# Vitamin D Status of Women Living in Ankara

## *Ankara'da Yaşayan Kadınlarda D Vitamini Durumu*

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**Abstract**

**Objective:** To evaluate vitamin D status and its implications on bone metabolism in Ankara, Turkey.

**Materials and Methods:** A population-based study was designed. Vitamin D status was evaluated in both elderly (≥65 years old) and reproductive-aged (20-40 years old) female population living in the same area. All subjects were given questionnaires asking for sunlight exposure and skin covering scores in order to estimate sunlight utilization score (SUS). Their serum 25-hydroxyvitamin D [25(OH)D], parathyroid hormone (PTH), alkaline phosphatase (ALP) Calcium (Ca), Phoshorus (P) levels were measured. The bone mineral density was determined by means of calcaneal quantitative ultrasound (QUS).

**Results:** Serum 25(OH)D levels were similar in both the elderly (n=251) and the younger (n=301) groups [16.8 (11.5-26.5) vs 18.6 (13.2-26.4) ng/ml]. Vitamin D status was sufficient in only 21.3% of the elderly, and in 18.3% of the younger group (p: 0.153). However, both secondary hyperparathyroidism (28.7 vs 15.3%, p<0.001) and osteopenia, determined by quantitative ultrasound measurements (46.9 vs 7.0%, p<0.001), were more prevalent in the elderly women compared to the younger females.

**Conclusions:** Since it has a high prevalence of approximatelyz 80% in both the reproductive-aged and the elderly women, vitamin D insufficiency seems to be a public health problem in Ankara, Turkey. Insufficient vitamin D status beginning at early adulthood may predispose to secondary hyperparathyroidism that is, at least, contributing to bone loss observed during postmenopausal period. *Turk Jem 2010; 14: 39-43*

**Key words:** Vitamin D Deficiency, quantitative ultrasonography, secondary hyperparathyroidism, sunlight exposure

**Özet**

**Amaç:** Ankara'da D vitamini durumu ve bunun kemik metabolizması ile ilişkisini değerlendirmek.

**Gereç ve Yöntemler:** Toplum-tabanlı bir çalışma planlandı. Vitamin D düzeyi, aynı bölgede yaşayan yaşlı (≥65 yaş) ve üreme çağındaki (20-40 yaş) kadınlarda karşılaştırmalı olarak değerlendirildi. Tüm bireylere güneşlenme ve giyim skorlarını içeren anketler verilerek güneşten faydalanma skoru tahmin edilmeye çalışıldı. Bireylerin serum 25-hidroksivitamin D [25(OH)D], parathormon, alkalen fosfataz, kalsiyum, fosfor düzeyleri ölçüldü ve kantitatif kalkaneal ultrasonografi ile değerlendirmeleri yapıldı.

**Sonuç:** Serum 25(OH)D düzeyleri yaşlı (n=251) ve üreme çağındaki (n=301) kadınlarda benzerdi [16,8 (11,5-26,5) ve 18.6 (13,2-26,4) ng/ml]. Vitamin D düzeyi yaşlıların yalnızca %21,3'ünde, ve daha genç kadınların %18,3'ünde yeterliydi (P=0,153). Bununla beraber, sekonder hiperparatiroidizm (%28,7'e %15.3, p<0,001), ve kantitatif ultrason indeksi ile tayin edilen osteopeni (46,9 vs 7,0%, p<0,001) yaşlılarda daha sıktı.
**Tartışma:** Hem yaşlı, hem üreme çağındaki kadınlarda %80'e yaklaşan sıklığı olmasından dolayı vitamin D yetersizliği Ankara'da bir halk sağlığı problem gibi görünmektedir. Erken erişkin dönemden itibaren başlayan D vitamin yetersizliği -postmenopozal dönemde görülen kemik kaybına en azından katkıda bulunan- sekonder hiperparatiroidizme zemin hazırlayabilir. *Türk Jem 2010; 14: 39-43*

**Anahtar kelimeler:** Vitamin D eksikliği, kantitatif ultrasonografi, sekonder hiperparatiroidizm, güneşlenme

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## Introduction

Vitamin D is very important for health and well-being. Its deficiency may lead to serious musculoskeletal disorders including rickets in children, osteomalasia and osteoporosis, followed by fractures in adults. However, its deficiency seems to be pandemic (1). In fact, in the new millennium, prevalence of vitamin D deficiency is still high, even in developed and sunlight-abundant countries, and not onlAy in elderly and housebound people, but also in young adults and in children (2). Unfortunately, this worldwide pandemic remains generally unrecognized and untreated.
25-hydroxyvitamin D [25(OH)D] is the best predictor of endogenous vitamin D status (3). Although a consensus regarding the optimal level of serum 25(OH)D has not yet been established, it is generally agreed that vitamin D deficiency is detrimental to bone health when this level is below 20 ng/ml (4). However, the optimal concentration of 25 (OH)D is estimated to be at least 30 ng/ml (5). The levels below 10 ng/ml are defined as severe decifiency (6).
A maximum bone mineral density (BMD) is achieved when the 25(OH)D levels are ≥40 ng/ml. On the other side, when the level is ≤30 ng/ml, intestinal calcium absorption significantly decreases (7), which is associated with increased parathyroid hormone (PTH) levels (8,9). PTH activates osteoblasts, which stimulate the transformation of preosteoclasts into mature osteoclasts, a process associated with elevation of bone-specific serum alkaline phosphatase (ALP). Activated osteoclasts dissolve the mineralized collagen matrix in bone, resulting in the mobilization of the calcium stores out of the skeleton (1, 4). Additionally, PTH causes phosphaturia, resulting in a low-normal or low serum phosphorus level. In case of inadequate calcium/phosphorus product, mineralization of the collagen matrix is diminished, leading to classic signs of rickets in children (3,10) and painful osteomalacia in adults (9,11,12).
Elderly people are at increased risk of vitamin D insufficiency due to insufficient dietary intake, limited exposure to sunlight, reduced synthesis of vitamin D in the skin, diminished alpha-hydroxylation in the kidneys, and altered intestinal absorption (13). On the other hand, young adults do not seem to be at less risk. The modern human culture brings about increasing indoor lifestyles, obesity, smoking, and efforts to minimize sunlight exposure by sunscreens. In Turkey, additionally, excessive clothing in the outdoors due to socio-cultural and traditional reasons may increase the risk of vitamin D deficiency, even in young adults. We aimed to document the prevalence of vitamin D deficiency in both reproductive-aged and elderly women, and to analyze its implications on bone metabolism.

## Materials ve Methods

The study was carried out in a primary health care region (Park Primary Health Care Center, Abidinpasa district) in Ankara (40°N), the capital city of Turkey, in March. All women aged ≥65 years (the elderly group) who between 20 and 40 years (the younger group) and admitted to the health care center were candidates to participate in the study. Subjects who were on medications that may influence the bone metabolism (calcium, vitamin D, bisphosphonates, selective-estrogen receptor modulators, strontium, hormone replacement therapy, calcitonin, glucocorticoids, thyroid hormone, etc.), and who were known to have diseases that may cause secondary osteoporosis (malabsorption, rheumatoid arthritis, malignancy, etc.) were excluded. Laboratory measurements compatible with primary hyperparathyroidism were also excluded. All eligible subjects were asked to fill out questionnaires. Blood samples were obtained from the participants, and calcaneal quantitative ultrasound parameters were determined.
Questionnaires: The study participants were individually interviewed by experienced nurses using a preprepared questionnaire and a checklist to estimate their sunlight exposure scores (SES) and their skin coverage scores (SCS) and to document if they have disorders or history of drug use that can influence bone metabolism. The subjects were graded and scored according to their habits in an average day (13).
SES 1: Not directly exposed to sunlight at all.
SES 2: Exposed to sunlight outside the period between the hours 1100 and 1500.
SES 3: Regularly exposed to sunlight during the period between 1100 and 1500.
SES 4: Exposed to sunlight during the whole day.
SCS 1: Daily clothes leaving the head, face, neck, arms, hands, and legs exposed to sunlight and sunbathing in swimming outfit for at least one week in summer
SCS 2: Daily clothes leaving the head, face, neck, arms, hands, and legs exposed
SCS 3: Daily clothes leaving the head, face, neck, arms, and hands,
SCS 4: More protective way of dressing.
The sunlight utilization score (SUS) was calculated as SES divided by SCS for each person examined.
**Anthropometrical measurements:** The heights and body weights of the subjects were measured, and the body mass index (BMI) was calculated according to the formula BMI=(weight in kilograms)/(height in meters)$^2$. They were also examined with the Tanita instrument, and the body fat percentage was estimated based on electrical impedance.
**Blood Samples:** All blood samples were obtained at 0900 A.M. following an overnight fast and serum samples were stored at -80° C until assay. Serum 25(OH)D, calcium, inorganic phosphorus, ALP and PTH levels were measured in the Endocrinology Laboratory, Ankara University, Faculty of Medicine, Ibn-i Sina Hospital. Serum 25(OH)D concentrations were measured by radioimmunoassay using the BIOSOURCE 25OH-VIT.D3-RIA-CT commercial kit. With this method, the smallest measurable concentration is 0.6 ng/ml. The coefficients of intraassay and interassay variations were 6.1-7.9% and 7.1-8.2%, respectively. PTH measurements were done by immunoradiometric assay using the Gamma-BCT Intact PTH IRMA commercial kit. Serum ALP, calcium and phosphorus levels were measured colorimetrically in Express Plus-550 Ciba Cornig autoanalyzer using DIALAB DIAPACK fluid reactants.
**Quantitative ultrasound (QUS) measurements:** Calcaneal Quantitative ultrasound (QUS) measurements were performed in the Department of Endocrinology and Metabolic Diseases, in the same university hospital. Speed of sound (SOS, in meter per second) and broad band ultrasonic attenuation (BUA, in dB/MHz) measurements were taken at the right calcaneus using the dry-system device Sahara Clinical Bone Sonometer-Hologic. This device automatically calculated the quantitative ultrasound index (QUI, a unitless proprietary linear combination of BUA and SOS), a parameter indicating stiffness, according to the formula QUI=0,41 (BUA+SOS)-571. The respective coefficients of variations were 0.22%, 3.7%, 2.6%, and the respective absolute precision

values were 3.4 m/sec for SOS, 2.6 dB/MHz for BUA, and 2.2 for QUI. The T scores related to SOS, BUA, and QUI were calculated according to the formula t=(measured value-mean of young female population)/(standard deviation of young female population). Using the results of our previous study where the mean±standard deviation in a young Turkish female population was found as 1553±29.1 m/sec for SOS, 76.42±16.70 dB/MHz for BUA, and 97,49±17,99 for QUI (14) T scores <-1 were proposed as osteopenia or osteoporosis.

**Statistical Analyses**

Continuous variables compatible with normal distribution were described as mean values and standard deviation and were compared with t-test; those that are not compatible with normal distribution [age, 25 (OH)D, PTH] were given as median and interquartile ranges 25 and 75 (IQR 25 and 75) values, and were compared with Mann-Whitney U test. Categorical variables were compared with Pearson $X^2$. Pearson's correlation coefficients were computed to explore the relationship between measured continuous variables [e.g. 25(OH)D, PTH, body mass index, calcium, phosphorus, etc.). Normality distribution was computed with Kolmogorov-Smirnov test.

With the assumption of the prevalence of vitamin D deficiency as 30% in the elderly, a sample size power calculation indicated that 251 participants were sufficient to perform the study with a power of 99% and an alpha error of 5%. A p-value of <0.05 was considered to be significant for two-tailed tests. SPSS software v.13.0 (SPSS, Chicago, IL) was used for all statistical calculations.

**Ethics**

The study was approved by the local ethics committee and informed consent was obtained from the subjects prior to participation.

## Results

During the study period, 251 elderly and 301 reproductive-aged women found to be eligible for the study. The demographic and anthropometrical characteristics, laboratory values, and quantitative ultrasound measurements of the both groups are given in Table 1. The elderly women were shorter, heavier, more obese, and with higher fat content of body weight, compared to the younger women group. Although the SES was similar in the groups, due to the higher SCS, the SUS was slightly lower in the elderly group. However, this did not cause a difference neither in serum 25(OH)D, nor in serum calcium levels. On the other hand, serum PTH and ALP levels were higher in the elderly, and all of the quantitative ultrasound measurements (speed of sound, broad band ultrasonic attenuation, and quantitative ultrasound index) were lower in the elderly.

Vitamin D insufficiency prevalence was similar in both groups. It was 78.7% in the elderly, and 81.7% in the reproductive-aged women group (Table 2). However, the prevalence of secondary hyperparathyroidism, defined as elevation of PTH above the upper limits of normal range, was 28.7% in the elderly, whereas it was 15.3% in the younger group. The frequency of osteopenia was obviously higher in the elderly group (Table 2).

Serum 25(OH)D levels correlated with SES and SUS. On the other side, serum PTH levels correlated well with age, BMI, and fat mass. The laboratory parameters associated with calcium, phosphorus and bone metabolism were correlated with serum PTH levels, instead of 25(OH)D levels. ALP positively, whereas

Table 1. Demographic and anthropometrical characteristics of the elderly (≥ 65years) and the younger (20-40 years old) populations (n=552)

| | 20-40 years (n=301) | ≥65 years (n=251) | p-value |
|---|---|---|---|
| **Demograhic features** | | | |
| Age (years) | 35 (29-39) | 67 (65-70) | <0.001 |
| Height (cm) | 155.5 ± 5.7 | 150.3±5.9 | <0.001 |
| Body Weight (kg) | 67.2±12.7 | 71.9±12.7 | <0.001 |
| BMI (kg/m$^2$) | 27.8±4.9 | 31.8±4.8 | <0.001 |
| Body Fat (%) | 23.5±9.0 | 29.2±8.7 | <0.001 |
| SES | 2.37± 0.94 | 2.39±0.89 | 0.649 |
| SCS | 2.82±0.89 | 3.12±0.75 | 0.001 |
| SUS | 1.00±0.79 | 0.88±0.72 | 0.046 |
| **Laboratory** | | | |
| Calcium (mg/dl) | 9.4 ±0.7 | 9.5±0.6 | 0.100 |
| Phosphorus (mg/dl) | 3.6±0.6 | 3.7±0.6 | 0.151 |
| 25 (OH)D (ng/ml) | 18.6 (13.2-26.4) | 16.8 (11.5-26.5) | 0.070 |
| PTH (pg/ml) | 38.9 (26.1-55.4) | 49.4 (36.2-72.9) | <0.001 |
| ALP (U/L) | 121.2±39.0 | 160.4±45.0 | <0.001 |
| Calcium-phosphorus product | 34.5±8.4 | 35.9±6.3 | 0.053 |
| **Calcaneal ultrasonography** | | | |
| BUA | 79.0±16.8 | 64.2±20.8 | <0.001 |
| tBUA | 0.15±1.00 | -0.74±1.21 | <0.001 |
| QUI | 103.1±17.8 | 84.1±21.7 | <0.001 |
| tQUI | 0.31±0.99 | -0.75±1.20 | <0.001 |
| SOS | 1564±38 | 1533±35 | <0.001 |
| tSOS | 0.40±1.02 | -0.63±1.24 | <0.001 |

BMI: Body Mass Index; SES: Sunlight exposure score; SCS: Skin covering score; SUS: Sunlight utilization score; SOS: Speed of sound; BUA: broad band ultrasonic attenuation; QUI: quantitative ultrasound index; ALP: alkaline phosphatase.

Table 2. Prevalences of vitamin D deficiency, secondary hyperparathyroidism, osteopenia measured with calcaneal quantitative ultrasonography in the elderly (≥65 years old) and in the younger groups (20-40 years old)

| Vitamin D status | The younger (n=301) (%) | The elderly (n=251) (%) | p-value |
|---|---|---|---|
| Serum 25 (OH) D3 levels | | | |
| Sufficient (>30 ng/ml) | 18.3 | 21.3 | |
| Insufficient (20-29.9 ng/ml) | 25.6 | 20.1 | |
| Deficient (10-19.9 ng/ml) | 46.1 | 43.7 | 0.153 |
| Severe deficient (<10 ng/ml) | 10.0 | 14.9 | |
| Secondary hyperparathyroidism | 15.3 | 28.7 | <0.001 |
| Osteopenia (t≤-1,SOS) | 7.1 | 44.7 | <0.001 |
| Osteopenia (t≤-1,BUA) | 10.6 | 43.4 | <0.001 |
| Osteopenia (t≤-1,QUI) | 7.0 | 46.9 | <0.001 |

SOS: Speed of sound; BUA: broad band ultrasonic attenuation; QUI: quantitative ultrasound index;

calcium-phosphorus product and all calcaneal quantitative ultrasound measurements were negatively correlated with serum PTH levels. Serum 25(OH)D levels were inversely associated with serum PTH levels, as well (Table 3).

## Discussion

This study demonstrates an endemic of vitamin D deficiency in a Turkish female population, affecting both the reproductive-aged and the elderly women. The prolonged vitamin D deficiency beginning at young adulthood predisposes to secondary elevation of PTH level that is, at least, contributing to cortical bone loss seen in postmenopausal period.

We measured serum 25(OH)D levels in March, which reflects the vitamin D status in winter. We found the prevalence of vitamin D insufficiency to be 78.7% in the elderly and 81.7% in the reproductive-aged women. Moreover, 58.6% of the elderly and 56.1% of the younger women were vitamin D-deficient. Our results in both the elderly and younger women are consistent with the results of epidemiological studies reported from the United States, Latin America, Canada, and many European and Asian countries (15-20).

Since serum 25(OH)D levels were similar in both the reproductive-aged and elderly women and secondary hyperparathyroidism was obviously more prevalent in the elderly population, our results suggest that elderly women presumably are more susceptible to vitamin D deficiency, which susceptibility may result in rapid bone loss. Elevated ALP levels in the elderly also suggest increased bone turnover associated with increased PTH action. Garnero et al. have reported that serum levels of bone ALP in the highest quartile were associated with an RR of fracture of 2.4, while increased levels of intact parathyroid hormone were moderately associated with an increased risk of fracture. The mechanism by which some postmenopausal women have an increased rate of bone turnover leading to an increased risk of fracture remains to be elucidated (21). Whatever the mechanisms are, epidemiological studies have demonstrated that calcium and vitamin D supplementation along with physical activity, and fall prevention are the first line in fracture prevention (22). Our results imply the importance of vitamin D supplementation in our study population.

Table 3. Correlations of demographic, anthropometric and laboratory parameters with serum 25(OH)D and PTH levels

| | 25 (OH) D | | PTH | |
|---|---|---|---|---|
| | R | p-value | R | p-value |
| **Demographic and anthropometrical features** | | | | |
| Age (years) | 0.025 | 0.562 | 0.237 | <0.001 |
| BMI (kg/m$^2$) | -0.057 | 0.187 | 0.212 | <0.001 |
| Fat mass (kg) | -0.037 | 0.400 | 0.199 | <0.001 |
| Fat mass (%) | -0.027 | 0.531 | 0.217 | <0.001 |
| SES | 0.140 | 0.001 | 0.017 | 0.690 |
| SCS | -0.103 | 0.018 | 0.109 | 0.012 |
| SUS | 0.157 | <0.001 | -0.071 | 0.102 |
| **Laboratory and ultrasonography parameters** | | | | |
| Calcium-phosphorus product | 0.014 | 0.765 | -0.127 | 0.006 |
| ALP | -0.069 | 0.115 | 0.141 | 0.001 |
| 25(OH)D | - | - | -0.163 | <0.001 |
| PTH | -0.163 | <0.001 | - | - |
| tSOS | -0.039 | 0.376 | -0.112 | 0.010 |
| tBUA | -0.027 | 0.533 | -0.062 | 0.152 |
| tQUI | -0.034 | 0.427 | -0.093 | 0.031 |

The major cause of vitamin D insufficiency in our population is the decreased sunlight utilization in both the elderly and reproductive–aged women, mainly due to increased skin covering and decreased sunlight exposure. Obesity seems to be another important problem that lead to decreased bioavailability of vitamin D. National health policies should consider education of the public on importance of vitamin D for bone health and overall well-being. In high risk populations, simple supplementation for all women may also be considered.

Quantitative ultrasound (QUS) may offer an attractive possible alternative to the central dual-energy X-ray absorptiometry (DEXA) assessment, because it is radiation-free, relatively cheap and easily transportable (23). It may reflect not only bone density, but also other qualitative properties of bone (elasticity, structure, micro-architecture) that are strictly related to bone strength (24). When evaluating the QUS measurements of our sample populations, we assumed all women with T values ≤-1 as osteopenic or osteoporotic, using the World Health Organization criteria for DEXA measurements as a model. Using the QUS parameters, the frequency of osteopenia/osteoporosis in our elderly population reached almost 50%, whereas it was only 7.0% in the reproductive-aged study population. Frost et al. reported similar results in the elderly, using both the QUS and bone mineral density, in their study population of 549 postmenopausal women without risk factors in the United Kingdom (25). Recently, even a higher prevalence of osteopenia/osteoporosis has been reported in a study of 84 postmenopausal women without any risk factors for osteoporosis (26). The difference in frequency of osteopenia/osteoporosis between our elderly and younger women group may be a consequence of multiple factors, such as aging, and decreased serum estrogen levels. However, the contribution of secondary hyperparathyroidism-associated vitamin D insufficiency cannot be ignored since PTH was higher in the elderly compared to the younger study population, and laboratory and ultrasound measurements, i.e. ALP, BUA, SOS, and QUI correlated with PTH, as well.

Some limitations of our study should be noted. Firstly, this was a cross-sectional study, and it did examine the influence of vitamin D status on bone metabolism indirectly. However, it was a population-based study, and the participation was satisfying to make a conclusion regarding the vitamin D status of the studied area. Secondly, since the elderly group was postmenopausal, and the younger group was premenopausal, the net influence of vitamin D itself on bone metabolism cannot be predicted.

In conclusion, vitamin D insufficiency and even deficiency seem to be endemic in both the elderly and the reproductive-aged women living in Ankara, and this problem needs further attention.

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