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Research Article

The Relationship Between Vitamin D Deficiency and Prediabetes

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Abstract

Introduction and Aim: Prediabetes is defined as the initial stage of diabetes mellitus. Approximately 25 - 30% of patients with prediabetes progress to diabetes mellitus within the following 5 years. Vitamin D deficiency is an important and common health problem. Observational studies has shown a relationship between low blood 25-hydroxyvitamin D levels and diabetes risk, but it is unclear whether vitamin D supplementation reduces diabetes risk. This study aims to investigate the relationship between vitamin D levels and prediabetes.

Method: Forty-four patients with prediabetes and 40 healthy controls who attended the Departments of Endocrinology and Internal Medicine outpatient clinics of Antalya Training and Research Hospital between 2017 and 2021 were enrolled in the study. The levels of HbA1c, fasting blood glucose, creatinine, sodium, potassium, blood urea nitrogen, total cholesterol, low-density lipoprotein, very low-density lipoprotein, high-density lipoprotein, and triglycerides were measured during the biochemical analysis and if vitamin D deficiency is suspected calcium, phosphorus, albumin, and vitamin D levels were measured. Data of the patients were evaluated retrospectively.

Results: Serum vitamin D levels were significantly lower in patients than controls ($p = 0.02$). Serum calcium levels were lower in patients than controls but the result was not statistically significant ($p = 0.07$). A significant inverse or negative correlation was observed between HbA1c ($r: -0.32$ $p = 0.001$), fasting blood glucose ($r = -0.41$, $p < 0.001$) and vitamin D levels.

Conclusion: Vitamin D levels were found to be significantly lower in prediabetics. There is a significant inverse correlation between fasting blood glucose, HbA1c and vitamin D levels. Prospective studies with a large number of patients are needed to confirm the findings.

Keywords: *Prediabetes; Vitamin D; HbA1c; Fasting Blood Glucose*

Introduction

Prediabetes is defined as the initial stage of diabetes mellitus (DM). According to the definition of the American Diabetes Association (ADA), prediabetes is impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or a combination of both, with HbA1c between 5.7% and 6.4% [1]. Approximately 25 - 30% of patients with prediabetes progress to DM within the following 5 years [2]. Vitamin D (vit-D) is a steroid hormone that is mainly produced in the skin and regulates the expression of many genes [3]. Vit-D deficiency is an

important and common health problem [3]. The 25-hydroxy vitamin D [25(OH)D] level is used to assess vit-D status in patients at risk of vit-D deficiency. Vit-D deficiency is generally defined as 25(OH)D level < 20 ng/ml, and vit-D insufficiency as 25(OH)D level 20 - 29 ng/ml [4]. The main task of vit-D is to balance bone, calcium and phosphorus metabolism. However, in recent years, it has been reported that vit-D is an immunomodulatory molecule and plays a role in the formation of autoimmune diseases, heart diseases, cancer, inflammatory bowel diseases, rheumatological diseases and DM [5]. Recent studies have reported that low blood 25(OH)D level is a possible risk factor for type 2 DM and that vit-D supplementation may reduce the risk of DM [6,7]. It has been reported that there is a relationship between low blood 25(OH)D levels and impaired pancreatic beta cell function and insulin resistance [8]. Observational studies has shown a relationship between low blood 25(OH)D levels and DM risk, but it is unclear whether vit-D supplementation reduces the risk of DM [9-11].

Aim of the Study

This study aims to investigate the relationship between vit-D levels and prediabetes.

Materials and Methods

Forty-four patients with prediabetes and 40 healthy controls who attended the Departments of Endocrinology and Internal Medicine outpatient clinics of Antalya Training and Research Hospital between 2017 and 2021 were enrolled in the study. Patients from 18 to 60 years old were included in the study. The research was carried out retrospectively by examining the file data recorded in the patients' data processing system. Patients with fasting blood glucose (FBG) of 100 - 125 mg/dl were identified as IFG. Patients with a blood glucose of 140 - 199 mg/dl measured 2 hours after the oral glucose tolerance test were considered IGT. Patients with IFG, IGT or both (IFG+IGT) constituted the prediabetic patient group. HbA1c levels between 5.7% and 6.4% were identified as prediabetic. FBG < 100 mg/dl, and 2nd-hour glucose values < 140 mg/dl and HbA1c < 5.7% were taken as a control group. Subjects with prior history of cardiovascular diseases, autoimmune disease, cancers, obesity (body mass index ≥ 30 kg/m^2), chronic renal failure (glomerular filtration rate of < 60 ml/min), osteomalacia, any other bone diseases, patients who were on calcium (Ca), vit-D supplements, or those using metformin or any antidiabetic drugs, pregnant and lactating women were all excluded. All subjects underwent anamnesis and physical examination and laboratory tests related to their diseases. The levels of HbA1c, FBG, creatinine, sodium, potassium, blood urea nitrogen (BUN), total cholesterol, low-density lipoprotein (LDL), very low-density lipoprotein, high-density lipoprotein (HDL), and triglycerides (TG) were measured during the biochemical analysis and if vit-D deficiency is suspected Ca, phosphorus, albumin and vit-D levels were measured. Data of the patients were evaluated retrospectively. Blood was drawn after 12 hours of fasting. FBG, BUN, creatinine, AST, ALT, and other biochemistry tests were analyzed by a conventional spectrophotometric method using Beckman coulter commercial kits on a Beckman coulter AU5800 (Beckman coulter Inc. CA, USA) autoanalyzer. Vit-D and other necessary hormone tests were studied by chemiluminescence method on Beckman coulter DxI800 (Beckman coulter Inc. CA, USA). The Ca levels were corrected in patients with low serum albumin levels, using the following formula: Corrected Ca (mg/dL) = measured total Ca (mg/dL) + 0.8 (4-patient's albumin). Vit-D deficiency was defined as a 25(OH)D level lower than 20 ng/ml, and vit-D sufficiency was defined as a 25(OH)D level ≥ 30 ng/ml.

Statistical analysis

Descriptive statistics were used to define continuous variables (mean ± standard deviation, and median, minimum and maximum). The comparison of two independent groups with a normal distribution was performed using ANOVA. Correlation of vit-D with study parameters analyzed by spearman's correlation. A 'p' value less than 0.05 was considered statistically significant. Data analysis was performed with IBM SPSS version 20.

Results

In this study data of forty-four prediabetic patients (prediabetic group) and 40 healthy controls (control group) were analyzed. Both groups were statistically similar in terms of age, gender, body weight and BMI (body mass index) (Table 1). As expected in the prediabetes group, the value of FBG and HbA1c was statistically significantly higher than the control group ($p < 0.001$ for FBG and $p < 0.001$ for HbA1c). TG and LDL levels were significantly higher in prediabetic group than controls ($p = 0.004$ for TG and $p = 0.04$ for LDL). HDL was significantly lower in prediabetic group than controls ($p = 0.03$). Serum vit-D level was significantly lower in patients than controls ($p = 0.02$). Serum Ca levels were lower in patients than controls but the result was not statically significant ($p = 0.07$) (Table 2). A significant inverse or negative correlation was observed between HbA1c (r: -0.32, $p = 0.001$), FBG ($r = -0.41$, $p < 0.001$) and vit-D levels.

	Prediabetic group	Control group	P value
N	44	40	
M/F	20/24	19/21	0,33
Age (yrs.)	36 ± 8	34 ± 9	0,12
BMI, kg/m^2	27 ± 2,8	26,0 ± 3,2	0,41
Weight, kg	84 ± 15	83 ± 14	0,96

Table 1: *Demographic data.*

BMI: Body Mass Index.

	Prediabetic group	Control group	P value
N	44	40	
Fasting blood glucose (mg/dl)	114 ± 5	89 ± 4	< 0.001*
Creatinin (mg/dl)	0,73 ± 0,1	0,76 ± 0,1	0,18
Total kolesterol (mg/dl)	198 ± 38	195 ± 31	0,63
Trigliserid (mg/dl)	181 ± 89	129 ± 41	0,004*
HDL (mg/dl)	42 ± 8	46 ± 5	0.03*
LDL (mg/dl)	146 ± 24	118 ± 24	0.04*
HbA1C (%)	5,9 ± 0,4	5,1 ± 0,2	< 0.001*
Vitamin D (ng/ml)	15.2 ± 7.1	19.4 ± 7.2	0.02*
Calcium (mg/dl)	9.1 ± 0.4	9.3 ± 0.2	0.07

Table 2: *Laboratory values.*

**: $p < 0.05$ is statistically significant. HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.*

Discussion

In our study, we found that patients with prediabetes had lower vit-D levels than controls. There was a significant inverse correlation between HbA1c, FBG and vit-D levels. Various studies have shown that vit-D levels are lower in patients with diabetes [7,8,10,11]. The Third National Health and Nutrition Examination Survey (NHANES) reported an inverse association between vit-D and metabolic syndrome risk, particularly for hyperglycemia, hypertriglyceridemia, and abdominal obesity [12,13]. The European prospective Investigation into Cancer (EPIC)-Norflok study reported an inverse relationship between circulating 25(OH)D and type 2 DM [14]. Studies conducted in prediabetes patients also showed that vit-D levels were low, as in our results and recommended measuring vit-D levels in prediabetes

[9,15,16]. In a meta-analysis, Lu Yu., *et al*. showed that low serum 25(OH)D levels increase the risk of prediabetes, and vit-D supplementation improves impaired glucose tolerance in prediabetes. Vit-D exerts its effect through vit- D receptors. These receptors are found in many tissues [17,18]. Molecular studies have found that pancreatic β-cells both express cytolic/nuclear vit-D receptor and improve β-cell function [19]. In addition, 25(OH)D, which has been shown to be an immunomodulator, protects pancreatic β cells from the attacks of the immune system [20]. 25(OH)D inhibits the release of TNFα, which are proinflammatory cytokines, and regulates the activity of TLR 2 and TLR 4 proteins [21-23]. A few studies support that vit-D supplementation can affect glucose homeostasis and improve insulin resistance [24-26]. Our study is compatible with literature studies and emphasizes that vit-D deficiency may play a role in the pathogenesis of prediabetes. The small number of patients and the retrospective nature of the study are limitations of our research.

Conclusion

Vitamin D levels were found to be significantly lower in prediabetics. There is a significant inverse correlation between fasting blood glucose, HbA1c and vit-D levels. Prospective studies with a large number of patients are needed to confirm the findings.

Conflict of Interest

There is no conflict of interest.

Presentation/Support Information

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