

Association between 25-Hydroxyvitamin D Levels and Glycemic Status



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Abstract

Aim: A significant body of literature supports that 25(OH) vitD deficiencies is associated with insulin resistance.

Methods: We studied the prevalence of 25(OH) vit D deficiencies across the spectrum of glucose metabolism. The study participants 441 total, 362 females (82.1%) had a mean age (\pm SD) of 64.59 (\pm 9.44) years. The study population was divided into 2 groups: Individuals with Diabetes (n=184), and controls with normal glucose levels (n=257).

Results: The mean 25(OH) vitD (\pm SD) levels were significantly lower in subjects with diabetes (18.6 \pm 10.6mg/ml) compared to normal subjects (24.2 \pm 12.2mg/ml), p=0.035. 25(OH) vitD deficiency was observed in 49.7% of the entire study population and was significantly more frequent in patients with diabetes compared to controls (60.9 vs 41.6% respectively).

Conclusion: This study illustrates the higher prevalence of 25(OH) vitD deficiencies among patients with diabetes.

Keywords: Diabetes; Vitamin D; HbA1c

Introduction

Diabetes is widely prevalent globally and around 285 million people have diabetes this number is expected to reach 438 million by the year 2030 [1]. Vitamin D deficiency is also an important public health problem globally [2]. Exposure to ultraviolet light and consumption of foods rich in fat-soluble vitamin D (egg, oily fish, meat and eggs) are the main sources of vitamin D and its levels can be measured by concentration of serum 25-hydroxyvitamin D (25(OH) vitD) [3]. 25(OH) vitD levels are positively related to bone mineral density [4], muscle mass and strength [5]. Moreover, there is a possible association of 25(OH) vitD with certain types of cancer [6,7] infections [8], autoimmune diseases [9] and cardiovascular disease [10]. 25(OH) vitD levels vary with age [11], obesity [12], skin type [13] and ethnicity [14], season [15], liver and kidney disease, medication, nutritional habits and others [16]. Moreover, there is an association of 25(OH) vitD levels with type 2 diabetes mellitus [17,18]. The aim of this study was to examine the association of vitamin D levels with glycemic status in two groups of subjects: patients with diabetes and normal subjects.

Methods

This study was conducted at the Outpatient and Inpatient Departments of the Endocrinology Unit of a tertiary cancer center (Metaxa Anticancer Hospital). The study was approved by the Scientific Committee of the hospital. A total of 441 randomly selected Greek Caucasian individuals, 79 males (17.9%) and 362 (82.1%) females were recruited between August 2013 and October 2015 including all four seasons. Their mean age was 64.59 \pm 9.44 (range=32-92 years).

A fasting venous blood sample after an overnight fast of over 8 hours was collected to determine blood glucose, HbA1c and serum 25(OH) vitD levels. Plasma glucose was estimated by the Photometric method, Abbott's ARCHITECT Abbott's ARCHITECT c16000 Clinical Chemistry Analyzer, Abbott Diagnostics, North Chicago, Illinois, USA. HbA1c was estimated by high pressure liquid chromatography method Menarini's ADAMS A1c HA-8160 Analyzer. The prevalence of vitamin deficiency (<20mg/ml), insufficiency (20-30mg/ml) and sufficiency (\geq 30mg/ml) was

estimated, as described by the Endocrine Society Clinical Practice guidelines [19]. The analytical assay for the determination of total 25(OH)D was the Roche electrochemiluminescence binding assay (ECL) on Elecsys immunoassay analyzers, Roche Diagnostics GmbH, Mannheim, state D-68305, Germany.

Exclusion criteria were major illness (end stage kidney disease, cirrhosis, pancreatitis, cancer and cardiovascular disorders), recent surgery or diabetic keto acidosis in the last

6 months, use of glucocorticoids and secondary diabetes. The control population was derived from patients of the obesity and thyroid clinic with normal glucose and HbA1c levels (Glu<100mg/dl and HbA1c<5.7%) and without any systemic illness. Data were analyzed using the SPSS analytical software 22 (SPSS Inc-IBM Corporation, New York, United States). Data are presented as mean, standard deviation (SD) and descriptive statistics were used for the data analysis. Variables with p-values of less than 0.05 were considered significant.

Results

The study population was divided into 2 groups

Table 1: Mean values ± SD of 25(OH) vit D age, plasma glucose levels and HbA1c in the two groups of patients.

	Male (N/%)	Age in Years	25(OH) vitD (mg/ml)	Glu (mg/dl)	Hba1c (%)
		Mean (±SD)	Mean (±SD)	Mean (±SD)	Mean (±SD)
Diabetes n=184	33 /17.9%	64.48 (±10.83)	18.6 (±10.6)	165.9 (±60)	7.81 (±1.35)
Normal n=257	46 / 17.9%	64.66 (±8.32)	24.2 (±12.2)	91.2 (±8.6)	5.38 (±0.2)
p-values			P=0.035	P<0.001	P<0.001

Table 2: Counts and percentages of subjects with 25(OH) vitD deficiency, insufficiency and sufficiency, in each group of subjects.

		25(OH) vitD_Status		
		Deficiency count (percent)	Insufficiency count (percent)	Sufficiency count (percent)
Diabetes Status	Diabetes (n=184)	112 (60.9 %)	46 (25%)	26 (14.1%)
	Normal (n=257)	107 (41.6 %)	76 (29.6%)	74 (28.8%)

Patients with Diabetes Type 2 (n=184, 33 males) and subjects with normal fasting blood glucose and HbA1c (n=257, 46 males). The mean 25(OH) vitD values for males and females patients was 22.9±11.6 and 21.6 ±11.9mg/ml respectively, p=0.815. The mean 25(OH) vitD levels were higher in the control group when compared with patients with diabetes (24.20±12.2, vs 18.6±10.6mg/ml, p=0.035, respectively). There was no difference in the mean age of patients and sex distribution between the two groups. Table 1 shows the mean values±SD for 25(OH) vitD, age, plasma glucose levels and HbA1c for each group. 25(OH) vitD deficiencies were seen in 49.7% of the entire study population. The majority of diabetic patients studied had 25(OH) vitD serum levels below the recommended threshold of 30mg/ml and only 26 of 184 (14.1%) of patients with diabetes had 25(OH) vitD sufficiency, compared to 28.8% of subjects with normal glucose (p<0.001). Table 2 shows the counts and percentages of subjects with 25(OH) vitD deficiency, insufficiency and sufficiency, in each group of subjects. There is statistically significant difference in the prevalence of vitD deficiency and insufficiency between the three groups (p-value is <0.001).

Discussion

There is a relationship between 25(OH) vitD deficiency and risk of diabetes mellitus [20-23]. A high prevalence of 25(OH)

vitD deficiencies has been reported in association with the metabolic syndrome [24]. Type 1 and Type 2 Diabetes Mellitus are multifactorial diseases and both genetic predisposition and environmental factors contribute to their development. 25(OH) vitD deficiency is linked to type 1 and type 2 diabetes development, and receptors for its activated form-1alpha, 25-dihydroxyvitamin D3-have been identified in beta cells and immune cells. 25(OH) vitD deficiencies impair insulin synthesis and secretion in humans and in animals, suggesting a role in the development of type 2 diabetes. Besides, epidemiological studies suggest a link between vitamin D deficiency in early life and the later onset of type 1 diabetes [25].

There is also compelling evidence that 1, 25(OH)2D regulates beta-cell function by different mechanisms, such as influencing insulin secretion by regulating intracellular levels of Ca²⁺, increasing beta-cell resistance to apoptosis, and possibly also increasing beta-cell replication. The capacity of vitamin D, more specifically 1, 25(OH)2D, to modulate immune responses is of particular interest for the prevention and the therapy of diabetes [26]. Diabetes itself can also result in lower circulating 25(OH) vitD concentrations [27]. Moreover, lower serum 25(OH) vitD levels are associated with prediabetes [28]. Vitamin D supplementation in prediabetes subjects has been shown to

decrease fasting plasma glucose, 2-h plasma glucose and HbA1c levels [29].

Another important observation of our study is that the majority of the study population has 25(OH) vitD deficiency in general and respective of the underlying glycemic status. Greece is considered a country of high sunlight levels. Based on the important contribution of sunlight exposure to the production and maintenance of serum 25(OH) vitD levels, one might consider that 25(OH) vitD deficiency may be a problem limited to countries located at higher latitudes and not Greece (Athens, Greece: 37.9°C north of the equator). Nevertheless, we observed a high prevalence of 25(OH) vitD deficiency and insufficiency, especially among patients with diabetes.

The sample of our study represents Greek individuals and there are some limitations. The data are aggregated and do not permit analysis by body mass index, personal medical history, complete medication of each patient or other covariates, multivitamin use, skin pigmentation, clothing style, place, duration of outdoor stay of each patient. Finally, we only had one spot measurement for each participant.

However, our study has an important strength: We included a large sample of individuals and divided them in two separate groups, taking into account the underlying glycemic status. Prospective studies with a large number of patients including a representative Greek sample are required to study the link between vitamin D deficiency and other factors related to the diabetes mellitus. Since many individuals are vitamin D deficient and at high risk of diabetes, vitamin D supplementation may contribute to prevent diabetes and insulin resistance. Recent observational data reports a positive effect of vitamin D on preventing the onset of diabetes [18]. Nevertheless the possible benefits of vitamin D supplementation on glycemic control are still questioned. There is a need to conduct further studies to evaluate the impact of vitamin D deficiency in relation to many chronic diseases such as diabetes, and answer whether this link is causative or not.

Conclusion

This study examined the relation between 25(OH) vitD levels and glycemic status in Greek patients with diabetes and normal subjects. We found that patients with diabetes had a significantly higher prevalence of vitamin D deficiency compared to normal subjects. From a clinical standpoint, specific advice needs to be provided especially to people with diabetes. Vitamin D supplements on a regular basis over the year and adequate sun exposure could be also recommended in order to achieve sufficient levels of 25(OH) vitD.

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