Journal of Diabetes & Metabolism

OPEN ACCESS Freely available online

Opinion

The Effects of Serum 25-Oh Vitamin D Level and Lipid on Type 1 Diabetic Young Armenians

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ABSTRACT

Objective: Vitamin D supposed to be associated with cardiovascular disease and diabetes mellitus via its effect on lipids profile. The main aim of current study is to determine the association of 25-OH vitamin D status and lipid changes in type 1 diabetic young Armenians with the diabetes duration of more than 5 years.

Materials and Methods: 48 type 1 diabetic patient with duration of diabetes >5 years, aged 20-35 years old, were investigated. Serum 25-OHvitamin D, TSH, lipid fractions and HbA1c were measured, BMI, weight, duration of diabetes were determined. Values of $P<0.05$ were considered statistically significant.

Results: 52.1% of all investigated patients showed insufficiency of vitamin D, regardless the season, and had significantly higher cholesterol and LDL in negative correlation with 25-OH vitamin D levels, compared with vitamin D sufficient group ($P<0.05$). HbA1c also had a positive correlation with the cholesterol, and the HDL showed negative correlation with weight ($P<0.05$). Interestingly all the investigated patients had 25-OH vitamin D level <25ng/ml (suboptimal sufficiency level). Vitamin D status showed no association with the season of the year and sunlight exposure ($P>0.05$).

Conclusion: 25-OH vitamin D correlates with poor glucose control and dyslipidemia in type 1 diabetic young patients. Moreover, absolute value of 25-OH vitamin D didn't exceed 25ng/ml, indicating low-sufficiency of vitamin D in type 1 diabetic young patients in Armenia. Further interventional investigations are needed to reveal also the precise relationship of 25-OH vitamin D absolute levels with diabetes-related complications in type 1 young diabetics. In this context, treatment and preventive recommendations of vitamin D supplementation should follow other guidelines from those for the general population.

BACKGROUND

Recent years many important issues of vitamin D status from fast-moving basic medicine area emerge into clinical medicine. Vitamin D aims to open new insights on the follow-up of important life-threatening systemic disorders such as diabetes mellitus, cardiovascular diseases etc.

Type 1 diabetes mellitus is an autoimmune disorder, resulting in islet beta-cells destruction and absolute insulin deficiency. It mostly occurs in children and adolescents, which requires intensified insulin therapy with daily multiple insulin injections. Recent years type 1 diabetes showed tendency to increase in prevalence and incidence in many countries [1]. Moreover, growing evidence is gathered, indicating the importance of glucose control in order to prevent and to slow the development and progression of later chronic diabetic complications. Several studies show an increase in vitamin D deficiency in many countries, particularly in young population [2,3]. Armenia is known to be a country with sufficient sun exposure, where almost half of the year is warm and sunny. However, there is a lack of investigations showing the vitamin D status neither in the healthy population, nor in diabetic in Armenia.

As it is shown in numerous studies, vitamin D plays a number of important roles in the organism, including bone metabolism, as well as extra-bone impact on immune, nervous systems, body weight correction etc. Sufficient 25-OH vitamin D level references are widely discussed by specialists during past years. Last year the lower limit of vitamin D sufficiency, appeared to be safe and

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Received: November 08, 2021; **Accepted:** November 22, 2021; **Published:** November 29, 2021

Citation: Anna G, Lusine N, Artashes T (2021) The Effects of Serum 25-Oh Vitamin D Level and Lipid on Type 1 Diabetic Young Armenians. J Diabetes Metab. 12:906. doi: 10.35248/2252-5211.21.12.906

sufficient for skeletal health in the healthy general population, was decreased by Endocrine Society and was documented as 20-50 ng/ml (50-125nmol/l) [4]. In fact, this is given for the general, so called healthy population, but not for the patients with chronic disorders, having high risk of other complications and vitamin D associated disorders. But less is known about sufficient threshold levels of vitamin D in chronic disorders such as diabetes. However, in our study we refer to the International Conference Statement, that vitamin D sufficient level should be encountered as >20 ng/ml.

The mechanism for the reduced bone turnover in diabetes is likely multifactorial, where the 25-OH vitamin D plays one of the major roles. Although some studies didn't find significant relationships [5], but others revealed an increased fracture risk in type 2 diabetic patients [6-10]. Vitamin D is carried out to have important roles in many non-skeletal disorders, such as hypertension [11], immune disorders, cardiovascular disorders [12], diabetes type 2, and cancer [13]. It is suggested that vitamin D deficiency is associated with high cardiovascular risk in type 2 diabetics through the action on lipid metabolism [14]. Several studies are performed to reveal the potential link of vitamin D status to glucose control in type 2 diabetes [15-18] and to lipid profile, as well as to CV risk in type 2 diabetes, where insulin-resistance and hyperinsulinemia mostly present, which can influence on lipid metabolism [19,20]. But, there is a lack of studies investigating those connections in type 1 diabetes, especially in young population with long duration of diabetes.

In the current study we investigate the 25-OH vitamin D status and lipid metabolism in a limited number of diabetic patients having 5 years and longer diabetes duration and its connection with diabetes compensation.

MATERIALS AND METHODS

Materials and study description

We have investigated 48 type 1 diabetic patients with duration of diabetes >5 years at the age 20-35 years old. This is the post-pubertal age of bone plateau, when the maximal bone mineral density is already achieved and is relatively stable period for the bone metabolism, when normally osteoformation should be in homeostatic balance with osteolysis. Patients were selected randomly according to the study criteria. All participants underwent clinical examination and anthropometric measurements. Weight was measured on the Seca scale (Seca 713; GmbH&Co., Hamburg, Germany) in light clothing without shoes, and height was measured using a Harpenden stadiometer (Holtain, Model 602VR, UK). Body Mass Index (BMI) was defined as weight (kg) divided by height (m) square. Pubertal assessment was scored according to Tanner stages, and in the study only patients with pubertal development of Tanner stage 5 were included. Exclusion criteria included hypogonadism, pregnancy, lactation, chronic liver and/or kidney diseases, use of drugs affecting lipid profile and/or calcium and bone metabolism, primary hypo- and hyperparathyroidism, use of calcium and/or vitamin D supplementations, as well as insulin-resistance. The family history of metabolic bone disorders and/or fractures was recorded. The sunny-season was determined as from May to October, when the direct sunlight exposure on the skin is known to be sufficient, and not sunny-season- from November to April.

All participants signed a written inform consent, approved by Ethical Committee of Yerevan State Medical University.

To investigate whether the vitamin D status correlates with the diabetes compensation and dyslipidemia the patients were divided into two groups depending on their vitamin D levels: in 1st group the 25-OH vitamin D was ≤20ng/mL, and in 2nd it was >20 ng/mL.

Performed laboratory analyses

Venous blood samples were collected in the morning after an 8-h of fasting. Serum 25(OH)-vitamin D, calcium, phosphorus, thyroid stimulating hormone (TSH), lipid profile (triglyceride-TG, high– and low-density lipoproteins- HDL, LDL, and total cholesterol) and glycosylated hemoglobin (HbA1c) were measured. HbA1c was measured by an automated high-performance liquid chromatography instrument (HLC-723 G7, Tokyo, Japan). 25-OH vitamin D was measured by chemiluminescent-microparticle immunoassay method (Cobas E411, 2013, Germany). Diabetes mellitus type 1 was defined based on ISPAD guideline diagnostic requirements [21]. Lipid profile levels were determined via enzymatic methods on an automatic analyzer (Cobas Integra 400+, 2009, Germany).

Statistical analysis

Numeric data of patients' characteristics and Standard Error of each group were reported as mean values with 95% confidence intervals. All analyses were performed using statistical software (IBM SPSS Statistics for Windows, Version 21.0; IBM Corp., USA). Values of $P<0.05$ were considered statistically significant. After checking of equality of variances using Levene's test, appropriate t-test was performed.

RESULTS AND DISCUSSION

Patients' characteristics

A total of 48 patients aged 20-35 years with type 1 diabetes were clinically evaluated and included in the study. The male/female ratio was as 25/23.

In 52.1% (n=25) of all investigated diabetics vitamin D insufficiency, and in 47.9% (n=23) - vitamin D sufficiency was revealed. Mean 25-OH vitamin D and HbA1c levels were 18.41±6.28 and 8.99±1.94, respectively.

Interestingly in 64.6% (n=31) of patients vitamin D was investigated in months from May to October, when the sun exposure of the skin is known to be sufficient in Armenia, and 97% of patients indicated to have more than 30 min/day sunlight exposure. In addition, no significant difference was noted between 25-OH vitamin D levels and the season of its measurement (P>0.05), which indicates that the vitamin D status in this population is not sufficient or low-sufficient, regardless the season.

Interestingly, none of the investigated patients had vitamin D level >30 ng/ml, the range of its value was from 20.0-25.0 ng/ml, showing that, if the vitamin D3 lower limit wouldn't be decreased [4], all the investigated patients would be either vitamin D deficient or vitamin D insufficient. Thus, we can assume that either the 30min/day sun-exposure is not sufficient in vitamin D status in this population, or the diabetes itself worsens the vitamin D status in the organism. This needs to be further investigated and approved or rejected by larger and more profound studies, including also

healthy population as a control group.

Pearson's correlation index was calculated, and negative correlations between vitamin D and cholesterol, as well as with LDL were revealed (P=0.028* and P=0.003*, respectively), which indicates the dependence of total cholesterol and LDL from the vitamin D levels in type 1 diabetic patients. Cholesterol, and more specifically LDL, are closely associated with atherosclerotic processes in the organism. Based on the results of current work we can conclude that the low vitamin D status indirectly can increase the atherosclerotic risk in type 1 diabetic patients by increasing the total cholesterol and LDL.

Another positive correlation was found between HbA1c and total cholesterol level (P=0.017*), which shows the impact of diabetes poor compensation on the lipids profile changes, particularly on cholesterol levels.

Interestingly a negative correlation between HDL and weight (P=0.003*), but not BMI (P=0.19) was revealed, showing that as high the body weight as lower the protective lipid fraction in type 1 diabetic patients (who are not known to be on a high risk of excess weight or obesity).

No correlations of vitamin D and HbA1c, age, diabetes duration, TSH, weight and BMI were found in the general study group.

Investigated groups comparison

The main characteristics of the groups are presented in the table 1. The groups are comparable by the age, diabetes duration and male/female ratio.

As it is seen from the table 1, in the 1st group with vitamin D insufficiency the glucose control is poorer than in the 2nd group, even if the level of 25-OH vitamin D doesn't reach >25ng/ml. Although in the 1st group serum levels of TG, total cholesterol, LDL and HDL were higher, than in the 2nd group, this association was statistically significant for only LDL and cholesterol, which are known to be more atherogenic lipid fractions. BMI was also higher in the 1st group compared with the vitamin D sufficient group.

Correlations within the separate groups

We have also investigated the correlation connections between above-mentioned variables separately within the 1st and 2nd groups. In the 1st group with low vitamin D status two correlations were found: HDL correlated with weight negatively, and, interestingly, TG positively correlated with age (P=0.006*), but not with the diabetes duration (P=0.6). So we can conclude that low vitamin D predicts decrease of HDL level.

In the 2nd group the level of vitamin D negatively correlated with cholesterol (P=0.03*) and LDL (P=0.04*), as well as LDL positively correlates with weight (P=0.02*). Vitamin D sufficiency plays a role in development of dyslipidemia, and prevents the increase of atherogenic lipid fractions levels. Another positive correlation was found between HbA1c and age (P=0.047*), and HDL with the diabetes duration (P=0.023*).

CONCLUSION

Today vitamin D deficiency seems to be prevalent not only among the elderly but also in younger population, including adolescents and children as well. It is still unclear whether the vitamin D deficiency in type 1 diabetes is due to systemic affection of vitamin D metabolism, lifestyle changes, insufficient sunlight exposure or increased use of sunscreen. However, vitamin D status has shown associations and correlations with poor glucose control and lipid changes in type 1 diabetic young patients. Moreover, absolute value of 25-OH vitamin D didn't exceed 25 ng/ml, indicating low-sufficiency of vitamin D in type 1 diabetic young patients in Armenia. Taking into account the skeletal and extra-skeletal roles of vitamin D in the organism, we believe that the recommendations for threshold values of 25-OH vitamin D in the normal population are not necessarily applicable to the patients groups with high-risk diseases for the bone metabolic, cardiovascular and atherogenic disorders, such as diabetes. In this context, we suppose that in the lack of studies, specifically targeting vitamin D status and its role in individuals with diabetes, treatment and preventive recommendations of vitamin D supplementation should follow other guidelines from those for the general population.

DECLARATIONS

Ethics approval and consent to participate

All participants gave their written informed consent after a complete explanation of this study before participating in the study. The study was performed in accordance with the guidelines of the Declaration of Helsinki and was approved by the ethics committee of the Yerevan State Medical University.

Table 1: Compared main characteristics of type 1 diabetic patients with 25-OH vitamin D ≤20ng/mL (1st group) and >20ng/mL (2nd group).

Mean parameters	1st group (n=25)	2nd group (n=23)	*P*-value
Vitamin D level (ng/mL)(mean±SE)	13.79±1.0	23.43±0.52	P<0.001*
Age at time of study (years)(mean±SE)	24.89±1.19	23.38±1.28	P=0.81#
Duration of diabetes (years)(mean±SE)	12.6±1.08	10.56±0.91	P=0.16
Weight (kg) (mean±SE)	61.92±1.85	61.13±1.75	P=0.76
BMI (kg/m^2)(mean±SE)	23.32±0.47	21.96±0.46	P=0.04*
HbA1c (%)(mean±SE)	9.96±0.83	8.26±0.64	P=0.01*#
Total cholesterol(mmol/l)(mean±SE)	4.42±0.21	3.96±0.15	P=0.81
TG (mmol/l)(mean±SE)	1.19±0.88	1.16±0.08	P=0.81
HDL (mmol/l)(mean±SE)	1.39±0.74	1.3±0.06	P=0.94
LDL (mmol/l)(mean±SE)	3.13±0.15	2.6±0.9	P=0.006*
TSH (mlU/l)(mean±SE)	3.29±0.66	2.54±0.36	P=0.32

#Nonparametric Man-Whitney test was performed due to non-equality of variances.

Consent for publication

Not applicable.

Availability of data and materials

All data generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding

This work was not funded.

Acknowledgements

The authors are grateful to all participants taking part in the study and the authorities of the "Muratsan" University Hospital.

Competing interests

The authors declare that they have no competing interests.

Author's contribution

AG participated in the study design and material collection. LN participated in the material collection and drafted the manuscript. AT participated in the design of the study and performed the statistical analysis. All authors read and approved the final manuscript.

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