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Research Article

A Study on Vitamin D Levels in Patients with Type II Diabetes compared to Normal Subjects

Mahboobe Taghipur[1], Hajieh Shahbazian[2], Homeira Rashidi[3], Zeinab Dehghan Mohamadi[4], Reza Amani[5], Bahman Ghaderian[6], Seyed Mahmoud Latifi[7]
Health Research Institute, Diabetes Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Khuzestan, Iran

***Corresponding author**
Hajieh Shahbazian
Email: hjb_shahbazian@yahoo.com

Abstract: Vitamin D deficiency is highly prevalent in the world and in Asian countries including Iran. There is a great deal of evidence suggesting the relationship between serum Vitamin D level and prevalence of type II diabetes. The objective of this study was to assess the serum level of Vit D in diabetics and non-diabetics and to compare the results of the two groups. This descriptive epidemiological study was carried out on 79 participants including 40 diabetic patients and 39 healthy individuals. The participants were randomly selected from the participants of the Ahwaz Metabolic Syndrome project. The serum vitamin D level, FBS, PTH, and insulin level were measured in the participants. The insulin resistance (HOMA-IR index) was also calculated for all participants. In general, 97.1% of healthy participants and 88.1% of diabetics were diagnosed with vitamin D deficiency or inadequacy. No difference was observed between the levels of vitamin D in the two groups (P=0.23). There was a statistically significant difference in the average levels of HOMA-IR, insulin level, and FBS of the two groups (P<0.0001). in conclusion Research results revealed the equally high prevalence of the disorder in the two study groups.
Keywords: Vitamin D, Diabetes Mellitus, HOMA-IR

INTRODUCTION

Diabetes is one of the most common endocrine disorders and an important global issue for the society's health [1]. The estimated prevalence of this condition in the U.S. will rise from 6% (16 million patients) in 2005 to 12% in 2050 (48 million patients) [2]. Vitamin D is a fat-soluble substance that was discovered in 1930 and named as Calciferol. In addition to its crucial role in the bone health, vitamin D has been recognized for several other functions. For instance, it prevents the proliferation of malignant cells in colorectal, breast, and prostate cancers, and also plays a role in autoimmune diseases [3]. Although the major role of vitamin D lies in maintaining the calcium balance, there are numerous findings suggesting its role in the immune system function and type I and II diabetes [4]. Studies have demonstrated that the prevalence of diabetes and diabetic blood sugar variations dramatically increases in the UK during the cold seasons when vitamin D level lowers [5]. In animal models and in humans, vitamin D deficiency has been shown to alter the production and secretion of insulin [6]. Vitamin D deficiency increases the PTH levels, which in turn, heightens the intracellular calcium ions, thus inhibiting the insulin receptors in target tissues and blocking Glat 4, which is an internal critical gateway for glucose in muscle and adipose tissues [7]. The presence of vitamin D receptors and vitamin D-binding protein in the pancreas and the link between certain genes of vitamin D receptors and the vitamin D-binding protein highlights such a role through glucose tolerance and insulin secretion [8]. Increased insulin secretion is a response to administration of oral glucose with vitamin D in both diabetics and healthy individuals with vitamin D deficiency [10]. Some studies have reported evidence of improved blood sugar indicators in patients with osteomalacia treated with vitamin D [11].

METHODOLOGY

In this descriptive-epidemiologic study, subjects were randomly selected from the participants in Ahvaz Metabolic Syndrome Plan [12], where a total of 2700 subjects had been called through cluster sampling by multiple health centers in Ahwaz. At the end, 79 cases were selected randomly (39 cases diabetic and 40 cases healthy). The fasting blood sugar (FBS) was measured through the glucose oxidase method using the MAN kit called supplied by Tehran-Iran Co. It was administered by the luminescence method using the relevant kit (Diasorin, U.S.). The PTH measurement involved the immunoradiometric assay (IRMA) using a DIASORIN kit, the natural range of which is 13-54 nmol/L. The vitamin D level was measured by the luminescence method developed in the US. The insulin resistance was assessed through the homeostasis model using the H0MA-IR formula (insulin x FBS)/22.5 [13]. The insulin level was measured through IRMA (Biosora, Denmark).

The data were analyzed by SPSS. The variables were evaluated through the Student's t-test. In this study, the subjects were divided into three groups based on vitamin D levels. The group with vitamin D level lower than 20 ng/dl was assigned to the deficiency group, while the groups with vitamin D level of 20-30 ng/dl and vitamin D level over 30 ng/dl were assigned to the insufficiency and sufficiency groups, respectively [14]. The FBS≥126 was considered diabetic, whereas FBS<126 was considered normal [15].
Furthermore, HOMA-IR<3.2 was defined normal, 3.9<HOMA-IR<3.19 was intermediate and HOMA-IR>3.9 was the insulin-resistant group [16].

FINDINGS

A total of 79 subjects were divided into two groups of diabetic and non-diabetic. In this respect, 39 subjects were placed in the diabetic group, and 40 subjects were placed in the normal group. Moreover, 75% of the subjects were men and 35% were women. The normal vitamin D level was observed only in 2.9% of healthy subjects and 11.7% of the diabetic patients. The mean age of patients in the healthy and diabetic groups were 39.3±16 and 52.3±26.7 years, respectively, where there was no statistically significant difference (P=0.28). There was no significant difference between the two groups in terms of gender frequency, body mass index (BMI), and serum PTH level, (P=0.63), (P=0.73), and (P=0.9) (Table 1). This study intended to examine the vitamin D levels in diabetics and non-diabetics. The mean vitamin D serum level in patients was 11 ng/ml, while it was 10 ng/ml in non-diabetics.

The evaluation of vitamin D levels in the experimental and control groups revealed no significant difference (Table 2) (P=0.23). The mean FBS, mean insulin level and mean HOMA-IRF in the diabetic group was higher than those in the control group. This difference was statistically significant at P=0.02, P=0.001, and P=0.001.

Mean of FBS and insulin resistance with Vit. D had significant difference in diabetic and normal group (P= 0.001, 0.001 respectively) (figure1, 2)

Table 1: Patient characteristics in normal and deficient group

Variable	Normal Vit D	Deficient	P value
Age	39.53±16.5	52.3±26.7	0.28
Sex M/F	48/25	3/3	0.43
PTH	32.2±13.2	27.7±31.12	0.73

Table 2: Frequency of Vit D level in normal and diabetic group

Group	Deficient<20(%)	20-30(%)	Normal>30(%)	Total (%)
Normal	32(94.1)	1(2.9)	1(2.9)	34(100)
Diabetic	25(73.5)	5(14.7)	4(11.8)	34(100)

Table 3: Comparison mean of FBS, Insulin level And HOMA-IR in diabetic and normal group

Variable	Normal Group	Diabetic group	P Value
FBS	85.5±8.9	208.3±70.6	0.02
Insulin	5.27±2.8	9±8.6	0.001
HOMA-IR	1.1±0.61	3.4±2.5	0.001

DISCUSSION

The role of vitamin D in the pathogenesis of type II diabetes has been proved through the involvement of vitamin D receptors and vitamin D-binding proteins in the pancreas. Moreover, there is a link between certain alleles of vitamin D-receptor genes and the binding proteins, which farther establishes the role of vitamin D through glucose tolerance and insulin secretion.

The role of vitamin D in type II diabetes is not evident only in regulating the serum calcium, which in turn, regulated the insulin secretion and synthesis, but also in the direct effect on beta-cell function. The engagement of vitamin D receptors and gene expression of alpha-hydroxylase in the pancreas beta cells produces an active form of vitamin D, the involvement of a factor responding to Vitamin D Response Element (VDRE) in insulin gene promoter in humans and the role of vitamin D in activation of factors contributing to insulin gene translation in humans. Vitamin D can stimulate the expression of insulin receptor and promote the response from factors transporting glucose to insulin in vitro and activation of the PPARδ, which contributes to the regulation of metabolism of fatty acids in skeletal muscle cells and adipose tissues.

In this descriptive-epidemiological study conducted on diabetics and non-diabetics, the mean vitamin D level in the diabetic group was 11 ng/dl, while it was 10 ng/dl in the normal subjects, which showed no statistically significant difference (P=0.16). The vitamin D deficiency in the healthy group and the patient group were 1.95% and 2.88, respectively. In a study, Hosseinnejad *et al.* examined a total of 646 healthy adults 20-79 years of age residing in Tehran. The overall prevalence of vitamin D was 72.3% (73.1% among men and 72% among women). The mean serum vitamin D level in subjects with type II diabetes was higher than that in healthy subjects and patients with type I diabetes [15].

In another study, Shirinzadeh [16] *et al.* observed that the mean vitamin D serum level in 61 patients with type II diabetes in Tehran was 10.87±56% mol/liter. Moreover, the calcium serum level was 9.45±23%. mg/dL. In this study, a high percentage (78.8%) of type II diabetics suffered from vitamin D deficiency. In contrast to the current study, Shirinzadeh's study did not involve any control group. In their study based in Isfahan, Taheri [17] *et al.* reported a relationship between vitamin D level and glycemic index in those with type II diabetes as compared to healthy subjects. Even though the vitamin D serum level in patients was lower than that in control group, there was no significant difference according to HOMA-IR results and the vitamin D levels. The percentage of healthy subjects with vitamin D deficiency was 94.5% (HOMA-IR<3.9), while it was 84.6% in subjects with insulin resistance (HMA-IR>4), which showed no significant difference (P=0.21). There was no statistically significant difference between the vitamin D level and HOMA-IR in both groups, which is consistent with the reports provided by Taheri *et al.* [17]in Isfahan. Numerous studies have so far been conducted on the relationship between vitamin D level and metabolic syndrome through the HOMA-IR index. In a NHANES III survey, Scrayg *et al.*[18] evaluated the vitamin D serum levels in a total of 6228 men and women 40 to 74 years of age with type II DM, including 1726 Mexican-Americans, 1726 African-Americans and 2766 non-Hispanic Whites. The vitamin D serum level was inversely correlated with HOMA-IR. Luo *et al.* [19] examined a total of 3262 Chinese subjects 50 to 70 years of age and reported an inverse relationship between HOMA-IR and vitamin D level. Furthermore, Gannage *et al.;* [20] carried out a study on 381 non-diabetic men in the Middle East. In general, the vitamin D serum level was in a significantly inverse correlation with BMI, systolic blood pressure, waist circumference, fasting blood glucose, insulin serum level, and HOMA-IR (P<0.01). It has been argued that the insignificant relationship between vitamin D and insulin serum level and HOMA-IR in the study by Taheri *et al*[17]. could be due to the fact that the participants were in the early stages of diabetes. In the current study, the duration of diabetes was unknown. It was reported in New Zealand that patients recently diagnosed with type II diabetes had lower vitamin D levels compared to the control group [19]. The prevalence of type II diabetes tends to be higher in obese patients, which is usually associated with low vitamin D level. It is suggested that vitamin D is stored in adipose tissues which is not beneficial in terms of biological accessibility [20].

In this study, however, there was no statistically significant difference between vitamin D and BMI. In terms of gender, there was no significant difference between men and women and vitamin D levels in the two groups of diabetic and healthy subjects. In a study conducted in Netherlands, vitamin D level in older men was reported to be lower than that in younger men. The lack of a gender difference in this study between the two groups can be associated with the high prevalence of vitamin D deficiency in both genders

The results obtained by the Third National Health and Nutritional Examination Survey suggested that vitamin D level is inversely correlated with diabetes among White non-Hispanics and Mexican Americans. In case of the Black Hispanics, however, there was no such an inverse correlation

In a study in UK, no relationship was observed between vitamin D level and FBS in the study population [2, 17]. All these findings suggest that Hypovitaminosis D can be a risk factor for impaired glucose tolerance and diabetes, but not in all populations. The relationship between vitamin D level and diabetes varied across ethnicities [3, 17]. According to some studies, the sensitivity to vitamin D and the involved hormones, such as PTH, might have been diminished [4, 17]. In another study, the sensitivity level of non-Hispanic Blacks and Caucasians were compared and a reduction in sensitivity to PTH was reported [5, 17]. Since the vitamin D levels in the current study were low for both diabetic and healthy groups, no decisive judgment can be made in this regard. It is therefore recommended that the treatment of deficiency be followed by further cohort studies on diabetics and non-diabetics under strict control conditions of vitamin D level. In this light, the population can be better judged concerning the relationship between vitamin D and diabetes or insulin resistance. In addition, vitamin D increases the insulin secretion while reducing the vitamin D level. Thus, a sharp decline in insulin level in diabetics can decrease the vitamin D level. Insulin resistance and glucose level are improved following para thyroidectomy [5, 17]. Therefore, there are multiple metabolic relationships between lower vitamin D levels and insulin secretion variation and type II diabetes, which can vary in different populations.

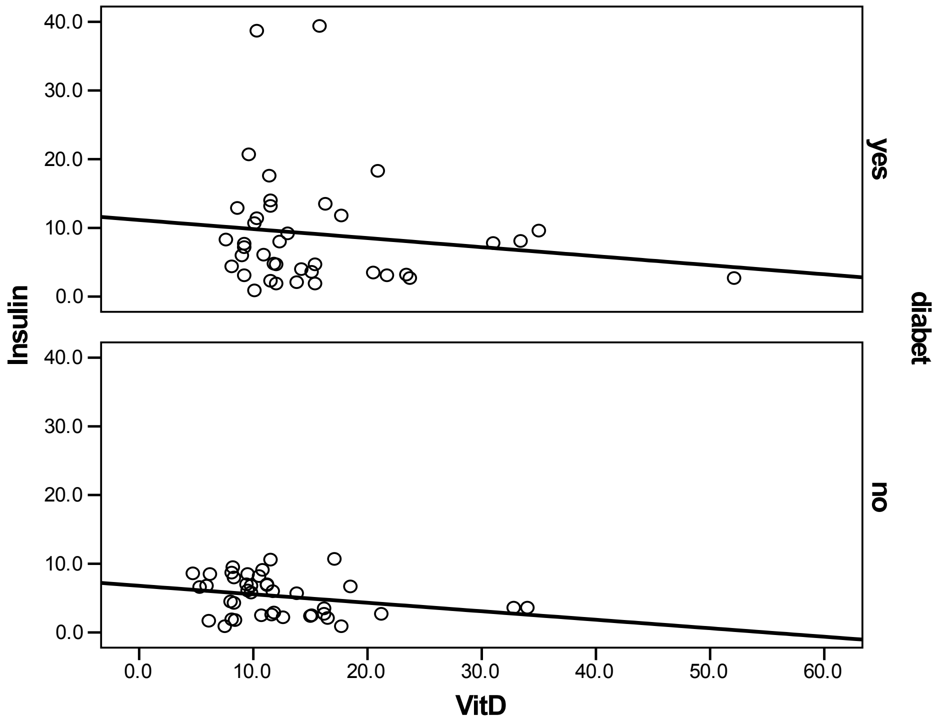

Fig-1: Relation between Vit D and Insulin level in diabetic and non diabetic group

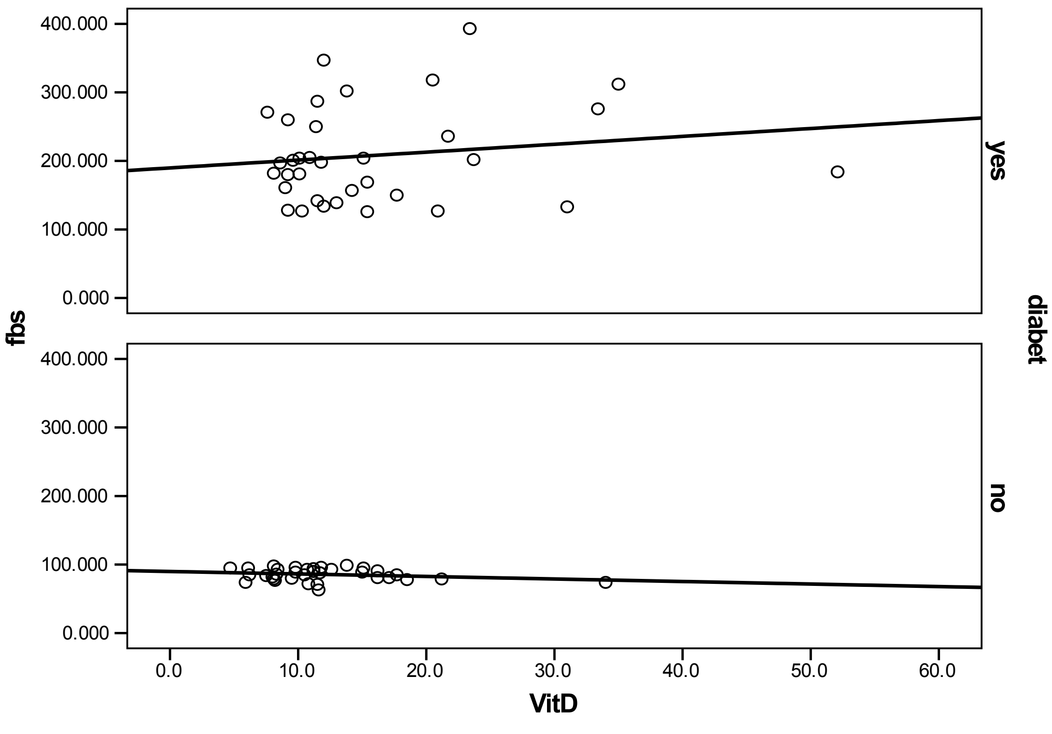

Fig-2: Relation between Vit D and FBS level in diabetic and non diabetic group

CONCLUSION:

The results of this study showed we have Vit. D deficiency in both diabetic and healthy group. Treatment of this deficiency recommended.

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