47
	>25	17	16.7
Place of residence	City	88	86.3
	Village	14	13.7

Table 2: The mean of quantitative variables in patients studied

Variable	*n*	Mean±SD	Min	Max
Age	102	15.38±48.95	19	82
Disease duration	102	1.91±3.58	1	9
Weight	102	9.55±71.43	50	95
Height	102	8.2±167.14	141	190
FBS	102	64.15±139.48	59.3	433
A1C	102	1.91±7.31	5.1	13.4
D3	102	8.77±19.75	1.3	46.1
BMI	102	3.11±21.47	16.98	30.34

Discussion and Conclusion

Based on the findings, the serum level of vitamin D was low in diabetic individuals, and in these patients, there was no significant relationship between serum level of vitamin D with diabetes duration and HbA1C.

The findings of this study indicated an inverse linear relationship between vitamin D with HbA1C ($P < 0.37$), FBS, ($P < 0.64$), BMI ($P < 0.59$), and disease duration ($P < 0.1$). There was also a direct linear relationship between HbA1C with FBS and disease duration ($P < 0.000$ and $P < 0.000$) and an inverse linear relationship between HbA1C and BMI ($P < 0.41$). Given the role of this vitamin in secretion and the effect of insulin, it seems useful to monitor the serum level of vitamin D diabetic patients and prescribe its supplements if necessary.

In the present study, 53.9% of the patients suffered from vitamin D deficiency, and this is more or less similar to the findings of the study conducted by Taheri *et al.*; vitamin D deficiency plays an important role in the pathogenesis of type 2 diabetes.

Table 3: Mean and standard deviation of HbA1C in patients studied according to different variables

Variables		*n*	Mean±SD	*P*
Smoking	Yes	24	1.95±7.39	0.74
	No	78	1.91±7.28	
Age	<30	11	1.36±6.47	0.18
	30-60	66	1.86±7.29	
	>60	25	2.17±7.73	
Gender	Male	28	2.06±7.14	0.58
	Female	74	86.1±37.7	
FBS	<70	1	10.3	0.000
	70-115	46	1.9±8.45	
	>115	55	1.22±6.3	
BMI	<20	37	2.33±7.67	0.35
	20-25	48	1.64±7.1	
	>25	17	1.56±7.11	

Table 4: Mean and standard deviation of the serum level of vitamin D in patients studied according to different variables

Variables		*n*	Mean±SD	*P*
Smoking	Yes	24	10.79±20.27	0.04
	No	78	8.15±21.44	
Age	<30	11	8.04±20.78	0.93
	30-60	66	9.2±21.41	
	>60	25	8.33±20.68	
Gender	Male	28	10.82±22.79	0.25
	Female	74	7.9±20.55	
FBS	<70	1	15.3	0.78
	70-115	46	8.92±21.04	
	>115	55	8.82±21.37	
BMI	<20	37	8.88±23.36	0.003
	20-25	48	6.68±20.08	
	>25	17	10.12±15.89	

Table 5: The correlation coefficient between serum level of vitamin D and HbA1C with the indices studied

		Age	Vitamin D	HbA1C	FBS	BMI	Disease duration
Age	Pearson	1	0.038	0.221	0.315	0.102	0.080
	P		0.7	0.02	0.001	0.3	0.42
Vitamin D	Pearson	0.038	1	−0.088	−0.047	−0.187	−0.164
	P	0.703		0.378	0.643	0.059	0.1
HbA1C	Pearson	0.221	−0.088	1	0.670	−0.082	**0.693
	P	0.02	0.378		0.000	0.411	0.000
FBS	Pearson	0.315	−0.047	0.670	1	−0.144	**0.401
	P	0.001	0.643	0.000		0.149	0.000
BMI	Pearson	0.102	−0.187	−0.082	−144.0	1	0.017
	P	0.309	0.059	0.411	149.0		0.869
Disease duration	Pearson	0.080	−0.164	0.693	0.401	0.017	1
	P	0.424	0.1	0.000	0.000	0.869	

The findings of the study conducted by Hidayat *et al.* on elderly people suffering from type 2 diabetes in Indonesia revealed that the serum level of vitamin D is higher in men than that of women, and this difference is significant.[31]

The findings of the present study are similar to those of the study conducted by Bonakdaran and Varasteh; the serum level of vitamin D reduces as the BMI increases, and there is a significant statistical relationship between serum level of vitamin D and BMI.[32]

Pearson's correlation coefficient test indicated an inverse linear relationship between vitamin D with HbA1C ($P < 0.37$), FBS (0.64), BMI ($P < 0.59$), and disease duration ($P < 0.1$); the relationship was not statistically significant. Moreover, Pearson's correlation coefficient indicated that there was a direct linear relationship between HbA1C with FBS and disease duration, and the relationship was statistically significant ($P < 0.000$ and $P < 0.000$, respectively). However, the relationship between HbA1C and BMI was an inverse linear one, and the relationship was not significant ($P < 0.41$).

In the present study, there was an inverse relationship between BMI and HbA1C. However, it was not statistically significant. There was a direct and an indirect significant relationship between diabetes and HbA1C.

Pearson's correlation coefficient indicated no significant relationship between diabetes duration and vitamin D ($P < 0.1$ and $r = 0.164$). Moreover, this test indicated a linear and significant relationship between diabetes duration and HbA1C ($P < 0.000$ and $r = 0.693$). Longer duration of suffering from the disease will bring about an increase in HbA1C. This is not surprising, since given progressive process of diabetes, the patient will be at a more developed stage of the disease as the duration of diabetes increases, and it will be more difficult to control the disease. These findings confirm those of the studies conducted by Carter *et al.* (2000), Patti *et al.* (1995), and Simon *et al.* (1989).[33-35] However, statistically speaking, in the present study as well as that of Simon *et al.*[36] no significant relationship was found between HbA1C with factors such as age, gender, BMI, and smoking.

In the present study, no significant relationship was observed between serum level of vitamin D and HbA1C. However, in the study conducted by Danaei *et al.* (2014), a significant negative relationship has been reported between serum level of vitamin D and HbA1C.[37]

According to the present study as well as other studies conducted in this regard, since vitamin D necessary for human body is supplied through receiving foods, vitamin D supplements, and sunshine, and given the high prevalence of vitamin D deficiency in diabetic patients, it is recommended to adopt special measures to compensate the deficiency of this vitamin in diabetic patients.

Ethical considerations

The present study was conducted after acquiring the necessary permit from the University Ethics Committee as well as letter of consent from the patients participated.

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Conflicts of interest

There are no conflicts of interest.

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