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The relationship between obstructive sleep apnea syndrome severity and vitamin D levels in sera

Emire Pınar Seyfettin Çelik[1], Ayşe Elif Küpeli[2]

[1]Department of Chest Diseases, Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Turkiye
[2]Department of Chest Diseases, Faculty of Medicine, Başkent University, Ankara, Turkiye

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Corresponding Author: Emire Pınar Seyfettin Çelik, pinarseyfettin@yahoo.com.tr

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ABSTRACT

Aims: Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by complete or partial upper airway obstruction episodes and frequently decreased arterial oxygen saturation. Etiological factors and risk factors of OSAS are still investigated and studies in this topic continue. Until recently, researches were focused on the major effects of vitamin D on the bone metabolism and calcium homeostasis. Today; it has been found that vitamin D plays roles in many cells and tissues of human body additional to its functions in the musculoskeletal system. In our study, we aimed to examine vitamin D levels in patients who are diagnosed as OSAS and to investigate the relationship between OSAS and vitamin D deficiency.

Methods: 83 volunteers, who were suspected to have OSAS, were included in the study. They all underwent polysomnography (PSG) in the sleep disorders center in pulmonary department, between January 2015 – May 2015. Twenty cases with apnea hypopnea index (AHİ) <5/hour were evaluated as simple snoring/control group. Cases with AHİ >5/hour were diagnosed as OSAS; 22 patients were diagnosed as mild, 20 patients were diagnosed as moderate and 21 patients were diagnosed as severe OSAS. Blood samples of these patients were studied for the measurement of vitamin D 25(OH)D3, parathormone (PTH) , calcium (Ca), phosphor (P) levels and the samples were quickly delivered to biochemistry laboratory

Results: A statistically significant difference in vitamin D levels were observed ($p<0.05$) between the control and OSAS groups. However, no statistically significant difference was found in PTH, Ca, P levels among these groups ($p>0.05$). Vitamin D levels in the control group were significantly higher than the mild and the severe OSAS patients. No statistically significant difference was observed in PTH, Ca, P levels between these patients.

Conclusion: Our study indicates that there is a significant relationship between vitamin D deficiency and OSAS. This finding suggests that vitamin D deficiency may play a role in the OSAS physiopathology. There are few studies exists about the association between vitamin D deficiency and OSAS. In this regard, we think our study will contribute to the literature. Moreover; prospective, randomized, controlled studies with large series were needed.

Keywords: Obstructive sleep apnea syndrome, vitamin D, parathormone, calcium, phosphor

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by recurrent episodes of complete or partial upper airway obstruction during sleep and often a decrease in oxygen saturation in arterial blood.[1] It results in excessive daytime sleepiness, cognitive dysfunctions, and low quality of life.[2] Obesity is the leading risk factor in OSAS, and other risk factors are advanced age, male gender, ethnicity, family history, anatomical anomalies, and impaired respiratory control during sleep.[3,4]

Polysomnography (PSG) is the gold standard for the diagnosis and treatment of OSAS. According to the American Academy of sleeping diseases classification that uses the apnea-hypoapnea index (AHI), OSAS is divided into three categories as mild OSAS (AHI=5-15), moderate OSAS (AHI=15-30), and severe OSAS (AHI >30).[5]

Vitamin D is a fat-soluble vitamin. Unlike other vitamins, it is synthesized in the body and is also called a hormone. Also,

25-Hydroxycholecalciferol 25(OH)D3, which is the product of 25 hydroxylation, is the main circulating form of vitamin D and its levels in human plasma vary between 10-80 ng/ml (25-200 nmol/L). The most important parameter that shows the sufficiency of vitamin D is serum 25(OH)D3 level. Vitamin D and its metabolites have important clinical roles in calcium balance and bone metabolism.[6]

Studies conducted in recent years report that vitamin D has many more functions than its already known effects on calcium, phosphorus, and bone metabolism with its physiological effects on bones, intestines, kidneys, and parathyroid glands. It was reported that vitamin D deficiency plays roles in the development of autoimmune diseases, inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, diabetes, tonsillar hypertrophy, many cancers, and heart diseases. Also, vitamin D deficiency is reported to be at a high prevalence in patients with Chronic Obstructive Pulmonary Disease (COPD) in recent studies and is stated to cause susceptibility to lung infections.[7,8] It is also among the discussed topics that vitamin D deficiency might predispose individuals to OSAS by causing adenotonsillar hypertrophy, airway muscle weakness, and/or chronic rhinitis.[9] Myopathy and associated widespread muscle pain caused by vitamin D deficiency are also considered to disrupt sleep quality.[7] Based on previous studies, it is expected that as the OSAS severity increases, the calcium and phosphorus levels in the serum will decrease and the parathormone level will increase.

In the present study, the levels of 25(OH)D3, which is the serum form of vitamin D and which was proven to play roles in metabolism and the physiopathology of many diseases, were measured in patients diagnosed with OSAS. PTH, calcium, and phosphorus levels were also evaluated. The study also aimed to investigate whether there is a relationship between OSAS severity and vitamin D deficiency. We believe that the study will contribute to the literature because there are not enough studies on OSAS-vitamin D levels.

METHODS

The study was carried out with the permission of Ethics Committe of the Başkent University Faculty of Medicine (Date: 03.02.2015, Decision No: KA14/311). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was conducted within the scope of research project KA14/311 after the approval of the Ethics Committee of Başkent University Researches board between January 2015 and May 2015 with 83 volunteers who were hospitalized for one night at the Sleep Disorders Center of the Department of Chest Diseases and underwent PSG examinations with a preliminary diagnosis of OSAS.

Before the examinations, the identity data, gender, height, and body weight of the individuals were recorded by the technician on duty who would perform the examinations. The body mass index (BMI) of the patients was calculated. The patients were hospitalized at the sleep disorders center for one night and a polysomnographic examination was made with a polysomnography (PSG) device (astro-med grass-telefactor, RI, USA) and 2-channel EEG (C3A2 or C4A1), 2-channel EOG, ECG, EMG recordings (from chin and tibialis anterior muscle), oronasal airflow with thermistor and nasal cannula, thoracoabdominal movements, body position, oxygen saturation from fingertip with pulse oximeter measurements were made.

Patient Groups

The study included 83 cases whose polysomnographic examinations were scored manually, aged between 18 and 75, and did not meet exclusion criteria, considering their AHI values. Those with AHI <5/h were evaluated as the simple snoring/control group. Patients with AHI >5/h were considered OSAS and were grouped according to their stages as follows.

- AHI <5/hour: Simple snoring (20 cases)
- AHI=5-15/hour: Mild OSAS (22 cases)
- AHI=16-30/hour: Moderate OSAS (20 cases)
- AHI >30/hour: Severe OSAS (21 cases)

Exclusion Criteria

Among the patients who were diagnosed with OSAS by polysomnography, those with diseases or medication use known to affect vitamin D and calcium levels (parathyroid disease, sarcoidosis, chronic kidney disease, acute myocardial infarction, chronic liver disease, calcium and/or vitamin D use) were not included in the study.

Laboratory Examinations

Serum samples taken from the cases were quickly delivered to the laboratory without waiting for the study. A total of 25-hydrocholecalciferol, phosphorus, calcium, and parathormone were studied from serum samples and 25-hydroxycholecalciferol was studied with the chemiluminescent microparticle immunoassay (CMIA) method on the "abbott architect i2000" device and the reference value was taken as 9.4-52.4 ng/ml. Phosphorus was examined with the Phosphomolybdate method on the "abbott architect c8000" device and the reference value was taken as 2.3-4.7 mg/dl. Calcium was examined with the arsenazo III method on the "abbott architect c8000" device and the reference value was taken as 8.8-10 mg/dl. Parathormone was examined with the chemiluminescent enzyme immune method on the "intact PTH" device and the reference range was accepted as 15-68.3 pg/ml.

Statistical Analysis

Before the analyses, the suitability of the data to some assumptions was investigated. The "Kolmogorov Smirnov normality test" was used to analyze the suitability of normal distribution, and the "Levene test statistics" were used to test the suitability of the homogeneous variance assumption. In the analysis of the relevant data, the test to be applied was decided by considering whether the assumptions were met and the structure of the data. Descriptive statistics of continuous variables were given as mean ± standard deviation or median (minimum value-maximum value), and descriptive statistics of categorical variables were shown as number of patients and percentage (%). Blood parameters and sleep parameters between the control group and OSAS groups, the one way ANOVA test was used when the assumptions were met for continuous variables, and the Kruskall Wallis H test was used when the assumptions were not met in comparing demographic variables. For the

variables with a significant difference as a result of the one-way ANOVA test, the tukey test and tamhane test were used for pairwise comparisons between the groups, and for the variables with a significant difference as a result of Kruskall Wallis H-test, m Whitney U test was used for pairwise comparisons. Also, the Chi-square test was used to compare categorical variables between groups. The spearman correlation coefficient was used to investigate the relationship between continuous variables. Statistical analyses were performed by using the SPSS Statistics 20.0 statistical package program in the present study and the p values obtained in the test results were evaluated at the 95% confidence level and the α=0.05 significance level.

RESULTS

A total of 20 cases with AHI <5/hour, 22 cases with AHI=5-15/hour, 20 cases with AHI=16-30/hour, and 21 cases with AHI >30/hour were included in the study prospectively among those who underwent PSG. 83 cases were included. Although there were no statistically significant differences between the groups in terms of height and gender (p>0.05), there were significant differences between the groups in terms of age, weight, BMI, and neck circumference (p<0.05) (Table 1).

There were no statistically significant differences between the groups in terms of phosphorus, parathormone, and calcium values (p>0.05). However, a significant difference was detected in terms of vitamin D (p<0.05) (Table 2).

There were no statistically significant differences between the groups in terms of snoring, waking up breathless, nocturia, morning dry mouth, headache, and daytime sleepiness (p>0.05). No statistically significant differences were detected between the groups in terms of the epworth sleepiness scale (ESS), total sleep time, sleep adequacy, maximum SPO_2, minimum heart rate, and maximum heart rate (p>0.05). However, statistically significant differences were detected between the groups in terms of apnea-hypopnea index, apnea index, hypopnea index, arousal index, obstructive apnea count, hypopnea count, total O2 desaturation, oxygen desaturation index, average SPO_2, minimum SPO_2, and SPO_2 <90% residence time (p<0.05).

The values of the four groups were significantly different from each other in terms of apnea index, arousal index, obstructive apnea count, total O_2 desaturation, oxygen desaturation index, and SPO_2<90% stay-fold. Although the control group had the lowest value in terms of the variables, it was found that as the degree of apnea increased among the OSAS groups, other values also increased. Hypopnea index values and hypopnea numbers are similar and at the highest values in the severe and moderate OSAS groups. These parameters were lower in the mild OSAS group than in the severe and moderate OSAS groups and were lowest in the control group.

Average SPO_2 values were similar and highest in the control group and the mild OSAS group, lower in the moderate OSAS group, and lowest in the severe OSAS group. Minimum SPO_2 values were similar in the control group and mild OSAS group. The values of these groups were significantly higher than the severe OSAS group. The values of the control group were significantly higher than those of moderate OSAS. Also, minimum SPO_2 values of moderate and severe OSAS groups were similar. No statistically significant relationships were found between AHI and vitamin D (r=0.031, p=0.791) and PTH (r=0.046, p=0.697). There was no statistically significant relationship between vitamin D and phosphorus, calcium, ODI, SPO_2<90% hospital stay-fold (p >0.05)

Table 1. Patient characteristics in OSAS groups

	Simple snoring n:20	Mild OSAS n:22	Modarate OSAS n:20	Severe OSAS n:21	p
Gender F/M	3 (15 %) / (82 %)	3 (13.6 %) /19(86.4 %)	3 (15 %) /17 (85 %)	3 (14.3 %) /18 (85.7 %)	0.999
Age	40.1±8.4	44.4±11.3	51.1±12.6	50.9±12.4	0.005*
Height (cm)	173.7±7.3	172.7±8.0	173.8±9.5	171.8±8.2	0.857
Weight (kg)	82.3±12	87.2±12.2	90.2±13.7	98.1±15.4	0.0003*
BMI (kg/m²)	27.3±3.6	29.2±3.5	30.1±5.4	33.3±4.9	0*
Neck circumference (cm)	39.1±3.1	39.8±2.7	40.8±2.1	41.8±2.5	0.0009*

OSAS: Obstructive sleep apnea syndrome; BMI: Body mass index. , *p: < 0.05

Table 2. Distribution of laboratory parameters according to OSAS groups

	Simple snoring	Mild OSAS	Moderate OSAS	Severe OSAS	p
Vitamin D (ng/ml)	20.7±13.3	12.7±3.6	15.2±5.5	13.1±6.4	0.037*
Phosphorus (mg/dl)	3.1±0.6	3.5±0.8	3.5±0.6	3.6±0.5	0.115
Parathormone (pg/ml)	45.7±29.6	57.2±22.4	44.7±21.2	64.4±41.9	0.111
Calcium (mg/dl)	9.6±0.3	9.6±0.3	9.5±0.3	9.4±0.3	0.119

OSAS: Obstructive sleep apnea syndrome

DISCUSSION

Although there are many known causes in the pathophysiology of OSAS, its pathogenesis is still not fully elucidated. The factors contributing to OSAS vary from individual to individual, and its pathophysiology is quite complex. It is already known that males are at 2-3-fold higher risk of OSAS than women and similar rates were found in many studies in the literature4 because pharyngeal and supraglottic airway resistance in the upper respiratory tract is higher in men.[2,10,11] The male/female rate was 6/1 in the present study. According to the literature data, we attributed our higher male/female ratio to the fact that women are less likely to visit our clinic with OSAS symptoms such as snoring and apnea and that vitamin D preparations are frequently used in our society, especially in the postmenopausal period, because of their protective effect against osteoporosis, and these cases were thus excluded from the study.

One of the known risk factors regarding OSAS is age. It is most common between the ages of 40-65 and plateaus after the age of 65. The reason for this increase with age has not been fully elucidated, but it is considered that the effect of aging on body fat distribution, tissue elasticity, ventilation control, and pulmonary and cardiovascular functions plays roles, and increasing comorbidities in old age also increase the tendency to URI obstructions. The average age was similar in the control group and mild OSAS group in the present study, but significantly higher in the moderate and severe OSAS group when compared to the control group.

One of the known and most common risk factors for OSAS is obesity.[12] It is already known that the frequency of OSAS increases as BMI increases. In the OSAS study of Nieto et al.[13] conducted with 6132 cases, in which demographic characteristics and the presence of hypertension were questioned, it was found that BMI levels were correlated with AHI values, and as AHI increased, BMI also increased.

As it is already known, obesity is a major risk factor for OSAS and causes vitamin D deficiency. One of the reasons might be the decreased ability of obese individuals to go out because of their physical appearance and, as a result, the decrease in vitamin D synthesis. Another reason might be the increase in the active metabolite 1.25(OH)2D3, which acts on the liver with negative feedback and reduces the production of 25(OH)D3. Also, vitamin D, which is a fat-soluble molecule, accumulates in excess amounts in the fatty tissue in obese individuals, and thus its amount in circulation decreases.14 However, some studies examined the relationships of both OSAS and vitamin D deficiency with Type 2 diabetes mellitus and metabolic syndrome, separately from each other.

Neck circumference is also an important risk factor for OSAS. If the neck circumference is >43 cm in men and 38 cm in women, it increases the risk.[25] Neck circumference measurement shows the soft and fatty tissue in the URI. Fat tissue accumulates mostly in the lateral pharyngeal wall and lateral pharyngeal fat pads.[15] In hoffstein and mateika's study, neck circumference was found to be significantly higher in the OSAS group than in the control group (42.7 cm and 38.4 cm, respectively).[16] In another study conducted by Uyar et al.[17] in our country to examine the clinical profiles of patients with OSAS, they found the neck circumference to be 41 cm in the mild OSAS group, 42.8 cm in the moderate OSAS group, and 45.5 cm in the severe OSAS group. In the present study, the mean neck circumference showed a positive correlation with AHI values and was statistically significantly higher in the severe OSAS group than in the control group. In our study, patients diagnosed with OSAS had larger neck circumferences compared to the control group, which was consistent with literature data.Vitamin D regulates calcium and phosphorus metabolism and exerts this effect on the parathyroid glands, kidneys, bones, and intestines.[18,19] It also regulates bone mineralization and calcium homeostasis by showing a synergistic effect with PTH.[20] Until recently, the emphasis was placed on the major effects of vitamin D (especially on bone metabolism and calcium and phosphorus homeostasis). In our present day, after the discovery that vitamin D is present in many tissues and cells of the body, it is not understood that it has many functions other than the musculoskeletal system. Vitamin D receptors (VDR) are found in almost all tissues (i.e., heart, breast, skin, brain, pancreas, lymphocytes, etc.) except target organs such as bone, kidney, and intestine, which proves that vitamin D has many other functions besides its known functions. The main functions of these are the regulation of immune functions, cell profiling and differentiation, and hormone secretion.

Studies conducted on the functions of vitamin D continue today. The relationship between obstructive sleep apnea syndrome (OSAS) and vitamin D is a recently researched topic, and there are several studies on this subject.[21-25] Particular attention is being paid to whether vitamin D deficiency is involved in the etiology of OSAS and whether it contributes to the severity of OSAS.[21] In a previous review by McCarty et al.,[26] the relationship between vitamin D deficiency and sleep disorders was discussed, and it was reported that the deficiency of this vitamin might be involved in the etiology of OSAS and other sleep disorders through different mechanisms. It was also emphasized that vitamin D deficiency, which develops because of various reasons, causes bone pain secondary to bone demineralization. Bone pain causes sleep disruptions and insufficient sleep, causing daytime fatigue and physical inactivity in people, and prepares the ground for obesity in the future, indirectly creating a risk factor for OSAS. In the same review, it was also emphasized that myopathy caused by vitamin D deficiency was directly and indirectly involved in the physiopathogenesis of OSAS. It paves the way for obesity through similar mechanisms and constitutes a risk factor for OSAS by indirectly causing peripheral muscle pain. It directly causes weakness in the upper respiratory tract muscles as a result of myopathy and is involved in the etiology of OSAS. Recently, aside from the known effects of vitamin D, its functions in the immune system have also been emphasized. Studies report that vitamin D deficiency causes immune dysfunction. Immune system dysfunction causes tonsillar hypertrophy, which paves the way for upper airway obstruction and thus constitutes a risk factor for OSAS. It is already known that immune dysfunction causes upper respiratory tract infection, allergy, and systemic inflammation, which predisposes to chronic rhinitis in the future, which in turn constitutes a risk factor for OSAS.

There are few studies conducted in the literature examining the relationships between vitamin D and OSAS, which are summarized in Table 3. Some studies speculated that vitamin D deficiency is secondary to OSAS, and some studies argued that OSAS is secondary to vitamin D deficiency. Mete et al.[27] examined the relationships between OSAS and vitamin D deficiency and reported that vitamin D was significantly lower in the severe OSAS group than in the other groups. It has been argued that this finding might be because of several different mechanisms (one of which is associated with TNF-α, an inflammatory marker). TNF-α is observed at high levels throughout the day in OSAS, which is an inflammatory process. In a previous study that was conducted by Peterson et al.,[21] a negative correlation was found between serum vitamin D levels and TNF-α levels. On the other hand, decreased ability to go outside in patients with OSAS because of daytime sleepiness and therefore restricting sun exposure was shown to be a reason for vitamin D deficiency. It was also emphasized that hypoxemia caused by OSAS might also cause vitamin D deficiency. In the same study, parathormone,

Table 3. Polysomnography parameters in OSAS groups

	Simple snoring n:20	Mild OSAS n:22	Moderate OSAS n:20	Severe OSAS n:21	p
Epworth sleepiness scale	5.9±2.9	7.9±4.7	7.9±5.2	6.8±4.4	[a]0.406
Snore	20 (% 100)	21 (% 95.5)	20 (%100)	21 (%100)	[c]0.507
Waking up unable to breathe	9 (%45)	11 (% 50)	9 (%45)	17 (%81)	[c]056
Notruria	9 (%45)	8 (% 36.4)	9 (%45)	11 (%52.4)	[c]0.772
Morning mouth dryness	12 (%65)	14 (% 63.6)	9 (%45)	16 (%76.2)	[c]0.259
Headache	14 (% 70)	9 (%40.9)	10 (%50)	8 (%38.1)	[c]0.164
Daytime sleepiness	12 (% 60)	10 (%45.5)	10 (%50)	11 (%52.4)	[c]0.820
TST	344.8+55.6	332.8±52.6	328.1±40.2	313.6±73.8	[a]0.375
Sleep adequacy %	82.4±11.4	81.5±10.8	84.1±9.9	77.6±17.1	[a]0.404
AHI	1.1 0-4.9)	9.4 (5.4±14.3)	19.9 (15.2-29.1)	59.7 (32.9-109.1)	[b]0*
Apnea index	0 (0-06)	0.7 (0-3.1)	2.1 (0-8.16)	42.5 (1.1-105)	b0*
Hypopnea index	0.9 (0-4.7)	7.4 (4.2-13.5)	16.1 (5.2-25.8)	19.4 (2.8-64.7)	[b]0*
Arousal Index	6.8 (1.6-14.2)	11.8 (3.5-21.6)	16.4(4.5-28.8)	42.5 (1.1-101.2)	[b]0*
Obstructive apnea number	0 (0-3)	3 (0-13)	10.5 (0-69)	157 (6-353)	[b]0*
Hypopnea number	5.5 (0-25)	44 (19-88)	91.5 (29-140)	127 (12-395)	[b]0*
Total O_2 desaturation	5 (0-14)	25.5 (13-59)	67.5 (26-111)	219 (97-523	[b]0*
ODI	0.6 (0-2.1)	3.9 (2-8.6)	10.5 (4.1-17.8)	32.5 (15-76.3)	[b]0*
Average SPO_2	94.3±1.8	93.0±2.1	91.2±2.4	88.8±3.9	[b]0*
Minimum SPO_2	87.6±8.8	78.5±12.2	75.9±10.8	68.4±12.9	[b]0*
Maximum SPO_2	98.3±0.7	97.9±1.1	97.6±1.9	97.6±0.9	[a]0.199*
SPO_2 <90% stay time	0.22 (0-20.7)	3.8±(0-82.9)	18.3 (1-99.5)	64.6 (11.4-96.2)	[b]0*
Minimum heart rate	52±11	50.6±7.0	51.5±8.9	50.0±7.2	[a]0.886
Maximum heart rate	108.3±12.9	99.4±9.7	99.1±11.1	100.3±15.6	[a]0.68

OSAS: Obstructive sleep apnea syndrome TST: Total sleep duration; AHI: Apnea hypopnea index; ODI: Oxygen desaturation index. *p: < 0.05 , a: Anova, b: Kuruskall wallis H, c: Chi square test

phosphorus, and calcium levels were compared in the OSAS and control groups, and no significant differences were reported, as in our study. In another study conducted by Bozkurt et al.,[22] where vitamin D levels and glucose metabolism disorders in OSAS were compared, they showed that vitamin D levels decreased as AHI values increased. They found the vitamin D levels to be below 20 ng/ml in all groups, which they attributed to seasonal reasons because they conducted the study in the winter months. The adverse effects of vitamin D deficiency on glucose metabolism in OSAS were investigated in the present study. For this reason, it was argued that giving vitamin D to cases with OSAS might prevent abnormal glucose metabolism and inflammation. In a study by Barceló et al.,[23] where diabetes, obesity, hypertension, and metabolic syndrome components and vitamin D levels were compared in patients with OSAS, statistically significant relationships were found between obesity, hypertriglyceridemia, metabolic syndrome, and vitamin D deficiency. It was observed that vitamin D levels were lower in the severe OSAS group than in the other groups, but the difference was not statistically significant. They also argued that vitamin D deficiency might be a result of OSAS and that in obese individuals with OSAS, this fat-soluble vitamin might accumulate in adipose tissue and cause deficiency in serum emphasizing that obese individuals with OSAS go out less because of immobility and that vitamin D deficiency might occur because of reduced sunlight exposure. In the same study, it was also stated that parathormone increased as AHI values increased, and they considered that this was secondary to low vitamin D. In a previous study conducted by Erden et al.,[24] it was found that as AHI values increased in individuals with OSAS, vitamin D levels decreased, and vitamin D levels in the moderate and severe OSAS group were statistically and significantly lower than the control group. One of the known causes of vitamin D deficiency is old age, and in their study, they stated that the average age of the severe OSAS group was higher than in other groups, and they considered advanced age to be the cause of vitamin D deficiency. They also examined parathormone, calcium, and phosphorus levels and found the values to be similar between the groups, which is similar to our study. In a study by Gozal et al.,[25] vitamin D levels were compared in obese and normal-weight children with and without OSAS in the pediatric population. They found the lowest mean levels of vitamin D in children with OSAS who were obese. They also reported a negative correlation between AHI values and vitamin D and underlined that vitamin D deficiency causes an inflammatory process and increases inflammation in OSAS. They attributed the reason why vitamin D deficiency is more common in obese children to the relationship of both processes with insulin resistance. McCarty et al.[28] examined the relationship between EUS and vitamin D levels in 81 patients who applied to a sleep center with sleep problems and nonspecific pain. They found a negative correlation between vitamin D levels and EUS scores in individuals without vitamin D deficiency. When they divided the group with vitamin D deficiency into black and white races, they reported that EUS scores were higher in the black race, but they did not detect any correlations between EUS and vitamin D deficiency in both races. They also found lower vitamin D levels in black people and considered that this difference between races might be because of the difference in skin pigmentation, underlined that this was the first study in the literature examining the relationship between EUS and vitamin D deficiency, and stated that studies with larger study groups were needed. Liguori et al.[29] compared their patients who were diagnosed with OSAS with the control group and found that vitamin D was significantly higher in the control group. They applied CPAP treatment for 7 days to patients diagnosed with severe OSAS, and while post-treatment vitamin D levels were found to increase significantly in men, this increase was not detected in women. They considered that this difference between men and women might be because of the complex effects of sex hormones on vitamin D.

Snoring is among the most common symptoms that bring OSAS patients to the doctor. Snoring is observed in 70-95% of patients with obstructive sleep syndrome.[30] The most common symptom was snoring in our study. Snoring was detected as 100% in the control group, 95.5% in the mild

OSAS group, 100% in the moderate OSAS group, and 100% in the severe OSAS group.

Other symptoms of obstructive sleep apnea syndrome are daytime sleepiness, morning dry mouth, morning headache, waking up unable to breathe, and nocturia. We did not detect a statistically significant difference between the groups in these symptoms, which were questioned in our study. Total sleep time (TST) is the time spent asleep during a PSG recording, and it might decrease or remain normal in individuals with OSAS. The TST and sleep adequacy in the severe OSAS group were lower than the other groups in our study, but no statistically significant difference was found between the groups.

The lowest heart rate in ECG during sleep recording is called the minimum heart rate, and the highest heart rate is called the maximum heart rate. It is already known that bradyarrhythmias will occur during apnea as a result of increased parasympathetic activation in individuals with obstructive sleep apnea syndrome, and compensatory tachyarrhythmias will occur during the postapneic period. In a study conducted by Akdoğan to examine the heart rate variability in patients with OSAS, no statistically significant difference was detected between the minimum and maximum heart rates between the control group and patients with OSAS, and many other factors that affect the heart rate (age, gender, comorbidities, obesity, etc.) In our study, no statistically significant differences were found between the groups in terms of minimum and maximum heart rate.

It was found in the present study that as the OSAS severity increased, the apnea index, hypopnea index, arousal index, obstructive apnea number, hypopnea number, total oxygen desaturation, duration of saturation below 90%, and oxygen desaturation index increased. Also, in line with the literature data, it was found that as AHI values increased, minimum SPO_2, maximum SPO_2, and average SPO_2 values decreased.

Limitations

The factors limiting the study were that the total number of patients and the distribution between groups were lower compared to the literature because the study was conducted in a limited time. Another limiting factor was that the study was conducted between January and May, a period when sunlight is low in our country. Another limiting factor was that patients' daily vitamin D intake was not determined through diet. We would like to underline that in our literature review, we could not find a validated survey to show adequate vitamin D intake. For this reason, we are aware that we cannot fix this variable. The same limiting factor is seen in all studies. We believe that the cause of vitamin D deficiency in patients with OSAS will be revealed more clearly with future validated survey studies determining dietary vitamin D intake.

CONCLUSION

In conclusion, in the present study in which the relationships between vitamin D and OSAS were examined, it was found that vitamin D levels were significantly lower in patients with OSAS than in the control group. We think that the study contributed to the few studies on this subject in the literature. However, we believe that larger series, prospective, randomized, controlled clinical studies are needed to better elucidate the mechanism of vitamin D deficiency on OSAS. We would also like to point out that controlled studies to investigate the success of vitamin D replacement therapy in patients with excessive daytime sleepiness might open a new page in the treatment of OSAS.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethics Committe of the Başkent University Faculty of Medicine (Date: 03.02.2015, Decision No: KA14/311).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Buysse DJ. International classification of sleep disorders, version 2: diagnostic coding manual. American Academy of Sleep Medicine, Rochester. 2005.
2. Silva GE, Goodwin JL, Vana KD, Quan SF. Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest J Pulm Crit Care*. 2016;13(3):137-149.
3. Al Lawati NM, Patel SR, Ayas NT. Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. *Prog Cardiovasc Dis*. 2009;51(4):285-293.
4. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. *JAMA*. 2004;29(16):6.
5. Iber C. Israel AS, Chesson AL, Quan SF. The AASM manual for the scoring of sleep and associated events. Rules, terminology and technical specifications. 1st ed: wenchester, Illıonis: American Academy of Sleep Medicine. 2007.
6. Yavuz D, Mete T, Yavuz R, Altunoğlu A. D Vitamini, kalsiyum, mineral metabolizması, D vitaminin iskelet dışı etkileri ve kronik böbrek yetmezliğinde nütrisyonel D vitamini kullanımı. *Ankara Med J*. 2014;14(4):162-171.
7. Skaaby T, Husemoen LLN, Thuesen BH, et al. Vitamin D status and chronic obstructive pulmonary disease: a prospective general population study. *PloS one*. 2014;9(3):90654.
8. Persson LJP, Aanerud M, Hiemstra PS, et al. Chronic obstructive pulmonary disease is associated with low levels of vitamin D. *PLoS One*. 2012;7(6):38934.
9. David E, McCarty M, Andrew L et al. The link between vitamin D metabolism and sleep medicine. *Sleep Med Rev*. 2014;18(4):311-319.
10. Jennum P. SjØl A. Epidemiology of snoring and obstructive sleep apnoea in a danish population, age 30–60. *J sleep Res*. 1992;1(4):240-244.
11. Çiftçi B. Bakmak ve görmek; uykuda solunum bozukluğu-hekim farkındalığı. *Solunum Hastalıkları Derg*. 2009;19(3):95-98.
12. Banno K, Kryger MH. Sleep apnea: clinical investigations in humans. *Sleep Med Rev*. 2007;8(4):400-426.
13. Nieto FJ, Young TB, Shahar E, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *JAMA*. 2000;283(14):1829-1836.

14. Sözen T. D hormon: güncel gelişmeler. *Hacettepe Tıp Derg.* 2011;42(1): 14-27.
15. Köktürk O. Obstrüktif uyku apne sendromu fizyopatolojisi. Turk Toraks Derneği merkezi kurslar. *Turk Thorac J.* 2007;27(1)71-82.
16. Hoffstein V, Mateika S. Differences in abdominal and neck circumferences in patients with and without obstructive sleep apnoea. *Eur Respir J.* 1992;5(4):377-381.
17. Uyar M, Elbek O, Aydın N, et al. Clinical profiles of obstructive sleep apnea syndrome. Turk Thorac J. 2008;9(3):113.
18. Holick MF. McCollum award lecture, 1994: vitamin D-new horizons for the 21st century. *Am J Clin Nutr.* 1994;60(4):619-630.
19. Jameson JL, Weetman AP. Tiroid bezi hastalıkları. Harrison İç hastalıkları prensipleri (15. Edisyon). İstanbul: Nobel Matbaacılık. 2004;4(1):2060-2075.
20. Bordelon P, Ghetu MV, Langan R. Recognition and management of vitamin D deficiency. *Am Fam Physician*. 2009;15(80):841-846.
21. Mete T, Yalçın Y, Berker D, et al. Obstructive sleep apnea syndrome and its association with vitamin D deficiency. *J Endocrinol Invest*. 2013;36(9):681-685.
22. Bozkurt NC, Çakal E, Şahin M, et al. The relation of serum 25 hydroxyvitamin D levels with severity of obstructive sleep apnea and glucose metabolism abnormalities. *Endocrine*. 2012;41(3):518-525.
23. Barcelo A, Esquinas C, Pierola J, et al. Vitamin D status and parathyroid hormone levels in patients with obstructive sleep apnea. *Respiration*. 2013;86(4):295-301.
24. Erden ES, Genc S, Motor S, Investigation of serum bisphenol A, vitamin D, and parathyroid hormone levels in patients with obstructive sleep apnea syndrome. Endocrine. 2014;45(2):311-318.
25. Kheirandish Gozal L, Peris E, Gozal D. Vitamin D levels and obstructive sleep apnoea in children. Sleep Med. 2014;15(4):459-463.
26. Udwadia ZF, Doshi AV, Lonkar SG. Singh C.I. Prevalence of sleep disordered breathing and sleep apnea in middle-aged urban Indian men. *Am J Respir Crit Care Med*. 2004;169(2):168-173.
27. Peterson CA, Heffernan ME. Serum tumor necrosis factor-alpha concentrations are negatively correlated with serum 25 (OH) D concentrations in healthy women. *J Inflamm*. 2008;24(5):10.
28. McCarty DE, Reddy A, Keigley Q, et al. Vitamin D, race, and excessive daytime sleepiness. *J Clin Sleep Med*. 2012;8(6):693-697.
29. Liguori C, Romigi A, Izzi F, et al. Continuous positive airway pressure treatment increases serum vitamin D levels in male patients with obstructive sleep apnea. *J Clin Sleep Med*. 2015;15(11):603-607.
30. Schlosshan D, Elliott MW. Sleep. 3: Clinical presentation and diagnosis of the obstructive sleep apnoea hypopnoea syndrome. *Thorax*. 2004;59 (4):347-352.