The European Research Journal

http://www.eurj.org

Original Article

e-ISSN: 2149-3189

DOI: 10.18621/eurj.278518

Causes of elevated parathyroid hormone levels in postmenopausal women

Irfan Esen[1], Selin Akturk Esen[1], Soner Cander[2], Ozen Oz Gul[2], Gokhan Ocakoglu[3], Erdinc Erturk[2]

[1]Department of Internal Medicine, University of Health Sciences, Bursa Yuksek Ihtisas Traininig and Research Hospital, Bursa, Turkey
[2]Department of Endocrinology and Metabolism, Uludag University School of Medicine, Bursa, Turkey
[3]Department of Biostatistics, Uludag University School of Medicine, Bursa, Turkey

ABSTRACT

Objectives. In this study we aimed to investigate causes of hyperparathyroidism and related factors in postmenopausal women. ***Methods.*** The study was conducted on 156 postmenopausal women, 43 with normal serum parathyroid hormone (PTH) levels and 113 with elevated serum PTH levels. Serum levels of 25-OH vitamin D, calcium and phosphorus, 24-hour urine calcium, phosphorus and calcium/creatinine ratio were compared between study groups. Also, bone mineral density, age of menopause, educational level, occupation, clothing style, daylight exposure time and daily dietary calcium consumption of subjects and relationships of these parameters with parathyroid hormone levels were investigated. ***Results.*** Causes of elevated serum PTH level were vitamin D deficiency in 92.9% and primary hyperparathyroidism in 4.4% of study group. Serum PTH levels were significantly higher in housewives (p<0.001), women with less than a high school graduates (p=0.008), and the veiled women (p=0.025). Serum 25-OH vitamin D levels were significantly lower in the veiled covered (p=0.002) and participants with less than a high school graduate (p=0.041). Significant negative correlation was detected between serum 25-OH vitamin D and the logarithmic value of serum PTH levels (r= -0.188; p=0.019). ***Conclusions.*** Vitamin D deficiency was common in all postmenopausal women but especially in those with lower education level and the veiled. Postmenopausal women should be screened for vitamin D deficiency and encouraged to benefit more from sunlight. Also, enriching foods in the markets with vitamin D may be helpful for decreasing hyperparathyroidism in this population.

Eur Res J 2017;3(3):234-242

Keywords: Primary hyperparathyroidism, secondary hyperparathyroidism, vitamin D deficiency, postmenopausal women, parathyroid hormome

Address for correspondence:
Irfan Esen, MD., University of Health Sciences, Bursa Yuksek Ihtisas Training and Research Hospital, Department of Internal Medicine, Bursa, Turkey
E-mail: irfan_esen@yahoo.com
Received: December 17, 2016; Accepted: March 3, 2017; Published Online: May 30, 2017

Introduction

Primary hyperparathyroidism is a calcium metabolism disorder characterized by excessive production of parathyroid hormone (PTH) from the parathyroid glands without any stimulus known or described. Primary hyperparathyroidism affects 0.3% of the general population and 2.1% of the postmenopausal women [1]. Secondary hyperparathyroidism is described as increased secretion of PTH as a result of the stimulation of the calcium sensitive receptors secondary to a decrease in serum calcium level. Secondary hyperparathyroidism affects 1% of the general population and is usually secondary to low oral intake of calcium and/or vitamin D deficiency [2]. Secondary hyperparathyroidism secondary to vitamin D deficiency leads to mineralization disorders of the bones, low bone mineral density, osteoporosis and ultimately an increased risk of bone fracture in adults [3]. Calcium and vitamin D replacement leads to reduction in fracture incidence in elderly people but treatment with only vitamin D does not provide significant benefits [4].

In this study, we screened the etiologies of elevated PTH levels in postmenopausal women without concomitant diseases or use of drugs that may interfere with PTH levels. Also, we aimed to determine the incidence of clinically asymptomatic primary hyperparathyroidism, the causes of secondary hyperparathyroidism, social risk factors of hyperparathyroidism and the measures that can be taken to avoid hyperparathyroidism and its complications in postmenopausal women.

Methods

One hunded and fifty-six postmenopausal women, 113 with elevated PTH levels and 43 with normal PTH levels, admitted to the department of Internal Medicine outpatient clinics of Uludag University Hospital (from October 2010 to May 2011), aged ≥50 years, had no menstruation for at least two years and no disease to affect calcium metabolism were included. Premenopausal women aged <50 years, postmenopausal women aged ≥75 years, women with a previous diagnosis of parathyroid gland disease, chronic renal failure, malabsorption, biphosphonate, thiazid or corticosteroid drug use and acute infection were excluded. Serum PTH levels higher than 68.3 pg/ml was considered as hyperparathyroidism according to Uludag University Laboratory parameters. The study protocol was approved by Medical Research Ethics Committee of Uludag University (Date: 28.09.2010; Nr: 2010-9/15) and written informed consent were taken from all patients included to the study.

Education, occupation, average duration of exposure to sunlight per day during summer and winter, consumption of calcium-rich foods were recorded. Participants were divided into four groups according to their educational levels: had no formal education, primary school, high school and college graduates; two groups according to their clothings: veiled and non-veiled; three groups according to their occupational status as housewives, workers and retired people; two groups according to sunlight exposure insufficient (less than 20 minutes per day) and sufficient (more than 20 minutes per day); two groups according to daily calcium consumption adequate and inadequate. Daily calcium intake of subjects were calculated by using a questionnaire form which prepared by Turkish Dietitians' Association. The questionnare form was designed to assessment calcium content of dietary records.

Venous blood samples were collected after 10-hours of overnight fast and centrifuged. Levels of calcium, phosphorus, creatinine, alkaline phosphates, albumin and follicle stimulating hormone (FSH) were determined using commercially available assay kits with an Abbott Architect C16000 auto-analyzer. PTH levels were measured using Abbott G200 kits with an Abbott Architect i2000sr analyzer. 25-OH vitamin D levels were measured using THERMO HPLC analyzer. 24-hour urinary calcium, phosphorus and creatinine excretion were measured. Patients with high serum creatinine levels and FSH levels lower than 20 IU/ml were excluded from the study.

Bone mineral density measurements in all participants were detected by dual-energy x-ray absorptiometry (DEXA) method using with Hologic QDR-4500A S/N 45130 analyzer (Hologic Inc. Bedford, MA, USA). The measurements of the lumbar spine and the left femur were recorded. The mineral density (g/cm²) of the second lumbar (L) vertebra and the average mineral density of the L 1-4 vertebrae were compared statistically. Also the mineral density (g/cm²) of the left femoral neck and the average mineral density of the femoral neck, trochanteric and intertrochanteric regions were compared.

Statistical Analysis

Continuous variables were expressed as mean ± standard error, median, minimum and maximum values. Categorical variables were expressed as number and percentage values. The suitability of the normal distribution of continuous variables was analyzed by Shapiro Wilk test. According to the test results, in cases where there is compliance with the normal distribution, independent-samples t test was used for between groups comparisons. Correlation analysis was used for determination the relationship between continuous variables and Pearson correlation coefficient was calculated.

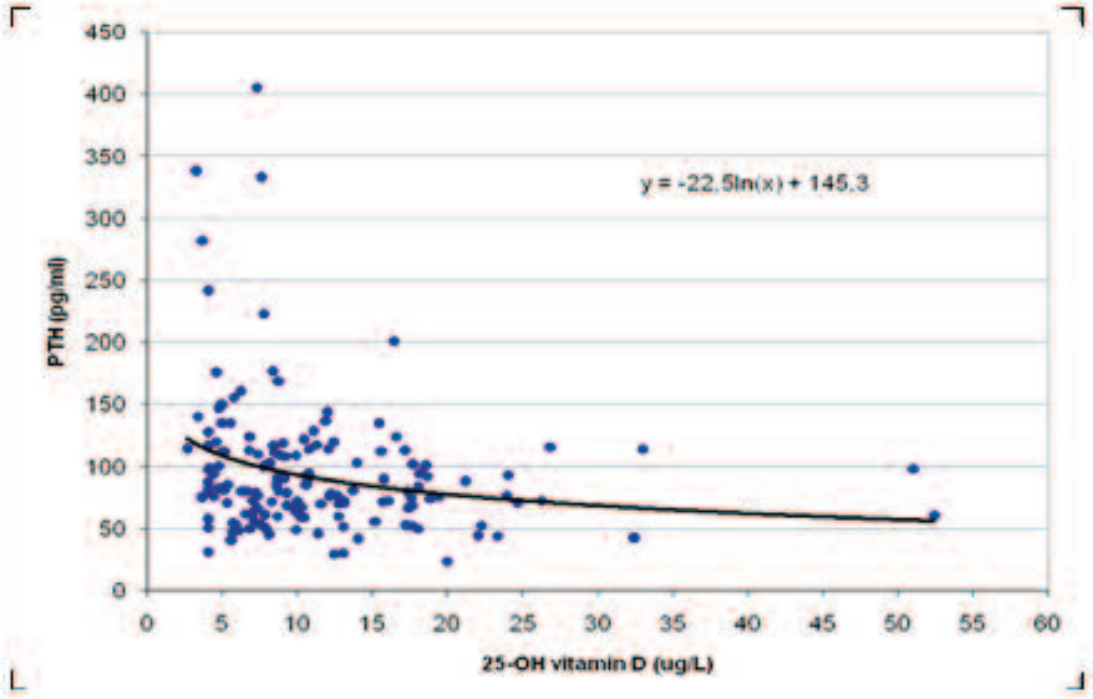

Figure 1. The relationship between 25-OH vitamin D levels and logarithmic values of serum PTH levels

Table 1. Comparison of some clinical and laboratory characteristics of the study group and the control group

	Study Group (n=113)	Control Group (n=43)	*p*
Age (year)	56.9±0.5	57.9±0.7	0.087
Menopausal age (year)	10.2±0.6	9.7±0.9	0.834
BMI (kg/m²)	30.2±0.5	29.4±0.5	0.753
Creatinine (mg/dl)	0.7±0.0	0.6±0.1	0.070
Chlorine (mmol/l)	104.2±0.2	104.2±0.3	0.865
ALP (IU/l)	83.6±2.3	81.3±3.1	0.362
Calcium (mg/dl)	9.5±0.04	9.5±0.05	0.588
Adjusted calcium (mg/dl)	9.6±0.04	9.6±0.05	0.355
Phosphorus (mg/dl)	3.3±0.04	3.6±0.7	**<0.001**
Creatinine clearance (ml/min)	110.6±2.2	108±3.5	0.530
24hUCa (mg/24s)	132.3 ± 7.3	168.5±11.8	**0.006**
24hUp (mg /24s)	637.6±23.4	653.4±42.7	0.956
TRp (%)	86.0±0.4	86.7±0.6	0.478
25- OH vitamin D (µg/l)	10.7±0.6	12.1±1.3	0.439
Uca /Ucr	0.009±0.004	0.012±0.004	**0.001**

Data are given as mean±SE (standart error). ALP=alkaline phosphates, BMI=body mass index, These parameters are statitistically insignificantly different, 24hUCa=24-hour urinary calcium excretion, 24hUp=24-hour urinary phosphorus excretion, TRp=tubular phosphorus reabsorption, Uca /Ucr=urinary calcium-creatinine ratio

Table 2. Comparison of the study group and the control group in terms of bone mineral density

	Study Group (n=113)	Control Group (n=43)	*p*
L2 (g/cm²)	0.90±0.12	0.89±0.12	0.840
L1-L4 total (g/cm²)	0.90±0.12	0.92±0.02	0.360
Femoral neck (g/cm²)	0.75 ± 0.11	0.75±0.01	0.680
Femur total (g/cm²)	0.95±0.01	0.95±0.01	0.970

Table 3. Social factors in the study and control groups

		STUDY	CONTROL	*p*
Social life	Living alone	(n=13; 11.5%)	(n=8; 18.6%)	0.294
	Living with partner/children	(n=100; 88.5%)	(n=35; 81.4%)	
Educational level	Less than a high school graduates	(n=93; 68.2%)	(n=25; 58.0%)	**0.003**
	More than a high school graduates	(n=20; 17.8%)	(n=18; 41.0%)	
Occupation	Housewives	(n=73; 64.6%)	(n=22; 51.1%)	0.144
	Workers / Retired	(n=40; 35.4%)	(n=21; 49.9%)	
Smoking	Yes	(n=16; 14.1%)	(n=9; 20.9%)	0.332
	No	(n=97; 85.9%)	(n=34; 79.1%)	
Be covered	Yes	(n=79; 69.9%)	(n=21; 48.8%)	**0.016**
	No	(n=34; 30.1%)	(n=22; 51.2%)	
Sunlight exposure	Sufficient	(n=40; 35.3%)	(n=23; 53.4%)	**0.046**
	Insufficient	(n=73; 64.7%)	(n=40; 46.6%)	

PTH=parathyroid hormone

Results

The mean age was 56.9 (range; 50-74) years in patients (n=113) with hyperparathyroidism and 57.9 (range; 50-72) years in the control group (n=43). There were no significant differences between the groups in terms of menopausal age, body mass index, serum calcium levels and serum 25-OH vitamin D levels but serum phosphorus levels were significantly lower in the study group (Table1). 24-hour urinary calcium excretion (24hUca) was reduced in the study group and 24-hour urinary phosphorus (24hUp) excretion was similar in both groups (Table1). Creatinine clearance was 110.6±2.2 ml/min in control study group and 108±3.5 ml/min in control group which was not statistically significant (p=0.530). 24hUca was 132.3±7.3 mg/24h in study group and 168.5±11.8 mg/24h in control group which was statistically significant (p=0.006). Tubular phosphorus reabsorption (TRp) was 86.0±0.4% in study group and 86.7±0.6% in control group, which was not statistically significant (p=0.478). Urinary calcium-

Table 4. Serum PTH levels of all participants

		PTH (pg/ml)	*p*
Social life	Living alone (n=21)	84.8±8.8	0.478
	Living with partner/children (n=135)	95.5±4.8	
Educational level	Less than a high school graduates (n=118)	101.4±5.4	**0.008**
	More than a high school graduates (n=38)	75.1±4.5	
Occupation	Housewives (n=95)	99.4±5.7	**<0.001**
	Workers / Retired (n=61)	88.0±6.5	
Smoking	Yes (n=25)	88.0±7.9	0.544
	No (n=131)	96.3±4.9	
Be covered	Yes (n=100)	103.2±6.1	**0.025**
	No (n=56)	80.2±4.1	
Calcium consumption	Sufficient (n=49)	94.7±6.4	0.680
	Insufficient (n=107)	95.1±4.3	

PTH=parathyroid hormone

Table 5. Serum 25-OH vitamin D levels of all participants

		25-OH vitamin D (µg/l)	*p*
Social life	Living alone (n=21)	12.4±1.6	0.242
	Living with partner/children (n=135)	10.9±0.6	
Educational level	Less than a high school graduates (n=118)	10.4±0.6	**0.041**
	More than a high school graduates (n=38)	13.2±1.4	
Occupation	Housewives (n=95)	10.3±0.7	0.439
	Workers / Retired (n=61)	12.2±1.0	
Smoking	Yes (n=25)	10.5±0.7	0.828
	No (n=131)	11.2±0.6	
Be covered	Yes (n=100)	9.9 ± 0.7	**0.002**
	No (n=56)	13.2±1.0	
Calcium consumption	Sufficient (n=49)	12.0±1.2	0.337
	Insufficient (n=107)	10.7±0.6	

Table 6. Causes of elevated serum PTH levels in patients with hyperparathyroidism

	n=113*
25-OH vitamin D deficiency	92.9%
Primary hyperparathyroidism	4.4%
Normocalcemic with hyperparathyroidism	3.5%
Calcium renal leak	1.8%
Hypocalciuric hypercalcemia	1.8%

*some patients have both of diseases, PTH=parathyroid hormone

creatinine ratio (Uca/Ucr) was 0.009±0.004 in study group and 0.012±0.004 in control group which was statistically significant (p=0.001) (Table 1).

Significant negative correlation were detected between logarithmic values of serum PTH levels and serum 25-OH vitamin D levels of both groups (r= -0.188; p=0.019) (Figure 1) but correlation coefficient was low showing a weak correlation.

There was no statistically significant difference between groups in terms of bone mineral density (Table 2). However, the mean mineral density of the L 1-4 vertebrae were in negative corerelation with the increase in serum PTH levels which was statistically significant (r= -0.175; p=0.029) despite this significance correlation coefficient was low showing a weak correlation, similarly the mean mineral density of the femoral neck, wards triangle and trochanteric region did not show any correlation.

Based on our data, serum PTH levels were significantly higher in housewives (p<0.001), women with less than a high school graduates (p=0.008), and the veiled women (p=0.025). Living alone and smoking were found to have no effect on serum PTH levels. PTH levels were not significantly different between groups with adequate calcium consumption and inadequate calcium consumption and also PTH levels were significantly different between groups with insufficient sunlight exposure and sufficient sunlight exposure (Tables 3 and 4).

Serum 25-OH vitamin D levels were significantly lower in the veiled covered (p=0.002); in participants with less than a high school graduate (p=0.041). Living alone, being a housewife or retired, smoking, sunlight exposure, calcium consumption found to have no effect on serum vitamin D levels (Table 5).

When the causes of elevated serum PTH levels were examined, 25-OH vitamin D deficiency was detected in 105 of cases and primary hyperparathyroidism was detected in five cases with 25-OH vitamin D deficiency (Table 6).

Discussion

Causes of elevated serum PTH levels are adenoma, hyperplasia and carcinoma of the parathyroid gland. Elevated PTH levels may be a physiological response which is called secondary hyperparathyroidism especially seen in cases with low serum calcium levels. Decreased oral intake or intestinal absorption of calcium, vitamin D deficiency,

increased renal calcium losses, impaired renal function results in elevated serum PTH levels. In our study, serum calcium levels were not statistically different between the study group and the control group but 24-hour urine calcium excretion was significantly lower in the study group. It was understood that vitamin D deficiency was the most important reason for this situation Reduction of renal phosphorus reabsorption is expected in vitamin D deficiency depending on the decreased intestinal absorption of phosphorus and the increased PTH activity leading to a decrease in serum phosphorus level. The levels of serum phosphorus were significantly lower in the study group than the control group. These results are expected in vitamin D deficiency. Although statistically significant reduction of the calculated rate of tubular reabsorption was not detected.

Serum 25-OH vitamin D levels were low in both control and study groups. A negative correlation was detected between serum PTH levels and 25-OH vitamin D levels. However, PTH levels were not increased in the control group with low 25-OH vitamin D levels Albertazzi *et al.* [5] divided the subjects in their study according to the levels of serum PTH and observed that serum 25-OH vitamin D levels were significantly lower in the group with high serum PTH levels. Sahota *et al.* [6] reported that vitamin D deficiency was common in active elderly people living at home but they also reported that secondary hyperparathyroidism was not so common among these elderly. In other studies, secondary hyperparathyroidism was observed in approximately only 30-50% of elderly people with low serum 25-OH vitamin D levels [7]. There may be several reasons for this situation. PTH levels may not be increased in people with vitamin D deficiency that consumes calcium-rich foods [8]. There may be personal differences in terms of intestinal calcium absorption, even if there is not a consumption of calcium-rich foods [9]. Also, the measured serum vitamin D is 25-OH vitamin D which is a reliable method in terms of showing the levels of stored vitamin D. However, the effect of serum PTH levels on [1.25(OH)2D], which is active vitamin D, is not clear [10].

One of the main problems encountered with increased levels of serum PTH is decrease in bone mineral density in long term. Decrease in bone mineral density is seen not only in hypercalcemic patients with primary hyperparathyroidism and also seen in normocalcemic patients with primary hyperparathyroidism [1]. Renjmark *et al*'s [11] study showed that bone mineral density was lower especially in the femoral neck and the risk of osteoporotic bone fracture was 59% in normocalcemic patients with hyperparathyroidism. Decrease in bone mineral density was seen not only in patients with primary hyperparathyroidism and also seen in patients with secondary hyperparathyroidism due to vitamin D deficiency. Nakamura *et al.* [12] showed a significant decrease in bone mineral density in patients with hyperparathyroidism but they also showed a decrease in bone mineral density in patients with vitamin D deficiency independently from PTH levels. There are no adequate data about what levels of increase in serum PTH may adversely affect bone mineral density [13]. Albettazzi *et al.* [5] compared the cases with elevated serum PTH levels and with normal serum PTH levels in their study but they could not detect a significant relationship between serum PTH levels and the bone mineral density of the lumbar spine and the femoral neck. Similarly, Kaya *et al.* [14] found no association between bone mineral density and elevated serum PTH levels in their study. But Silverberg *et al.* [15] demonstrated slightly decrease in bone mineral density with elevated PTH levels in their study. In our study, there is no significant difference between the study and control group in terms of bone mineral density and it may be related to the duration of hyperparathyroidism. Our study was a cross-sectional study and we did not know how long the patients had hyperparathyroidism. Probably, due to short-term exposure of elevated PTH levels and the small number of the study group, a significant difference could not be identified between the two groups in terms of bone mineral density. In addition, the levels of vitamin D deficiency in both groups were not very different. Therefore, it is considered that the levels of secondary hyperparathyroidism, the main factor that causes bone resorption, were not at the levels of negative effect on bone mineral density.

The reduction of bone mineral density is usually detected in all of the measurement regions in patients with primary hyperparathyroidism [16]. However, increase in bone resorption due to hyperparathyroidism is expected in cortical bones [15, 17]. Proximal radius is the region with highest cortical bone. In our study, due to the fact that the bone mineral densities of the lumbar vertebra, which is mainly trabecular, and femur, which is mainly cortical, were measured and the bone mineral density of proximal radius was not measured, a significant difference could not be identified in patients with hyperparathyroidism.

Vitamin D deficiency/insufficiency is one of the most discussed topics. What should be the normal range of serum 25-OH vitamin D levels are not exactly certain for the definition of vitamin D deficiency. The level that stimulates parathyroid gland for PTH secretion is generally accepted as cut off for vitamin D deficiency [18]. In 1985, Peacock *et al.* [19] defined vitamin D insufficiency in addition to vitamin D deficiency. They proposed to define serum vitamin D level less than 10 ng/ml as deficiency and serum vitamin D level less than 20 ng/ml as insufficiency. The minimum level of serum 25-OH vitamin D necessary to normalize the increased bone turnover due to elevated serum PTH was 20 ng/ml (80 mmol/l) [20, 21]. Generally, serum vitamin D level less than 20 ng/ml is defined as deficiency and serum vitamin D level less than 30 ng/ml is defined as insufficiency [15, 22-24]. In a study performed in our country, sufficient serum 25-OH vitamin D levels were observed in only 18% of postmenopausal women and elderly men. In addition, there was no relationship between the levels of serum 25-OH vitamin D and some parameters such as serum PTH levels, age, body mass index and dietary calcium content [25]. 25-OH vitamin D level less than 20 ng/ml was defined as vitamin D deficiency in our study. We detected sufficient serum 25-OH vitamin D levels in only eight patients (7.4%) with hyperparathyroidism and in only six patients (13.9%) without hyperparathyroidism.

The frequency of vitamin D deficiency was detected as 50-97% in several studies in different populations [26, 27]. This increased incidence was not only reported in countries with insufficient exposure to sunlight Vitamin D deficiency is detected up to 90% in countries such as Greece, Italy and Spain during winter [28]. The different results detected in the studies were thought to be associated with the habits of vitamin D-rich food consumption and the use of drugs containing vitamin D. In many studies synthesis of vitamin D has been shown to be decreased with increasing age [29, 30]. Therefore, the daily requirement of vitamin D is known to be increased in advanced age. In patients requiring vitamin D supplementation, daily 400 units of vitamin D supplementation is considered insufficient and it is accepted that this dosage should be increased to 800 units/day. Apart from all these, the reason for the detection of extremely low serum 25-OH vitamin D levels may be related to the adequacy of the study method. It was shown in studies that there may be significant differences between the assays used in the measurements of serum 25-OH vitamin D levels and also significant deviations were found between the measurements performed in different laboratories, although the same study method [31, 32]. HPLC (Recipe ®) method was used for the measurement of vitamin D in our study. It is a very reliable method with 2.7% intraassay deviation and 3.7% interassay deviation. In some studies, HPLC method has been reported to be more sensitive than chemiluminescent immunoassay or radio immunoassay methods [33].

In our study, participants were divided into groups based on various social features. Participants were mainly composed of people with hyperparathyroidism. The control group were only 27.5% of all participants. In our society, the most important factors leading to vitamin D deficiency were being veiled and having low levels of education. Since, living alone, being housewife or retired, smoking, sunlight exposure, calcium consumption found to have no effect on serum vitamin D levels Our study proved once more that vitamin D deficiency is the most important cause of hyperparathyroidism.

The incidence of primary hyperparathyroidism was calculated as 4.4% in our study group. It was a very high prevalence although the average age of the group was not very advanced. In comprehensive studies, the prevalence of primary hyperparathyroidism ranged from 3/1000 to 21/1000. However, in our study, patients with elevated levels of serum PTH were selected and there were sufficient numbers of patients as a control group. Therefore, the frequency of detected primary hyperparathyroidism reflected primary hyperparathyroidism frequency of patients with elevated PTH levels rather than primary hyperparathyroidism frequency of general population. Primary hyperparathyroidism was detected in 5 cases. The remaining 108 patients had elevated serum PTH levels but normal serum calcium levels. After vitamin D deficiency, calcium renal leak, and hypocalciuric hypercalcemia excluded; we evaluated 4 patients (3.5%) as normocalcemic with hyperparathyroidism. In studies on long-term follow-up these patients, it has been shown that the possibility of hypercalcemic hyperparathyroidism development was very low [1]. Some studies reported that there may be adverse effects on bone mineral density in these cases [34].

Conclusions

Consequently, the results of this study showed that the most important reason for the increase of PTH secretion in postmenopausal women was vitamin D deficiency. Additionally, vitamin D deficiency was common in patients with or without hyperparathyroidism. Especially, all postmenopausal women should be evaluated for vitamin D deficiency to be informed about vitamin D deficiency. The normal range of serum 25-OH vitamin D level is not exactly certain, vitamin D deficiency incidence shows seasonal changes, there are problems with the measurement accuracy and the measurements of vitamin D levels are quite expensive. Because of all these reasons vitamin D deficiency screening and treating are not easy. Vitamin D supplementation for all society is a more rational approach to avoid vitamin D deficiency. Enrichment of milk and milk products with vitamin D seems to be the most appropriate solution for the elimination of vitamin D deficiency.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

References

[1] Bolland MJ, Grey AB, Orr-Walker B, Home AM, Evans MC, Clearwater JM, et al. Prospective 10-year study of postmenopausal women with asymptomatic primary hyperparathyroidism. N Z Med J 2008;121:18-29.
[2] Saleh F, Jorde R, Sundsfjord J, Haug E, Figenschau Y. Causes of secondary hyperparathyroidism in a healthy population: the Tromso study. J Bone Miner Metab 2006;24:58-64.
[3] Holick MF. Vitamin D: importance in the prevention of cancers, type 1 diabetes, heart disease, and osteoporosis. Am J Clin Nutr 2004;79:362-71.
[4] Avenell A, Gillespie WJ, Gillespie LD, O'Connell DL. Vitamin D and vitamin D analogues for preventing fractures associated with involutional and post-menopausal osteoporosis. Cochrane Database Syst Rev 2005; 3:227.
[5] Albertazzi P, Steel SA, Purdie DW, Gurney E, Atkin SL, Robertson WS. Hyperparthyroidism in elderly osteopenic women. Maturitas 2002;43:245-9.
[6] Sahota O, Mundey MK, San P, Godber IM, Lawson N, Hosking DJ. The relationship between vitamin D and parathyroid hormone: calcium homeostasis, bone turnover, and bone mineral density in postmenopausal women with established osteoporosis. Bone 2004;35:312-9.
[7] Sahota O, Gaynor K, Harwood RH, Hosking DJ. Hypovitaminosis D and 'functional hypoparathyroidism'-the NoNoF (Nottingham Neck of Femur) study. Age Ageing 2001;30:467-72.
[8] McKane PJM, Khosla S, Egan KS, Robins SP, Burritt MF, Riggs BL. Role of calcium intake in modulating agerelated increases in parathyroid function and bone resorption. J Clin Endocrinol Metab 1996;81:1699-703.
[9] Cerrahoglu L, Duruoz MT, Tikiz C, Olcenler S, Tulukoglu N, Susin A. [The correlation between dietary calcium intake and bone mineral density in postmenopausal women]. Osteoporoz Dünyasından 2002;8:173-7. [Article in Turkish]
[10] McKenna MJ, Freaney R. Secondary hyperparathyroidism in the elderly: means to defining hypovitaminosis D. Osteoporos Int 1998;8:3-6.
[11] Rejnmark L, Vestergaard P, Brot C, Mosekilde L. Increased fracture risk in normocalcemic postmenopausal women with high parathyroid hormone levels: a 16-year follow-up study. Calcif Tissue Int 2011;88:238-45.
[12] Nakamura K, Tsugawa N, Saito T, Ishikawa M, Tsuchiya Y, Hyodo K, et al. Vitamin D status, bone mass, and bone metabolism in home-dwelling postmenopausal Japanese women: Yokogoshi Study. Bone 2008;42:271-7.
[13] Bates CJ, Carter GD, Mishra GD, O'Shea D, Jones J, Prentice A. In a population study, can parathyroid hormone aid the definition of adequate vitamin D status? A study of people aged 65 years and over from the British National Diet and Nutrition Survey. Osteoporos Int 2003;14:152-9.
[14] Kaya T, Ulutas O, Celebiler Cavusoglu A, Aslanca D, Karateper AG, Gunaydin R, et.al. [Serum levels of 25 (0H) vitamin D and hyperparathyroidism in healthy postmenopausal women]. Romatizma 2007;22:20-3. [Article in Turkish]
[15] Silverberg SJ, Shane E, de la Cruz L, Dempster DW, Feldman F, Seldin D, et al. Skeletal disease in primary hyperparathyroidism. J Bone Miner Res 1989;4:283-91.
[16] Khan A, Bilezikian J. Primary hyperparathyroidism: pathophysiology and impact on bone. JAMC 2000;163:184-7.
[17] Seeman E, Wahner HW, Offord KP, Kumar R, Johnson WJ, Riggs BL. Differential effects of endocrine dysfunction on the axial and the appendicular skeleton. J Clin Invest 1982;69:1302-9.
[18] McKenna MJ, Freaney R. Secondary hyperparathyroidism in the elderly: means to defining hypovitaminosis D. Osteoporos Int 1998;8:3-6.
[19] Peacock M, Selby PL, Francis RM, Brown WB, Hordon L. Vitamin D deficiency, insufficiency, sufficiency and intoxication. What do they mean? In: Norman AW, Schaefer K, Grigoleit H-G, Herrath DV, editors. , eds. Vitamin D: Chemical, Biochemical and Clinical Update. Berlin, Germany: Walter de Gruyter; 1985:569-70.
[20] Saliba W, Barnett O, Rennert HS, Lavi I, Rennert G. The relationship between serum 25(OH)D and parathyroid hormone levels. Am J Med 2011;124:1165-70.
[21] Sai AJ, Walters RW, Fang X, Gallagher JC. Relationship between vitamin D, parathyroid hormone, and bone health. J Clin Endocrinol Metab 2011;96:436-46.
[22] Silverberg SJ. Vitamin D deficiency and primary hyperparathyroidism. J Bone Miner Res 2007;22 Suppl 2:V100-2.
[23] Gaugrıs S, Heaney R, Boonen S, Kurth H, Bentkover JD, Sen SS. Vitamin D inadequacy among post-menopausal women:

a systematic review. QJM 2005;98:667-76.
[24] Souberbielle JC, Friedlander G, Kahan A, Cormier C. Evaluating vitamin D status. Implications for preventing and managing osteoporosis and other chronic diseases. Joint Bone Spine 2006;73:249-53.
[25] Basaran S, Guzel R, Benlidayi IC, Uysal FG. [Effects of vitamin D levels on quality of life in osteoporosis]. Osteoporoz Dünyasından 2006;12:35-8. [Article in Turkish]
[26] Matsuoka LY, Wortsman J, Dannenberg MJ, Hollis BW, Lu Z, Holick MF. Clothing prevents ultraviolet-B radiation-dependent photosynthesis of vitamin D3. J Clin Endocrinol Metab 1992;75:1099-103.
[27] Mishal AA. Effects of different dress styles on vitamin D levels in healthy young Jordanian women. Osteoporos Int 2001;12:931-5.
[28] Scharla SH. Prevalence of subclinical vitamin D deficiency in different European countries. Osteoporos Int 1998;8 Supp 2:S7-12.
[29] MacLaughlin J, Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. J Clin Invest 1985;76:1536-8.
[30] Holick MF, Matsuoka LY, Wortsman J. Age, vitamin D, and solar ultraviolet. Lancet 1989;2:1104-5.
[31] Binkley N, Krueger D, Cowgill CS, Plum L, Lake E, Hansen KR, et al. Assay variation confounds the diagnosis of hypovitaminosis D: a call for standardization. J Clin Endocrinol Metab 2004:89:3152-7.
[32] Zerwekh JE. The measurement of vitamin D: analytical aspects. Ann Clin Biochem 2004;41:272-81.
[33] Snellman G, Melhus H, Gedeborg R, Byberg L, Berglund L, Wernroth L, et al. Determining vitamin D status: a comparison between commercially available assays. PLoS One 2010;5:e11555.
[34] Adami S, Braga V, Squaranti R, Rossini M, Gatti D, Zamberlan N. Bone measurement in asymptomatic primary hyperparathyroidism. Bone 1998;22:565-70.