CukurovaMedicalJournal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

CukurovaMed J 2023;48(2):402-408
DOI: 10.17826/cumj.1184194

RESEARCH

Relationship between vitamin D and magnesium

Vitamin D ve magnezyum arasındaki ilişki

Semih Kalyon[1]

[1]Prof.Dr. Cemil Tascioglu City Hospital, Internal Medicine, Istanbul/Turkey

Abstract

Purpose: Vitamin D is a steroid hormone that plays an essential role in healthy bone structure. Magnesium plays a role as a cofactor for enzymes in vitamin D synthesis and degradation. The study aims to determine whether there is also accompanying magnesium deficiency, in patients with vitamin D deficiency or insufficiency.

Materials and Methods: Patients over the age of 18 who applied to the internal medicine outpatient clinic of our tertiary center for any reason between 01.10.2018 and 01.10.2020 were screened and patients whose serum glucose, ALT, creatinine, Vitamin D, and magnesium values were all present at the same time were selected. Pregnant and lactating women, patients with malignancy, chronic renal failure, hyperparathyroidism, or hypoparathyroidism, and patients under vitamin D or magnesium supplementation were excluded. Age, gender, and laboratory data of the included patients were recorded.

Results: A total of 5982 patients, 1197 male and 4785 female, were included in this study. The mean age of the cases was 42 years. There was no statistically significant relationship between Vitamin D values and magnesium or glucose levels However, there was a statistically significant relationship between serum vitamin D levels and age and serum creatinine and ALT levels. Both vitamin D and magnesium levels in women were found to be statistically significantly lower than in men.

Conclusion: Since there was no relationship between Vitamin D and magnesium levels, there is no need for a routine magnesium examination to be performed in patients with vitamin D deficiency or insufficiency who are planned to take vitamin D therapy.

Keywords: Vitamin D, magnesium, deiodinase

Öz

Amaç: Sağlıklı kemik yapısında önemli rol oynayan D Vitamini steroid yapıda bir hormondur. Magnezyum ise birçok görevinin yanısıra D vitamin sentezi ve yıkımı enzimlerin de kofaktörü olarak rol almaktadır. D vitamin eksikliği veya yetersizliğinde aynı zamanda Magnezyum düşüklüğünün de olup olmadığını anlamak bu çalışmanın amacıdır.

Gereç veYöntem: Herhangi bir sebeple 3. basamak hastanemiz dahiliye polikliniğine 01.10.2018-01.10.2020 tarihleri arasında başvuran 18 yaş üzerindeki hastalar taranıp gluko, ALT, kreatinin, D vitamini, magnezyum değerlerinin hepsi aynı anda test edilmiş hastalar seçildi. Gebeler ve emzirenler, malignitesi olanlar, kronik böbrek yetmezliği olanlar, hiperparatiroidisi, hipoparatiroidisiolanlar, D vitamin veya magnezyum desteği alanlar elendi. Geriye kalan hastaların yaş, cinsiyet ve laboratuvar değerleri kaydedildi.

Bulgular: Bu çalışmaya 1197'si erkekve 4785'i kadın 5982 hasta alınmıştır. Olguların yaşları ortalaması 42'dir. D vitamin değerleri ile magnezyum ve glukoz değerleri arasında istatistiksel olarak anlamlı bir ilişki bulunmamaktadır. Ancak D vitamin ile yaş, kreatininve ALT arasında istatistiksel olarak anlamlı bir ilişki mevcuttur ayrıca kadınlarda hem D vitamini hem de magnezyum düzeyi erkeklere göre istatistiksel olarak anlamlı düzeyde daha düşük bulunmuştur.

Sonuç: D Vitamini ile magnezyum arasında bir ilişki saptanamadığından dolayı D vitamin tedavisi başlanacak olan D vitamin eksik veya yetersiz hastalara rutin magnezyum tetkikinin de yapılmasına gerek yoktur.

Anahtar kelimeler: Vitamin D, magnezyum, deiyodinaz

Address for Correspondence: SemihKalyon, Prof.Dr. CemilTascioglu City Hospital, Internal Medicine, Istanbul/TurkeyE-mail:semihkalyon@hotmail.com
Received: 04.10.2022Accepted: 18.05.2023

INTRODUCTION

Vitamin D was discovered in 1922 by Dr. Elmer Mc Collum[1]. Vitamin D plays an important role in calcium and phosphate metabolism and takes part in the formation of a healthy bone structure. Vitamin D, which is in steroid form, has many cellular and molecular functions and is necessary for glucose homeostasis as well as its importance for the skeletal muscle system[2]. Its storage and inactive form, 25 OH D vit, is hydroxylated to become the active form, 1-25 OH D vit[3]. Vitamin D deficiency or insufficiency is a serious health problem both for our country and for the whole world and is seen quite frequently, due to low oral intake and insufficient exposure to UV light[4-5]. Vitamin D deficiency not only has a negative impacton skeletal system, but also facilitates development and progression of multipledisease, including cardiovascular diseases, diabetes, autoimmune disease, and cancer[6].

Magnesium is the second most cation in cell and fourth most abundant mineral in the human body. It is a cofactor for many enzymes[7]. Magnesium, an antioxidant, also plays a role in RNA and DNA synthesis and cellular repair. In addition, magnesium has important roles in the functions of the protein-based carrier that takes part in the intestinal absorption of vitamin D and its transport to the liver and hydroxylation and activation of vitamin D in the liver and kidney[8]. Also magnesium is important for bone and calcium metabolism[9]. A widerange of human diseases, including cardiovascular and metabolic diseases, skeletal disorders, respiratory illness and neurologic anomalies (stress, depression, andanxiety) are linked to magnesium inadequacy[10].

In 2016, in a review of Rosanoff et al., it was mentioned that the answer to the question "Does low magnesium levels affect vitamin D levels and/or activation?" has not yet been given[11]. Today, this question still has not been answered. In patients with vitamin D deficiency, the possible cause may be magnesium deficiency, or vitamin D deficiency may be accompanied by magnesium deficiency. Therefore; this study aims to understand whether there is also a magnesium deficiency in patients with vitamin D treatment indication and to examine the relationship between serum vitamin D and magnesium levels.

MATERIALS AND METHODS

Sample

For this study, which was carried out in a single-center, patients older than 18 years of age with a preliminary diagnosis of Vitamin D deficiency, whose blood vitamin D test was analyzed between 01.10.2018 and 01.10.2020 and whose serum magnesium level was also present in the period one month before or after this test, were retrospectively evaluated from the hospital data system. Pregnant and lactating women, patients with any malignancies, chronic renal failure, hyperparathyroidism, or hypoparathyroidism, and patients under vitamin D or magnesium supplementation were excluded. 5982 patients were included for this study out of total 10356 evaluated patients. Informed consent was obtained from all the participants.

Procedure

In this retrospective study, ethical approval was obtained from the Prof .Dr. CemilTaşcıoğlu City Hospital Ethics Committee with the number 153 and dated 05.04.2021. Age, gender, serum magnesium and Vitamin D levels of all patients, and creatinine, alanine amino transferase (ALT), and glucose levels, if they were measured at that time, were also noted. Glucose, creatinine, ALT, and magnesium tests were performed with the colorimetric method with the Autoanalyzer Beckman Coulter Brand, AU5800, USA device, and the 25-hydroxyvitamin D3 test was performed with the Autoanalyzer Beckman Coulter Brand, DXI800, USA using the chemiluminescence immunoassay method.

American National Academy of Medicine defined vitamin D level as deficient if below 12 μg/L, insufficient if between 12 and 20 μg/L, and normal if between 20 and 50 μg/Lfor bone health[12]. Therefore, all the cases were first divided into 2 groups according to their vitamin D (μg/L) level, those with a level below or above 20; and then divided into 3 groups according to their vitamin D levels, those below 12, between 12 and 20, and above 20 μg/L. Similarly, to compare those with and without magnesium deficiency, the cases were divided into two groups as those with serum magnesium levels of below or above 1.8 mg/dl, since the cut-off value for normal serum magnesium level was 1.8 mg/dl in our laboratory. Forrest et all.

defined magnesium level as deficient if below 1.8 mg/dl[13].

Statistical analysis

For evaluating the results obtained in the study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used for statistical analysis. The suitability of the study parameters to the normal distribution was evaluated with the Kolmogorov Smirnov test. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation, frequency), the Mann Whitney U test was used for the comparison of the parameters that did not show normal distribution in the comparison of quantitative data, the Kruskal Wallis test for the comparisons between the three groups, and the Dunn's test for the determination of the group that caused the difference. The chi-square test was used to compare the qualitative data. Spearman's rho correlation analysis was used to examine the relationships between parameters that did not conform to the normal distribution. Significance was evaluated at the $p<0.05$ level.

RESULTS

This study was conducted with a total of 5982 cases, 1197 (20%) male and 4785 (80% female) aged between 18 and 95 years. The mean age of the cases was 42.40±14.90 and the median was 41.

Vitamin D values ranged between 0.24 and 49.97 μg/L, with a mean of 18.38±8.87 and a median of 16.8 μg/L. Serum creatinine levels ranged from 0.12 to 0.99 mg/dl, with a mean of 0.68±0.13 and a median of 0.7 mg/dL. ALT values ranged from 2 to 79 IU/ml, with a mean of 18.66±10.54 and a median of 16 IU/ml. Serum glucose levels ranged from 63 to 99 mg/dl, with a mean of 87.37±7.29 and a median of 88 mg/dl. Magnesium values ranged from 1.09 to 2.6 mg/dl, with a mean of 2±0.17 and a median of 2 mg/dl. (Table 1)

Table 1.General information on study parameters

Variable		**Min-Max**	**Mean±SD (median)**
Age (years)		18-95	42.4±14.9 (41)
Vitamin D (μg/L)		0,24-49,97	18.38±8.87 (16.9)
Creatinine (mg/dl)		0,12-0,99	0.68±0.13 (0.7)
ALT (IU/ml)		2-79	18.66±10.54 (16)
Glucose (mg/dl)		63-99	87.37±7.29 (88)
Magnesium (mg/dl)		1,09-2,6	2±0.17 (2)
		n	%
Gender	Male	1197	20
	Female	4785	80
Vitamin D (μg/L)	<20	3763	62.9
	≥20	2219	37.1
Magnesium (mg/dl)	<1.8	579	9.7
	≥1.8	5403	90.3

ALT: Thealanineaminotransferase

There was no statistically significant relationship between serum Vitamin D levels and magnesium or glucose values ($p>0.05$). However, there was a statistically significant relationship between vitamin D levels and age, and serum creatinine and ALT levels ($p<0.01$) (Table 2).

Table 2. Evaluation of the correlation between Vitamin D and age, glucose, creatinine, ALT, and magnesium values

	Age (years)	Glucose (mg/dl)	Creatinine (mg/dl)	ALT (IU/L)	Magnesium (mg/dl)
Vitamin D (µg/L)	r:0.127 p:0.001	r:-0.008 p:0.542	r:0.142 p:0.001	r:0.084 p:0.001	r:-0.005 p:0.711

SpearmanRhoCorrelation Analysis

When the cases were divided into 2 groups according to their vitamin D (µg/L) levels, those with a level below or above 20; the mean age of the group with a vitamin D level below 20 was found to be statistically significantly lower than the group with a vitamin D level of 20 and above (p:0.0001; p<0.05). The mean creatinine level of the group with a vitamin D level below 20 was found to be statistically significantly lower than the group with a vitamin D level of 20 and above (p:0.0001; p<0.05). The mean ALT level of the group with a vitamin D level below 20 was statistically significantly lower than the group with a vitamin D level of 20 and above (p:0.0001; p<0.05). There was no statistically significant difference between the vitamin D groups in terms of the mean glucose or magnesium levels (p>0.05). There was no statistically significant difference between the vitamin D groups in terms of gender distribution (p>0.05) (Table 3).

Table 3.Evaluation of study parameters among vitamin D groups

	Vitamin D(µg/L)		Pvalue
	<20	≥20	
	Mean±SD (median)	Mean±SD (median)	
Age (years)	41.05±14.66 (40)	44.67±15.01 (44)	[1]0.000*
Creatinine (mg/dl)	0.67±0.13 (0.7)	0.69±0.13 (0.7)	[1]0.000*
ALT (IU/L)	18.29±10.31 (16)	19.23±10.91 (16)	[1]0.000*
Glucose (mg/dl)	87.47±7.25 (88)	87.21±7.37 (88)	[1]0.184
Magnesium (mg/dl)	2.01±0.17 (2)	2±0.17 (2)	[1]0.166
Gender$_{n(\%)}$			
Male	746 (%19.8)	451 (%20.3)	[2]0.641
Female	3017 (%80.2)	1768 (%79.7)	

[1]Mann Whitney U Test[2]Ki-Kare Test*p<0.05; ALT:Thealanineaminotransferase

When the cases were divided into 3 groups according to their vitamin D levels as those with a level below 12, those with a level between 12-20 and those with a level between 20-50 µg/L;

there was a statistically significant difference between the vitamin D groups in terms of mean age (p:0.0001; p<0.05). As a result of the pair-wise comparisons made to determine which group the difference originates from; the mean age of the group with vitamin D levels below 12 was found to be statistically significantly lower than the groups between 12-20 and 20-50 µg/L (p1:0.024; p2:0.0001; p<0.05). The mean age of the group with vitamin D levels between 12-20 was statistically significantly lower than the group between 20-50 µg/L (p:0.0001; p<0.05).

There was a statistically significant difference between vitamin D groups in terms of creatinine levels (p:0.0001; p<0.05). As a result of the pair-wise comparisons made to determine which group the difference originates from; the mean creatinine level of the group with vitamin D levels below 12 was found to be statistically significantly lower than the groups between 12-20 or 20-50 µg/L (p1:0.0001; p2:0.0001; p<0.05). The mean creatinine level of the group with vitamin D levels between 12-20 was found to be statistically significantly lower than the

group with a vitamin D level between 20-50 (p:0.0001; p<0.05).

There was a statistically significant difference between vitamin D groups in terms of ALT levels (p:0.0001; p<0.05). As a result of the pair-wise comparisons made to determine which group the difference originates from; the mean ALT level of the group with a vitamin D level below 12 was found to be statistically significantly lower than the groups with a vitamin D level between 12-20 or 20-50 μg/L (p1:0.000; p2:0.000; p<0.05). There was no statistically significant difference between the mean ALT levels of the groups with a vitamin D level between 12-20 and between 20-50 μg/L (p>0.05).

There was no statistically significant difference between vitamin D groups in terms of the mean glucose levels (p>0.05).

There was a statistically significant difference between the vitamin D groups in terms of the mean magnesium levels (p:0.007; p<0.05). As a result of the pair-wise comparisons made to determine which group the difference originates from; the mean magnesium level of the group with vitamin D levels between 12-20 was found to be statistically significantly higher than the groups below 12 and between 20-50 μg/L (p1:0.020; p2:0.023; p<0.05). There was no statistically significant difference between the mean magnesium levels of the groups with vitamin D levels below 12 and between 20-50 μg/L (p>0.05).

There was a statistically significant difference between the vitamin D groups regarding the gender distributions (p:0.0001; p<0.05). As a result of the pair-wise comparisons made to determine which group the difference originates from; the rate of female cases (85.1%) in the group with vitamin D levels below 12 was statistically significantly higher than the groups with vitamin D levels between 12-20 (76.7%) and 20-50 (79.7%) μg/L (p1:0.0001; p2:0.0001; p<0.05). The rate of being female (76.7%) in the group with vitamin D levels between 12-20 was found to be statistically significantly lower than the group with a vitamin D level between 20-50 (79.7%) μg/L (p:0.015; p<0.05) (Table 4).

Table 4. Evaluation of study parameters among vitamin D groups

	Vitamin D(μg/L)			P value
	<12	12-20	20-50	
	Mean±SD (median)	Mean±SD (median)	Mean±SD (median)	
Age (years)	40.41±14.73 (39)	41.52±14.61 (40)	44.67±15.02 (44)	[1]0.000*
Creatinine (mg/dl)	0.65±0.13 (0.64)	0.68±0.13 (0.67)	0.69±0.13 (0.68)	[1]0.000*
ALT (IU/L)	17.07±9.32 (14)	19.22±10.9 (16)	19.22±10.9 (16)	[1]0.000*
Glucose (mg/dl)	87.28±7.37 (88)	87.58±7.17 (88)	87.21±7.36 (88)	[1]0.321
Magnesium (mg/dl)	2.01±0.2 (2)	2.02±0.2 (2)	2±0.18 (2)	[1]0.007*
Gender$_{n(\%)}$				
Male	231 (%14.9)	516 (%23.3)	451 (%20.3)	[2]0.000*
Female	1323 (%85.1)	1693 (%76.7)	1768 (%79.7)	

[1]Kruskal Wallis Test [2]Ki-Kare Test *p<0.05
ALT:Thealanineaminotransferase

There was no statistically significant difference between the magnesium groups in terms of age, and serum vitamin D, ALT, and glucose levels (p>0.05). The mean creatinine level of the group with a magnesium level below 1.8 was found to be statistically significantly lower than the group with a magnesium level of 1.8 and above (p1:0.0001; p2:0.0001; p<0.05). The rate of being female (86%) in the group with a magnesium level below 1.8 was found to be statistically significantly higher than the group with a magnesium level of 1.8 or higher (79.3%) (p:0.0001; p<0.05) (Table 5).

Table 5. Evaluation of study parameters among magnesium groups

	Magnesium (mg/dl)		P value
	<1.8	**≥1.8**	
	Mean±SD (median)	Mean±SD (median)	
Age (years)	44.11±17.02 (41)	42.21±14.64 (41)	[1]0.140
Vitamin D(μg/L)	18.85±10.01 (17)	18.33±8.74 (16.8)	[1]0.750
Creatinine (mg/dl)	0.64±0.14 (0.6)	0.68±0.13 (0.7)	[1]0.000*
ALT (IU/L)	18.58±11.47 (16)	18.65±10.44 (16)	[1]0.211
Glucose (mg/dl)	87.44±7.7 (88)	87.37±7.25 (88)	[1]0.600
Gender$_{n(\%)}$			
Male	81 (%14.0)	1116 (%20.7)	[2]0.000*
Female	498 (%86.0)	4287 (%79.3)	

[1]Kruskal Wallis Test [2]Ki-Kare Test *p<0.05; ALT:Thealanineamino transferase

DISCUSSION

The hydroxylations required for the conversion of vitamin D3 produced by our skin owing to sunlight, and dietary vitamin D3 of animal origin and vitamin D2 of vegetable origin, into active vitamin D occur in two steps. While the first step is with 25 hydroxylase enzymes in the liver, the second step is with 1 alpha-hydroxylase enzyme in the kidney. Magnesium is a cofactor for both enzymes.

While magnesium plays such a key role in the formation of Vitamin D, active Vitamin D increases the absorption of magnesium from the gut.

There are a small number of publications in the literature that magnesium replacement reduces vitamin D resistance in pediatric rickets, although there are few similar studies in adult osteoporosis patients, there is no such study in patients with low or normal vitamin D levels. In their systematic reviews, Uwitonze et al. and Reddy et al. emphasized that sufficient magnesium level is requiredfor optimum vitamin D effect[8,14].

In their study, Dai et al. reported that in the group of patients diagnosed with malignancy magnesium supplementation increased the level of 25 OH vitamin D3 in patients with 25 OH vitamin D levels <30 μg/L, on the contrary, this supplementation decreased 25 OH D3 levels in patients with 25 OH vitamin D levels >30 μg/L. They attributed this to the fact that magnesium is a cofactor of both hydroxylation enzymes that activate vitamin D and other enzymes that inactivate it (such as 24 hydroxylase)[15].

Based on the data of our study to examine the relationship between magnesium and vitamin D, it can be said that; there is no relationship between serum magnesium and 25 OH vitamin D levels. Both magnesium and Vitamin D levels are lower in women than in men. However, the current negative correlation between age and vitamin D is quite interesting that the group of patients with lower vitamin D levels was younger. Therefore, the young population should be better screened for vitamin D deficiency. This should bring a different perspective to the clinician's conventional understanding of "I should screen an older patient for vitamin D deficiency". Regardless of age, every patient, especially women, who are thought to have vitamin D deficiency, should be examined.

There are some limitations of the study. The most important disadvantages of this study are that it was conducted in a single center and retrospectively. Secondly, since magnesium is an intracellular cation, the serum magnesium level may not exactly reflect the body's magnesium status.

In conclusion, There is no relationship between serum vitamin D and magnesium levels. Therefore, it is not necessary to have a routine magnesium examination in patients who are diagnosed with vitamin D deficiency or insufficiency and will be treated. However, it should be kept in mind that as well as elderly patients, especially young female patients should be screened for vitamin D.

Author Contributions: Concept/Design :SK; Data acquisition: SK; Data analysis and interpretation: SK; Drafting manuscript: SK; Critical revision of manuscript: SK; Final approval and accountability: SK; Technical or material support: SK; Supervision: SK;Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained from the Ethics Committee of Cemil Taşcıoğlu City Hospital with the decision dated 05.04.2021 and numbered 153.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support
Acknowledgement:I would like to thanks to EbruOsmanoğluAkyol (VARYANS Statistical Consultancy) for statistical consulting and data analyzing

REFERENCES

1. Dobson R, Cock HR, Brex P, Giovannoni G. Vitamin D supplementation. PractNeurol. 2018;18:35-42.
2. Erem S, Atfi A, Razzaque MS. An abolic effects of vitamin D and magnesium in aging bone. J Steroid BiochemMol Biol. 2019;193:105400.
3. Goltzman D. Functions of vitamin D in bone. Histochem Cell Biol. 2018;149:305-12.
4. Öksüz A, Kutlu R. Meram Tıp Fakültesi Hastanesi Aile Hekimliği Polikliniğine başvuran hastaların D vitamin düzeylerinin değerlendirilmesi. Konuralp Tıp Dergisi. 2018;10:160-4.
5. Holic MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention Rev EndocrMetabDisord. 2017;18:153-65.
6. Zmijewski MA. Vitamin D and human health. Int J MolSci. 2019;20:145.
7. Capozzi A, Scambia G, Lello S. Calcium, vitamin D, vitamin K2, and magnesium supplementation and skeletalhealth. Maturitas. 2020;140:55-63.
8. Uwitonze A.M, Razzaque M.S. Role of magnesium in vitamin D activation and function. J Am Osteopath Assoc. 2018;118:181-9.
9. AllgroveJ. Physiology of calcium, phosphate, magnesium and vitamin D. Endocr Dev. 2015;28:7-32.
10. Razzaque MS. Magnesium: are we consuming enough? Nutrients. 2018;10:1863.
11. Rosanoff A, Dai Q, Shapses SA. Essential nutrient interactions: does low or suboptimal magnesium status interact with vitamin D and/or calcium status? AdvNutr. 2016;7:25–43.
12. LeFevre ML, LeFevre NM. Vitamin D screening and supplementation in community-dwelling adults: common questions and answers. Am Fam Physician. 2018;15:254-60.
13. Forrest H. Nielsen, LuAnn K. Johnson, Huawei Zeng. Magnesium supplementation improves indicators of low magnesium status and inflammatory stress in adults older than 51 years with poor quality sleep. Magnes Res. 2010;23:158-68.
14. Reddy P,Edwards L. Magnesium supplementation in Vitamin D deficiency. Am J Ther. 2019;26:e124-32.
15. DaiQ, ZhuX, Manson J, Song Y, Li X , Franke A et al. Magnesium status and supplementation influence vitamin D status and metabolism: results from a randomized trial. Am J ClinNutr.2018;108:1249-58.