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Original Article

The Relationship Between Vitamin D Levels and Cardiovascular Risk Scores in Geriatric Patients with Type 2 Diabetes Mellitus

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Keywords: BNF Score; Framingham Risk Score; geriatric; risk scores; Type II Diabetes Mellitus, various cardiovascular; vitamin D deficiency.

ABSTRACT

Objective: The aim of this study is to evaluate the relationship between vitamin D levels and various cardiovascular risk scoring systems such as QRISK2, BNF, ASSING, SCORE and Framingham in geriatric diabetic patients.

Methods: 60 diabetic geriatric patients with vitamin D deficiency (10–30 ng/mL) and 40 geriatric patients with vitamin D deficiency (<10 ng/mL) were included in the study. The scores of the patients indicating cardiovascular disease risks such as QRISK2, BNF, ASSIGN, SCORE and Framingham were calculated. All values were compared between these two groups.

Results: While the Framingham risk score (p<0.001), BNF (p=0.001) and SCORE (p<0.001) were found to be significantly higher in patients with vitamin D deficiency, other scores did not significantly differ between the groups. There was a weak but statistically significant negative correlation between 25[OH] D levels with Framingham risk score (p<0.001 r=-0.384), BNF score (p=0.003 r=-0.299), and Score score (p=<0.001 r=-0.407).

Conclusion: In the present study, we found a close relationship between the Framingham, BNF and ASSIGN cardiovascular risk score and serum vitamin D concentrations in diabetic geriatric patients.

INTRODUCTION

It is known that vitamin D deficiency is common in patients with type II diabetes mellitus.[1] Cardiovascular diseases are of particular importance in predicting and preventing risks, especially in asymptomatic people in terms of predicting and preventing the risks, as they are often associated with multiple risk factors. Inflammation plays a major role in the development of atherosclerosis. Inflammatory cells produce foam cells that are involved in the development of atherosclerosis. This poses a predisposition to cardiovascular diseases. Vitamin D suppresses the production of pro-inflammatory cells by controlling the immune system, thus preventing the development of inflammatory diseases. Vitamin D is a hormone that has major effects on the cardiovascular system as well as its effects on the skeletal system.[2,3] Vitamin D deficiency can cause peripheral vascular disease, coronary artery disease, and cerebrovascular accidents and it indirectly contributes to mortality.[3] It has also been found that vitamin D levels are associated with hypertension, obesity, and diabetes. Type II diabetic patients, the risk of developing atherosclerosis than patients without diabetes are higher than 2-fold. Diabetic patients are at greater risk of cerebrovascular disease, coronary artery disease and sudden death risk than non-diabetic patients.[4] While vitamin D plays an important role in bone metabolism, it also plays a major role in cancer prevention, glucose and lipid metabolism, and cardiovascular diseases. The present study investigated the relationship between vitamin D levels and cardiovascular disease risk assessed by various cardiovascular risk scoring systems such as QRISK2, BNF, ASSIGN, SCORE and Framingham in diabetic geriatric patients.

MATERIALS AND METHODS

The present study is a cross-sectional study. As a result of the power analysis, 100 consecutive patients with type 2 diabetes mellitus (DM, between the ages of 65–80 admitted to our outpatient clinic were included in the study. The study was approved by the local ethics committee of Umraniye Training and Research Hospital (Date: 18.02.2016; Number: B.10.1.TKH.4.34.H.GP.0.01/14). All procedures performed in studies involving human participants comply with the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and subsequent amendments or comparable ethical standards. Patients with severe cardiovascular, type I diabetes mellitus, uncontrolled diabetes (diabetic ketoacidosis, hyperosmolar hyperglycaemic coma, or hypoglycaemia in the last 3 months), acute or chronic infection, liver disease, thyroid disorders, acute infections, hyperparathyroidism, neurologic disease, and those who have received or are currently receiving vitamin D replacement and supplement therapy were excluded from the study. Since vitamin D levels are generally low in the Turkish population, a separate 3rd group with normal vitamin D levels was not included in the study. Therefore, the present study was conducted on patients with vitamin D levels below 30 ng/mL. The patients were divided into two groups. There were 60 patients with vitamin D insufficiency (30–10 ng/mL) in the first group and 40 patients with vitamin D deficiency (<10 ng/mL) in the second group. Since vitamin D levels are known to vary seasonally, blood samples were collected in December, January and February.

Measures

A detailed medical history was obtained from the patients, and all patients underwent a physical examination. Anthropometric measurements such as weight, height, body mass index (BMI, kg/m^2), and waist circumference of the patients were measured. The blood pressures were measured twice in the morning according to the standard protocol. Hypertension was considered as diastolic blood pressure >90 or systolic blood pressure >140 mmHg or the presence of antihypertensive drug use. The presence of coronary artery disease was evaluated by examining the medical documents of the patients. 25- (OH) vitamin D, Glycated haemoglobin A1c (HbA1c), fasting blood glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, alkaline phosphatase, creatinine and urea levels were measured after at least 8 hours of fasting. Blood samples were drawn into LH PST II, SST II, and EDTA tubes and all samples were analysed at the same time. Cardiovascular risk scores of the patients such as QRISK2, BNF, ASSIGN, SCORE and Framingham risk score were calculated using a calculation program. Cardiovascular risk scores and vitamin D levels were compared.The relationship between vitamin D status and different cardiovascular risk scores was evaluated. Blood glucose levels were studied in whole blood by enzymatic colorimetric methods (with an intra-assay coefficient variance of 6% and an inter-assay coefficient variance of 8%).Total cholesterol, triglyceride, and HDL levels were measured using the enzymatic colorimetric test (Hitachi 747 autoanalyzer Mito, Ibaragi, Japan). LDL cholesterol levels were calculated using Fried Ewald's formula. levels were measured by high-performance liquid chromatography (HPLC) as described in the NHANES Laboratory Procedure Manual HbA1c. Measurement of 25-OH vitamin D was performed through a chemiluminescence assay (Liaison XL, Dia Sorin, Stillwater, MN) (Intra-assay coefficients of variation were 3.8% at a vitamin D concentration of 7.85 ng/ml, 2.3% at 19.6 ng/ml and 2% at 51.9 ng/ml). Vitamin D concentration <10.0 ng/mL is considered "deficient", and between 10.0–30.0 ng/ml is considered "insufficient".

Cardiovascular Risk Scores

Parameters such as age, gender, diabetes status, smoking status, chronic kidney disease status, angina or heart attack status, blood pressure treatment status, atrial fibrillation status, cholesterol/HDL ratio, systolic blood pressure, body mass index, rheumatoid arthritis status, and ethnicity were used to calculate the Q risk 2 score.[5] Parameters such as year, age, smoking status, blood pressure, sex, total cholesterol, and HDL were used for the BNF score.[6] Infırmation such as sex, age, rheumatoid arthritis status, diabetes status, systolic blood pressure, smoking status, total cholesterol, and HDL cholesterol were used to calculate the ASSIGN score.[7] Parameters such as sex, age, systolic blood pressure, smoking status, and total cholesterol were used for the SCORE score.[7] Parameters such as gender, age, HDL cholesterol, total cholesterol, diabetes status, systolic blood pressure, smoking status, and blood pressure treatment status were used to calculate the Framingham risk score.[8]

Statistical analysis

It is expressed using descriptive statistics such as mean, standard deviation, minimum, median, and maximum for continuous variables. Mann-Whitney U test was used to compare two abnormally distributed independent variables, and Student's T-test was used to compare two normally distributed independent continuous variables. Chi-square test or Fisher's exact test (where appropriate) was used to assess the relationship between categorical variables. Spearman's rho correlation coefficients were used to assess the correlation between two abnormally distributed continuous variables. The statistical analysis was performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013). The statistical significance level was set at $p<0.05$.

RESULTS

The mean age of the patients included in the study was 70.8±5.2 years, of which 39 (39%) were male and 61 (61%) were female. The mean height was 158.5±12.6 cm, the mean weight was 80.4±16.6 kg, the mean waist circumfer-

Table 1. Comparison of the parameters between the deficiency group and insufficiency group

	Vitamin D <10 ng/mL (n=40)	Vitamin D ≥10–30 ng/mL (n=60)	All patients (n=100)	p-value
Glycolysis haemoglobin A1c (<6.5%)	8.3±2.1	9.0±2.3	8.7±2.3	0.16
Total cholesterol (<200 mg/dL)	205.1±49.3	205±45.9	205.1±47	0.99
LDL-cholesterol (<130 mg/dL)	130.2±40.7	130±39.4	130.1±39.7	0.98
HDL-cholesterol (40–60 mg/dl)	43±12	43.2±13.4	43.1±12.8	0.66
Systolic blood pressure (mmHg)	155.3±16.2	126.9±18.8	138.3±22.5	<0.001
Diastolic blood pressure (mmHg)	86.5±10	78.8±15.4	82.7±14.3	<0.001
Framingham risk score	45.9±13	33.6±11.3	38.5±13.4	<0.001
QRisk score	40.3±15.6	39.9±17.8	40.1±16.9	0.97
ASSIGN score	64.4±24.3	55.8±20.6	59.2±22.5	0.06
Score score	12.9±9.4	5.6±3.6	8.5±7.4	<0.001
BNF score	27.6±14.4	17.8±9.1	21.7±12.4	<0.01

LDL: Low density lipoprotein; HDL: High density lipoprotein.

Table 2. Correlation with Vitamin D Level and Risk Scoring

D Vitamin	Framingham	Q Risk	BNF	ASSIGN	SCORE
r*	-0.384	0.089	-0.299	-0.163	-0.407
P	<0.001	0.377	0.003	0.104	<0.001

*Spearman Rho Correlation Coefficient.

Table 3. Correlation of Framingham with Other Risk Scorings

Framingham risk score	Q Risk	BNF	ASSIGN	SCORE
r*	0.576	0.907	0.860	0.623
P	<0.001	<0.001	<0.001	<0.001

ence was 101.0±12.6 cm, and the mean BMI was 32.1±10.0 kg/m^2. There were 30 patients with coronary artery disease. The mean vitamin D level was 13.3±6.3 ng/mL and the mean HbA1c level was 8.7±2.2%. 11% of the participants in the study were smokers. There were statistically significant differences between deficiency group and insufficiency group regarding the HbA1c levels (8.3±2.1 versus 9.0±2.3), p=0.161), cholesterol levels (205.1±49.3 versus 205±45.9 mg/dl, 0.990), and SBP and DBP (155.3±16.2 versus 126.9±18.8 mmHg, <0.001; 86.5±10 versus 78.8±15.4 mmHg, p<0.001). The HbA1C levels of the patients do not differ regarding to their Vitamin D levels. Regarding the Vitamin D level, it is statistically significant in the renal failure stage. Cholesterol levels of the patients do not differ regarding to their Vitamin D levels. SBP and DBP levels of patients with Vitamin D levels of 10 or less are higher in terms of statistical significance. Drug use shows a statistically significant difference regarding vitamin D levels.

Their CAD histories do not show a statistically significant difference regarding to their vitamin D levels. Framingham risk score (45.9±13 versus 33.6±11.3, p<0.001), BNF score (27.6±14.4 versus 17.8±9.1, p=0.001) and SCORE score (12.9±9.4 versus 5.6±3.6, p<0.001) were significantly higher between the deficiency group and insufficiency group. The scores in other risk scoring systems did not significantly differ according to vitamin D concentrations (Table 1).

We found a weak but statistically significant negative correlation between the 25 [OH] D level and the Framingham risk score (r=-0.384). Vitamin D level has a weak, negative and statically significant difference correlation with BNF score (r=-0.299) and with Score score (r=-0.407) (Table 2). There is a moderate and statistically significant difference correlation between Framingham score and Score score (r=0.623). Framingham score has quite a strong and statically significant difference correlation with BNF (r=0.907) and ASSIGN score (r=0.860). The Framingham score is above the average level and has a statically significant difference correlation with the Score score (Table 3).

DISCUSSION

In the present study, we found a relationship between the Framingham, BNF and ASSIGN risk scores and serum vitamin D levels in geriatric patients with type II diabetes mellitus. However, we found that as the vitamin D level decreased the Framingham risk score increased. We could not show a correlation between the QRISK and SCORE score and the vitamin D level.

Vitamin D deficiency has been reported as a risk factor for the development of diabetes.[9] In the study by Lee et al.,[10] 89% of the study diabetic participants were found to have vitamin D deficiency. In the study by Gagnon et al.,[11] diabetic patients were found to have lower vitamin D concentrations compared to patients without diabetes mellitus. In a meta-analysis, a significant relationship was reported between insulin and HOMA-IR and vitamin 25 (OH) D levels.[12] In the study by Anderson et al.[13] reviewing the medical records of 41,504 patients, low vitamin D concentrations were found to be associated with cardiometabolic events and an increased risk of developing type II DM.

The studies have used different cut-off levels to evaluate vitamin D levels. In a study, the prevalence rate of 34% in diabetic patients for vitamin D deficiency was reported by taking a cut-off level of ≤37.5 nmol/L (15 ng/mL) for vitamin D concentration.[14] In this study, we considered vitamin D concentration <10.0 ng/mL as "deficient" and between 10.0 and 30.0 ng/ml as "insufficient".

Vitamin D slows down vascular smooth muscle proliferation and the development of atherosclerosis by affecting the rennin-angiotensin aldosterone system.[15] In the present study, vitamin D concentrations and various cardiovascular risk scores were evaluated in diabetic patients in order to determine the relationship between vitamin D deficiency and cardiovascular risk scores, and the study found that there was a significant correlation between vitamin D status and certain cardiovascular risk scores.

Epidemiological studies have reported increased triglyceride and LDL-cholesterol levels and decreased HDL-cholesterol in association with vitamin D deficiency. A recent study has reported different results regarding the relationship between vitamin D status and lipid profile.[16] Some authors have reported a positive correlation between HDL-cholesterol levels and vitamin D status.[17] The present study found no significant relationship between lipid profile and vitamin D status. Another study has found a weak correlation between heart failure and vitamin D supplementation. In this study, vitamin D supplementation was found to have no contribution to the decrease in systolic and diastolic blood pressure. Therefore, it was recommended to avoid the use of vitamin D as an anti-hypertensive agent. Some studies have found a correlation between vitamin D deficiency and cardiovascular diseases, atrial fibrillation, peripheral artery disease, and stroke; however, there is no evidence showing the benefits of vitamin D supplementation.[18] In the present study, systolic and diastolic blood pressures were higher in patients with vitamin D levels at or below 10 ng/ml. Various studies have found a relationship between vitamin D status-calcium metabolism and cardiovascular diseases. In one study, vitamin D receptors were shown to affect the matrix metalloproteinase and tissue inhibitor factor.[19] Furthermore, vitamin D receptors suppress foam cell formation by reducing the levels of oxidized LDL-cholesterol.[20] Low vitamin D concentrations were shown to be related to cardiovascular diseases and mortality.[21] As in our findings, Framingham risk scores were found to be higher in patients with low vitamin D concentrations.

The present study found a negative correlation has been found between vitamin D concentrations and cardiovascular diseases. However, there is no sufficient data regarding the relationship between vitamin D status and cardiovascular risk scores. The present study reports a positive correlation between vitamin D concentrations and certain cardiovascular risk scores.

Ethics Committee Approval

This study approved by the Umraniye Training and Research Hospital Clinical Research Ethics Committee (Date: 18.02.2016, Decision No: B.10.1.TKH.4.34.H.GP.0.01/14).

Informed Consent

Prospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: D.O., S.B.; Design: R.S.; Supervision: D.O.; Fundings: R.S., S.B.; Materials: R.S.; Data: D.O.; Analysis: R.S., S.B.; Literature search: R.S.; Writing: D.O.; Critical revision: S.B.

Conflict of Interest

None declared.

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Tip 2 Diabetes Mellitus Tanılı Geriatrik Hastalarda D Vitamini Düzeyi ile Kardiyovasküler Risk Skorları Arasındaki İlişki

Amaç: Bu çalışmanın amacı, geriatrik diyabetik hastalarda vitamin D düzeyi ile QRISK2, BNF, ASSING, SCORE ve Framingham gibi çeşitli kardiyovasküler risk skorlama sistemleri arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Çalışmaya D vitamini yetersizliği olan 60 diyabetik geriatrik hasta (10–30 ng/mL) ve D vitamini eksikliği olan 40 geriatrik hasta (<10 ng/mL) dahil edildi. Hastaların QRISK2, BNF, ASSIGN, SCORE ve Framingham gibi kardiyovasküler hastalık riskini gösteren skorları hesaplandı. Tüm değerler bu iki grup arasında karşılaştırıldı.

Bulgular: D vitamini eksikliği olan hastalarda Framingham risk skoru ($p<0.001$), BNF ($p=0.001$) ve SCORE ($p<0.001$) anlamlı olarak yüksek iken diğer skorlarda gruplar arası anlamlı farklılık yoktu. D vitamini düzeyi ile Framingham risk skoru ($p<0.001$ $r=-0.384$), BNF skoru ($p=0.003$ $r=-0.299$) ve SCORE skoru ($p=<0.001$ $r=-0.407$) arasında zayıf fakat istatistiksel olarak anlamlı negatif bir korelasyon vardı.

Sonuç: Bu çalışmada, diyabetik geriatrik hastalarda Framingham, BNF ve ASSIGN gibi kardiyovasküler risk skoru ile serum D vitamini konsantrasyonu arasında yakın bir ilişki bulduk.

Anahtar Sözcükler: BNF Skoru; Framingham Risk Skoru; geriatri; kardiyovasküler risk skorları; Tip II Diabetes Mellitus; vitamin D eksikliği.