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Diabetes Mellitus Relationship with Vitamin D and Vitamin B12 Levels: A Retrospective Analysis

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Abstract: To compare the levels of vitamin D and vitamin B12 in patients with type 2 diabetes mellitus (DM) versus those without diabetes mellitus. Serum hemoglobin A1c (HbA1c), 25-hydroxy vitamin D, vitamin B12, calcium and phosphate levels were studied in 1932 patients who applied to Adult Endocrinology Unit of Dicle University Medical Faculty Hospital between January 2016 and January 2018 the patients were taken to work and the results were retrospectively reviewed. According to HbA1c levels, two groups were categorized as non-diabetic and diabetic.The results were evaluated according to age, gender and seasonal variables as well as biochemical parameters. In the study group, the patients between 2016 and 2017 were classified as non-diabetic and diabetic according to their HbA1c values, whereas the diabetic patients (%41.04). Diabetic patients (HbA1c level>%6.5) with D vitamin-B12 and D vitamin-calcium were statistically significant (p <0.001) (p <0.001); A negative correlation between vitamin D- phosphorus and vitamin D-HbA1c was statistically significant (p <0.01) (p <0.01).In the statistical evaluation of the hemoglobin A1c (HbA1c) groups, it was seen that in the group of HbA1c> %6,5, vitamin D value was lower in males (p = 0,002) than in females (p = 0,093) and was meaningful in males. There was a statistically negative correlation significant (p <0,01). In the group of HbA1c> %6,5, B12 value (p <0,001) was lower in males than females (p <0,05), both of which were significant. These findings suggest that increased vitamin D deficiency in patients with Type 2 diabetes is important in examining vitamin D and B12 levels in such chronic diseases. The statistical significance of vitamin D in male diabetic patients suggests that this may be due to hormonal differences. Prospective studies are needed to clarify the relationship between vitamin D and vitamin B12 in patients with type 2 diabetes.

Keywords: Vitamin D, Diabetes mellitus, Vitamin B12, Calcium, phosphate.

INTRODUCTION

Diabetes is a multifactorial disease associated with carbohydrate and fat metabolism, especially associated with energy metabolism. There are complications due to the imbalance between natural antioxidants and free radical formation [1].

Vitamin D is a fat-soluble vitamins. In humans, the primary source of vitamin D is the natural source. Synthesis of vitamin D is induced by UV light at the bottom. It is converted to 25 hydroxyvitamin D by 25 hydroxylase enzymes in the liver and then 1.25 (OH) 2D which is the active metabolite in the kidney by the renal 1-25 hydroxylase enzyme [2]. The herbal sources Ergocalciferol identified as D2 and the animal origin known as D3, cholecalciferol, are converted into biologically active forms in the liver and kidney by two hydroxylation products. D vitamins, calcium homeostasis, bone metabolism and neuroimmune modulation [3]. In the prevention and treatment of Type 2 DM and impaired glucose tolerance, Vitamin D has been implicated in animal and human studies [4,5].

Vitamin B12 or cyanocobalamin is found in animal-derived foods. It has important roles in deoxyribonucleic acid synthesis and in many biochemical reactions[6]. Megaloblastic anemia, neuropathy, cognitive dysfunction, memory loss, nervousness, dementia and osteoporosis are seen in the absence of vitamin B12 [7- 9]. Type 2 DM is a disease in which oxidative stress is present. In diabetic patients, oxidative stress in vitamin B12 deficiency increases with hyperhomocysteinemia [10]. It is thought that impairment of calcium balance in both cases of deficient extracellular and intracellular intake of

vitamin D in dietary intake may lead to changes in insulin secretion [11].

There are studies in the literature about serum vitamin D and B12 levels in patients with diabetes using metformin. Our purpose in this study is; To investigate the effect of vitamin D and vitamin B12 on diabetes mellitus according to age, sex and seasonal variation in patients with DM.

MATERIALS AND METHODS

Between 01 January 2016 and 31 December 2017, 1306 women and 626 male patients aged 15-94 years who applied to Dicle University Hospitals Adult Endocrinology Unit were included in the study. HbA1c, 25 hydroxyvitamin D, vitamin B12, calcium and phosphate results of the patients included in the study were retrospectively examined. Ethical committee approval was obtained before the study (Dicle University 2018/136).

In the study, the patients were divided into two groups. Group I = Serum HbA1c>%6.5 were diabetic, Group II = Serum HbA1c ≤%6.5 were non-diabetic. The treatment they have received for diabetes patients (oral antidiabetics, insulin and diet therapy) have been questioned.

Exclusion Criteria

Those who use medications (calcium and D vitamins, calcitonin, selective estrogen receptor modulators, thyroid hormone drugs) that may affect calcium metabolism, those with additional diseases that affect calcium metabolism (liver and kidney disease, Cushing syndrome, bone disease) were excluded from the study.

Vitamin D, vitamin B12, Calcium, Phosphate, HbA1c Study Methods

25 hydroxyvitamin D levels were determined by high performance liquid chromatography (HPLC), B12 Vitamin levels ECL (ElectroChemiLuminescence-Roche) With the COBAS E 601 brand device, Calcium and phosphorus levels were studied in the autoanalyzer by the Architect 1600c brand Architect spectrophotometric method. HbA1c (Bray, Ireland/ Kansas City, MO, USA) was studied by Boronate Affinity High Pressure Liquid Chromatography (HPLC).

STATISTICAL ANALYSIS

In our study, the data were analyzed with 95% confidence using the SPSS 21 (Statistical Package for the Social Sciences) package program. The significance limit of all statistical tests used was determined to be 0.05. Kolmogorov-Smirnov and Shapiro Wilk tests were used for normality control. Nonparametric tests were used for those who did not show parametric tests for normal distribution data. Descriptive statistics were used for the demographic characteristics used in the study.

RESULTS

Group I diabetic patients (%41.04) included in the study were female / male (515/278) ranging in age from 17 to 94 years. The average age of 55.39 ± 13.61, while 515 female, 279 male patients with a mean age ranging between 15-87 was 56.15 ± 15.21. Group II non diabetic ones included in the study The mean age of the 791 women aged 15-95 was 46.24 ± 13.88, while the mean age of 348 men aged 15-83 was 47.04 ± 14.27 (%58.96).

There was a negative correlation between vitamin D and HbA1c in diabetic men and women ($p < 0.01$), which was significant only in males. Negative correlation between vitamin B12 and calcium was detected. There was a positive correlation between vitamin B12 and HbA1c ($p < 0.05$). when there is a negative correlation between HbA1c with calcium, calcium with a positive correlation was found between seasons ($p < 0.01$) (Table).

Table-1: Variables for men with a HbA1c> greater than %6.5

	D vitamin	B12 Vitamin	Calcium	Phosphorus	HbA1c	Seasons
D vitamin	1					
B12 Vitamin	0,000**	1				
Calcium	0,114	-0,018*	1			
Phosphorus	0,375	-0,416	0,551	1		
HbA1c	-0,002**	0,021*	-,000**	0,838	1	
Seasons	0,546	-0,279	,001**	0,345	-0,618	1

*p<0,05; **p<0,01

A positive correlation was found between vitamin D and vitamin B12 levels in the diabetic group ($p < 0.05$), vitamin D levels in diabetic women with serum calcium levels ($p < 0.01$) also found a positive correlation between levels of vitamin B12 and phosphorus and HbA1c levels (Table 2).

Table-2: Variables related to women with HbA1c> greater than %6.5

	D vitamin	B12 Vitamin	Calcium	Phosphorus	HbA1c	Seasons
D vitamin	1					
B12 Vitamin	0,038*	1				
Calcium	0,000**	0,219	1			
Phosphorus	0,766	0,003**	-0,069	1		
HbA1c	-0,093	0,011*	-0,480	-0,924	1	
Seasons	-0,277	-0,100	0,402	-0,622	-0,552	1

*p<0,05; **p<0,01

There was a positive correlation between vitamin B12 and vitamin D levels in non-diabetic women with serum HbA1c ≤ % 6.5 (p <0.01), a positive correlation was found between vitamin D levels and serum calcium levels in non-diabetic men and women (p <0.05), There was a negative correlation between serum vitamin D levels and serum phosphorus levels (p <0.05), (Table 3).

Table-3: Variables related to women with HbA1c ≤ less than %6.5

	D vitamin	B12 Vitamin	Calcium	Phosphorus	HbA1c	Seasons
D vitamin	1	0,001**	0,020*	-0,027*	-0,104	0,036
B12 Vitamin		1	-0,047	0,005	0,069	-0,011
Calcium			1	0,035	-0,038	0,093
Phosphorus				1	,026	-0,060
HbA1c					1	0,090
Seasons						**1**

*p<0,05; **p<0,01

In males with non-diabetes mellitus with HbA1c ≤ %6.5, a negative correlation was found between vitamin D levels and HbA1c levels (p <0.05). There was a positive correlation between vitamin B12 and phosphorus levels (p <0,05) and a negative correlation between calcium level and HbA1c (p <0.01) (Table 4).

Table-4: Variables for men with HbA1c ≤ less than %6.5

	D vitamin	B12 Vitamin	Calcium	Phosphorus	HbA1c	Seasons
D vitamin	1					
B12 Vitamin	0,628	1				
Calcium	0,010**	0,101	1			
Phosphorus	0,403	0,037*	0,462	1		
HbA1c	-0,034*	-0,362	-0,008**	-0,624	1	
Seasons	0,126	0,819	0,104	0,165	-0,287	1

*p<0,05; **p<0,01

DISCUSSION

We found in this study that there was a positive correlation between vitamin D and vitamin B12 and calcium in patients with Type 2 diabetes, and that vitamin D was lower in diabetic male patients.

Until the early 1980s, vitamin D was only being studied for Ca, P and bone mineralization, while studies conducted over the last 20-25 years have shown that they also function outside of bone metabolism. D vitamins have been associated with bone mineralization for many years, but have been associated with cancer, rheumatoid arthritis, multiple sclerosis, autoimmune diseases such as type 1 DM, heart diseases and metabolic syndrome [12,13].

The effect of vitamin D on the prevention of diabetes mellitus has been researched for the last two decades, and many studies have been conducted. Nevertheless, the inhibition of the development of vitamin D, DM, has not been fully elucidated. D vitamini is being investigated extensively in both human and animal studies as a risk factor [14]. Candido and the work done by friends, Vitamin D 'to increase the synthesis of insulin and pancreatic islets of Langerhans which protects and Type 2 diabetes has been stated that under control [15]. Anderson and colleagues studied 41504 patients' records and found that low vitamin D levels were associated with cardiometabolic events and increased risk of type 2 DM [16].

In most studies the prevalence in the adult Turkish population ranges from %29-90 [17, 18]. Turkey is one of the countries where endemic vitamin D deficiency (21). When analyzed studies about vitamin D levels less than 150 subjects in Turkey, male and most women mainly work in different clime cities in the studies, but not the same methods studied vitamin D levels in different seasons in our work together in the spring rastlanırk the lowest levels of vitamin D in patients with diabetes in men, while the women were at the lowest level in the autumn.

In our study, vitamin D levels were lower in diabetic male patients than in previous studies ($p < 0.001$), There was no relationship between vitamin D and HbA1c levels in female patients ($p > 0.05$).

In diabetic men, there was a positive correlation between vitamin D and B12 ($p < 0.001$) and a negative correlation between HbA1c ($p < 0.01$).

In diabetic men and women between vitamin D and vitamin B12 ($p < 0.05$), and in diabetic women between vitamin D and calcium ($p < 0.001$) positive correlation revealed.

CONCLUSION

Decreased insulin sensitivity, impaired beta cell function and systemic inflammation lead to glucose intolerance and Type 2 DM. Studies have shown that Vitamin D affects these functions. In our study, in patients with diabetes mellitus-especially in men- the statistically low and significant emergence of vitamin D and vitamin B12 levels, it can emphasize the importance of both vitamins to protect against such chronic diseases. Statistical significance in male patients may be due to hormonal differences.

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