Relationship Between Vitamin D, Calcium, and Phosphorus Levels

✉ Burcu Çaykara¹, ✉ Güler Öztürk¹, ✉ Hacer Hicran Mutlu², ✉ Ebru Arslan¹

¹Istanbul Medeniyet University Faculty of Medicine, Department of Physiology, İstanbul, Turkey

²Istanbul Medeniyet University Faculty of Medicine, Department of Family Medicine, İstanbul, Turkey

Cite this article as: Çaykara B, Öztürk G, Mutlu HH, Arslan E. Relationship Between Vitamin D, Calcium, and Phosphorus Levels. J Acad Res Med 2020;10(3):252-7

ABSTRACT

Objective: Our study aimed to determine the relationship between the prevalence of vitamin D deficiency and calcium and phosphorus levels by retrospectively obtaining vitamin D, calcium, and phosphorus values.

Methods: Vitamin D, calcium, and phosphorus levels of patients admitted to family medicine between October 2015 and December 2017 were evaluated. Shapiro-Wilk, Mann-Whitney U, and Spearman's rho tests were used for data analysis and p-values <0.05 were considered to be statistically significant.

Results: A total of 1,063 patients were included in the study. The percentage of patients with normal vitamin D levels was 20.5% and those with normal calcium and phosphorus levels were 97.1% and 84.9% of the study population, respectively. Positive correlation was found between vitamin D levels, calcium, and age.

Conclusion: In our study, the prevalence of vitamin D deficiency was found to be 49.6%.

Keywords: Vitamin D, calcium, phosphorus

INTRODUCTION

Vitamin D is synthesized in the skin by exposure to sunlight, but can also be obtained exogenously from the diet (1). Dehydrocholesterol in the skin is converted to previtamin D by exposure to sunlight. Previtamin D is transported to the liver where it is converted into 25-hydroxyvitamin D [25(OH)D], which is the major circulating form. 25(OH)D is further converted in the kidney into the active form 1,25-dihydroxyvitamin D [1,25(OH)₂D] (2). To assess vitamin D levels, measurement of serum 25(OH)D, which has a half-life of about three weeks is performed (3). Vitamin D, which is fat soluble, plays an important role not only

in the musculoskeletal system, but also in all tissues, which have vitamin D receptors (4). The main function of vitamin D is to maintain calcium (Ca) and phosphorus (P) balance in the body by promoting Ca and P absorption from the intestines and kidneys (5). In vitamin D deficiency, only 10%-15% of calcium and 50%-60% of phosphorus can be absorbed from ingested foods (6).

Serum 25(OH)D levels are interpreted as follows; <10 ng/mL-severe deficiency, <20 ng/mL-deficiency, 20-30 ng/mL-insufficiency, >30 ng/mL-sufficient, and >150 ng/mL-intoxication (7,8). It is reported that the main underlying cause of vitamin D deficiency, which is now considered to be a global health issue, is insufficient

ORCID IDs of the authors: B.Ç. 0000-0001-7063-2140; G.Ö. 0000-0001-6556-3662; H.H.M. 0000-0003-3712-0068; E.A. 0000-0001-5309-3931.

Corresponding Author: Burcu Çaykara,

E-mail: burcu.caykara@medeniyet.edu.tr

Received Date: 03.05.2020 **Accepted Date:** 05.11.2020

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exposure to sunlight (9). Vitamin D levels can also be affected by other factors such as age, sex, ethnicity, and seasonal variations (10). Low levels of vitamin D were found to be associated with hypertension, cardiovascular diseases, chronic musculoskeletal pain, and various malignancies (4). Our study aimed to determine the relationship between vitamin D deficiency and calcium and phosphorus levels.

METHODS

Vitamin D, calcium, and phosphorus levels from the hospital registries of İstanbul Medeniyet University, Göztepe Training and Research Hospital, Department of Family Medicine between October 2015 and December 2017 were retrospectively evaluated. Ethical approval was obtained from the Ethics Committee of İstanbul Medeniyet University, Göztepe Training and Research Hospital (approval number: 2018/0336, date: 12.09.2018). Since our study was retrospective, consent forms were not obtained from patients. All subjects who had been tested concurrently for vitamin D, calcium, and phosphorus levels were included in the study. In cases where there was more than one measurement of the subjects under follow-up, the date of the first measurement was taken into consideration, and other measurements of the same subject were not included in the study.

Statistical Analysis

SPSS 22 (IBM Corp.; Armonk, NY, USA) were used for statistical analysis. Data analyses were performed with Shapiro-Wilk, Mann-

Whitney U and Spearman's rho tests. P-value <0.05 was considered to be statistically significant.

RESULTS

The number of subjects who had undergone concurrent measurements of vitamin D, calcium, and phosphorus levels between October 2015 and December 2017 was determined to be 1,063, of which 298 were male and 765 were female. The mean age of the subjects admitted to the department of family medicine was 50.48 ± 17.51 , the mean vitamin D value was 22.24 ± 14.85 , the mean calcium value was 9.45 ± 0.46 , and the mean phosphorus value was 3.64 ± 0.56 . When these values were compared between men and women, it was determined that only phosphorus values in women were statistically significantly higher than men (Table 1). The vitamin D levels of the 1,063 subjects were as follows: 198 (18.6%) were at or below 10 ng/mL, 329 (31%) were between 10 ng/mL and 20 ng/mL, 317 (29.8%) were between 20 ng/mL and 30 ng/mL, 218 (20.5%) were between 30 ng/mL and 150 ng/mL, and only one subject had a vitamin D level (0.1%) above 150 ng/mL (Table 2). Vitamin D levels were similar between women and men. When grouped according to vitamin D levels, a statistically significant difference was found between men and women only at levels of 30 ng/mL and 150 ng/mL ($p=0.019$) (Table 3). Based on calcium levels, subjects were divided into hypocalcemia, normal, and hypercalcemia groups; 13 (1.2%) subjects had hypocalcemia, 18 (1.7%) subjects had hypercalcemia, and 1,032 (97.1%) subjects

Table 1. The mean values of patient data

Category	Number	Minimum	Maximum				Mean			SD	
Age (year)	1,063	3	94				50.48			17.51	
Vitamin D (ng/mL)	1,063	2.6	150.8				22.24			14.85	
Calcium (mg/dL)	1,063	5.9	11.7				9.45			0.46	
Phosphorus (mg/dL)	1,063	1.80	6.8				3.64			0.56	
Men						Women					
Category	Number	Minimum	Maximum	Mean	SD	Number	Minimum	Maximum	Mean	SD	p
Age (year)	298	3	93	51.57	18.69	765	4	94	50.05	17.02	0.109
Vitamin D (ng/mL)	298	5.1	89.2	22.22	11.54	765	2.6	150.8	22.25	15.96	0.086
Calcium (mg/dL)	298	7.2	11.1	9.48	0.43	765	5.9	11.7	9.44	0.47	0.239
Phosphorus (mg/dL)	298	2	6.1	3.49	0.59	765	1.8	6.8	3.7	0.54	<0.001
SD: standard deviation											

SD: standard deviation

Table 2. Serum 25(OH)D values

n=1,063	Minimum	Maximum	Mean	SD
	2.6	150.8	22.24	14.85
	n		%	
<10 ng/mL	198		18.6	
10-20 ng/mL	329		31	
20-30 ng/mL	317		29.8	
30-150 ng/mL	218		20.5	
>150 ng/mL	1		0.1	

SD: standard deviation, 25(OH)D:

had normal calcium levels (Table 4). When calcium levels were compared based on gender, no significant difference was observed between men and women (Table 5). Based on phosphorus levels, subjects were divided into hypophosphatemia, normal, and hyperphosphatemia groups; 98 (9.2%) subjects had hypophosphatemia, 63 (5.9%) subjects had hyperphosphatemia, and 902 (84.9%) subjects had normal phosphorus levels (Table 6).

When phosphorus levels were compared based on gender, phosphorus levels were found to be significantly higher in women compared to men. Furthermore, a significantly higher number of women (87.2%) were in the normal phosphorus level group (3-4.5 mg/dL) compared to men (78.9%) ($p<0.001$) (Table 7). Spearman's rho test showed that vitamin D levels were positively correlated with calcium and age ($p<0.001$) (Table 8).

Table 3. Serum 25(OH)D values to gender

Men					Women					
n=298	Minimum	Maximum	Mean	SD	n=765	Minimum	Maximum	Mean	SD	p
	5.1	89.2	22.22	11.54		2.6	150.8	22.25	15.96	0.086
	n		%			n		%		p
<10 ng/mL	36		12.1		<10 ng/mL	162		21.2		0.064
10-20 ng/mL	106		35.6		10-20 ng/mL	223		29.2		0.25
20-30 ng/mL	96		32.2		20-30 ng/mL	221		28.9		0.413
30-150 ng/mL	60		20.1		30-150 ng/mL	158		20.7		0.019
>150 ng/mL	0		0		>150 ng/mL	1		0.1		-

SD: standard deviation, 25(OH)D: 25-hydroxyvitamin D

Table 4. Calcium values

n=1,063	Minimum	Maximum	Mean	SD
	5.9	11.7	9.45	0.46
	n		%	
Hypocalcemia <8.5 mg/dL	13		1.2	
Normal 8.5-10.5 mg/dL	1032		97.1	
Hypercalcemia >10.5 mg/dL	18		1.7	

SD: standard deviation

Table 5. Calcium values to gender

Men					Women					
n=298	Minimum	Maximum	Mean	SD	n=765	Minimum	Maximum	Mean	SD	p
	7.2	11.1	9.48	0.43		5.90	11.7	9.44	0.47	0.239
	n		%			n		%		p
<8.5 mg/dL	1		0.3		<8.5 mg/dL	12		1.6		0.276
8.5-10.5 mg/dL	292		98		8.5-10.5 mg/dL	740		96.7		0.36
>10.5 mg/dL	5		1.7		>10.5 mg/dL	13		1.7		0.424

SD: standard deviation

Table 6. Phosphorus values

n=1,063	Minimum	Maximum	Mean	SD
	1.8	6.8	3.64	0.56
	n		%	
Hypophosphatemia <3 mg/dL	98		9.2	
Normal 3-4.5 mg/dL	902		84.9	
Hyperphosphatemia >4.5 mg/dL	63		5.9	

SD: standard deviation

Table 7. Phosphorus values to gender

Men					Women					
n=298	Minimum	Maximum	Mean	SD	n=765	Minimum	Maximum	Mean	SD	p
	2	6.1	3.49	0.59		1.8	6.8	3.7	0.54	<0.001
	n		%			n		%		p
<3 mg/dL	49		16.4		<3 mg/dL	49		6.4		0.813
3-4.5 mg/dL	235		78.9		3-4.5 mg/dL	667		87.2		<0.001
>4.5 mg/dL	14		4.7		>4.5 mg/dL	49		6.4		0.174

SD: standard deviation

Table 8. The correlation analysis for vitamin D, phosphorus, calcium, age, and gender

		Vitamin D	Phosphorus	Calcium	Age	Gender
Vitamin D	Correlation coefficient	1.00	0.016	0.125	0.303	0.053
	p-value	-	0.602	<0.001**	<0.001**	0.086
Phosphorus	Correlation coefficient	0.016	1.00	0.009	-0.068	-0.202
	p-value	0.602	-	0.777	0.026*	<0.001**
Calcium	Correlation coefficient	0.125	0.009	1.00	0.078	0.036
	p-value	<0.001**	0.777	-	0.011*	0.239
Age	Correlation coefficient	0.303	-0.068	0.078	1.00	0.049
	p-value	<0.001**	0.026*	0.011*	-	0.109
Gender	Correlation coefficient	0.053	-0.202	0.036	0.049	1.00
	p-value	0.086	<0.001**	0.239	0.109	-

*p<0.05, **p<0.001

DISCUSSION

The present study shows that the prevalence of vitamin D deficiency and insufficiency were 49.6% and 29.8%, respectively, in our study population. The proportions of subjects with normal calcium and phosphorus levels were 97.1% and 84.9%, respectively. Furthermore, vitamin D levels were found to positively correlate with calcium and age ($p<0.001$).

Vitamin D plays an important role in cellular growth and proliferation, homeostasis, oxidative stress and cellular transport (11). Vitamin D enhances calcium absorption in the intestine to maintain adequate serum calcium concentrations and is essential for bone growth and remodeling by osteoblasts and osteoclasts. A meta-analysis study found that synergistic administration of calcium and vitamin D could reduce general bone fractures by 15% and hip fractures by 30% (12). A study conducted in Spain reported that daily dietary intake of calcium and vitamin D alone was not sufficient to maintain adequate serum levels (13). Factors such as decreased vitamin D absorption, low vitamin D intake and little or no sun exposure, obesity, and darker skin pigmentation may increase risk of vitamin D deficiency, which is currently considered to be a global pandemic (14,15).

The prevalence of vitamin D deficiency was found to be 75.2% in northwestern China, and the predictors of vitamin D deficiency included dyslipidemia, coronary heart disease, obesity, smoking,

age, and sex (16). Another study in the United Kingdom showed that 61.5% of the study population was vitamin D deficient, and low socio-economic status, high body mass index, and cold season were associated with low vitamin D levels (17). The prevalence of vitamin D deficiency was found to be 87.1% in urban residents in Beijing and highly prevalent during the winter and spring seasons (18). Although one study found that vitamin D inadequacy and deficiency increased the odds of diabetes two-fold (19), another study conducted in Turkey found no difference between type 1 diabetics and healthy controls (20).

Yu et al. (21) found that 5.9%, 50%, and 38.7% of the study population were severely vitamin D deficient (<10 ng/mL), vitamin D deficient (10-20 ng/mL), and vitamin D insufficient (20-30 ng/mL), respectively. Only 5.4% of the participants were vitamin D sufficient (>30 ng/mL) and vitamin D deficiency was found to be higher in women (66.3%) compared to men (45.3%, $p<0.01$) (21). In our study, we found vitamin D levels of 198 subjects (18.6%) to be below 10 ng/mL, 329 subjects (31%) to be between 10-20 ng/mL, 317 subjects (29.8%) to be between 20-30 ng/mL, 218 subjects (20.5%) to be between 30-150 ng/mL, and only one subject (0.1%) had a vitamin D level ≥ 150 ng/mL.

In a study conducted in Saudi Arabia, vitamin D deficiency and insufficiency were found in 50% and 43.8%, respectively, among 160 pregnant women (22). Vitamin D deficiency was found in

about 44.6% of pregnant Turkish women in İzmir, which is a city in the Aegean region of Turkey (23). Another study found that 97.8% of pregnant women belonging to low socio-economic status were vitamin D deficient. 25(OH)D levels of maternal serum and cord blood were found to positively correlate. The findings of that study suggested that vitamin D stores of the mother directly affect neonatal vitamin D status (24). Öztürk et al. (25) found that 94.92% of participants had serum vitamin D levels <30 ng/mL and 75.54% of the participants were vitamin D deficient in Gaziantep, another city located in the southeastern province of Turkey. When vitamin D levels were compared between men and women, no significant difference was found in our study. We found that 79.4% of our study population had serum vitamin D levels below 30 ng/mL. Similarly, a study conducted in Oman found that 79% of the study population had vitamin D levels below 30 ng/mL and the study population had normal serum calcium and alkaline phosphatase levels (26). Furthermore, 80.3% of the study population were found to have levels <30 ng/mL in a study conducted in northern France, and 25(OH)D levels were found to correlate positively with 1,25(OH)₂D and negatively with parathyroid hormone, but did not correlate with serum calcium or phosphate levels (27). We observed that 97.1% and 84.9% of our study population had normal calcium and normal phosphorus levels, respectively. When phosphorus levels were compared based on gender, it was found to be significantly higher in women compared to men. Furthermore, a significantly higher proportion of women (87.2%) were in the normal phosphorus (3-4.5 mg/dL) level group ($p < 0.001$) compared to men (78.9%). We found that vitamin D levels were positively correlated with calcium and age but not with phosphorus levels.

Vitamin D deficiency was found in 73.9% of Turkish patients suffering from widespread musculoskeletal pain, and factors associated with hypovitaminosis included sex, age, and season (especially March) (28). A total of 75.2% of female and 33.7% male medical faculty students had vitamin D levels <20 ng/mL in Malatya (29). In our previous study, it was reported that 75% of the participants had levels <20 ng/mL, 16.1% had levels between 20-30 ng/mL, and 8.9% had levels ≥ 30 ng/mL (30). In the current study, we found sufficient vitamin D levels (≥ 30 ng/mL) in 20.5% of the study population (different study population and different timeline). Although our current as well as previous studies included subjects living in the Marmara region, the differing results may be due to the regular follow-up of the current subject group in a single department and more conscious practices to prevent vitamin D deficiency.

Study Limitations

The limitations of our study include not knowing the underlying disease condition of the subjects, absence of age restriction while selecting the participants, addition of triple test (vitamin D, calcium, phosphorus) for the first time, not including subjects who had these same tests before October 2015, and including only subjects who applied to the department.

CONCLUSION

Our study showed that prevalence of vitamin D deficiency is high in the Turkish population despite Turkey being a sunny country and presence of awareness about vitamin D deficiency among the population. Our study population generally had normal calcium and phosphorus levels.

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of İstanbul Medeniyet University, Göztepe Training and Research Hospital (approval number: 2018/0336, date: 12.09.2018).

Informed Consent: Since our study was retrospective, consent forms were not obtained from patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.Ç., G.Ö., H.H.M., E.A.; Design - B.Ç., G.Ö., H.H.M., E.A.; Data Collection and/or Processing - B.Ç., G.Ö., H.H.M., E.A.; Analysis and/or Interpretation - B.Ç., G.Ö., H.H.M., E.A.; Literature Search - B.Ç., G.Ö., H.H.M., E.A.; Writing Manuscript - B.Ç., G.Ö., H.H.M., E.A.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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