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Relation between carotid intima media thickness and vitamin D in hypertension.

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Abstract

Purpose: Subclinical atherosclerosis defined as endothelial dysfunction, coronary calcification, and increased carotid intima media thickness is related to cardiovascular events independent from blood pressure. There are data showing possible relation between low vitamin D levels and subclinical atherosclerosis. In this study we aimed to find out the relation between vitamin D level and intima media thickness and the presence of atherosclerotic plaques.

Materials and methods: Fifteen male and 148 female subjects with essential hypertension aged between 30-76 were included to the study. Intima media thickness was measured and the presence of plaque was evaluated by real time B mode ultrasonography (MyLab 70 XVG, Esaote SpA, Genoa, Italy) using 4.0-13.0 MHz linear probe. Serum parathormone was measured by chemiluminiscence immunoassay and 25 OH vitamin D level by radioimmunassay.

Results: Eighty patients (49%) had plaques. Seventy three patients (45%) had severe vitamin D deficiency defined as level below 10 ng/ml and 64 (39%) had insufficiency, (10-20 ng/ml). Vitamin D levels were similar in plaque +ve and –ve groups (p=0.44). Intima media thickness was positively correlated with age (r=0.399, p=0.0001), fasting glucose (r=0.165, p=0.036), and Hemoglobin A1c (r=0.384, p=0.002). There was no correlation between intima media thickness and vitamin D level (p=0.75) and LDL (p=0.581).

Conclusion: We did not find any relation between vitamin D level andintima media thickness in hypertensive subjects. The lack of significance may be due to high prevalence of vitamin D deficiency.

Keywords: Vitamin D, Hypertension, Subclinical atherosclerosis.

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Introduction

High blood pressure is associated with increased risk of cerebrovascular disease and coronary artery disease [1]. Hypertension leads to arterial and arteriolar sclerosis via endothelial cell changes and remodelling of smooth muscle cells underlining endothelium [2]. As a result target organ damage ensues. Subclinical atherosclerosis is defined as endothelial dysfunction, coronary calcification, and increased carotid intima media thickness (IMT).IMT is related to cardiovascular events independent from conventional vascular risk factors including blood pressure [3].

Increased IMT and plaque formation are biologically and genetically distinct entities [4]. IMT is mainly caused by hypertensive medial hypertrophy and weakly associated with traditional coronary risk factors. IMT is more predictive of stroke than of myocardial infarction. On the contrary plaque formation is more strongly associated with traditional risk factors and is more predictive of myocardial infarction than of stroke [5]. It was shown that after adjustment for age, gender, blood pressure, cholesterol, smoking, diabetes mellitus (DM), and treatment of lipids and blood pressure, patients in the top quartile of plaque area had 3.5 times the risk of those in the lowest quartile [5].

Plaques grow along the carotid arteries 2-4 times faster than they thicken [4]. Both calcified and non-calcified plaques are independent predictors of vascular disease at all ages. Measurement of IMT is a non-invasive, simple, reliable, and safe method in detecting subclinical atherosclerosis [3]. IMT is measured in vascular segments free of plaque [4].

Beyond established cardiovascular risk factors epidemiologic studies indicate that vitamin D deficiency is an independent risk factor for cardiovascular events [6-8].

Similarly, there are data showing possible relation between low vitamin D levels and subclinical atherosclerosis [6,9]. Vitamin D (vitamin D) receptors are expressed by endothelial cells and vascular smooth muscle cells [9].

Low vit D level also activates renin angiotensin system (RAS) that is upregulated in essential hypertension [6,10]. Although some data favours the role of vitamin D in subclinical atherosclerosis, the relation has not been established yet.

In this study we aimed to find out the relation between 25 hydroxy (OH) vitamin D level and subclinical atherosclerosis (IMT and atherosclerotic plaques) in hypertensive patients.

Materials and Methods

A total number of 176 patients (15 male and 161 female subjects) with essential hypertension aged between 30-76 were included to the study. The patients were already on hypertensive medication.

Secondary hypertension was excluded in case of clinical suspicion (such as age and resistant hypertension). Neither of patients were hypokalemic even some of them were on diuretic therapy. None of the patients were on steroid medication. The patients with any known or suspected metabolic bone disease except osteoporosis and vitamin D deficiency were excluded. History of coronary artery disease (established by angiography, nuclear scanning, suspicous ECG, and angina pectoris), cerebrovascular disease, transient ischemic attack, peripheral artery disease, chronic liver disease, collageneous tissue disease, and type 1 DM were other exclusion criteria.

Serum lipid levels, urea, creatinine, sodium, potassium, *alanine aminotransferase* (ALT) values, total albümin, calcium, hosphorus, and haemoglobin A1c measured by photometric method using autoanalyzer (Siemens, Advia 1800) within preceding year were documented. After an overnight fast venous blood sample was studied for serum PTH by chemiluminiscence immunassay (Siemens, Advia 1800, Centour XP). TSH and 25 OH vitamin D were also studied using chemiluminiscence immunassay (Siemens, Advia 1800).

Corrected calcium level was calculated according to the formula

[0.8*(4.0-patient's albumin)]+patient's serum calcium

The subjects with corrected calcium above normal level, any biochemical and clinical suspicion of parathyroid adenoma were excluded.

Parathormone (PTH) begins to rise as glomerular filtration rate (GFR) falls below 60 mL/min. Therefore GFR was calculated according to the MDRD formula [11]. GFR lower than 30 ml/min were excluded.

IMT was measured and the presence of plaque was evaluated by real time B mode ultrasonography (MyLab 70 XVG, Esaote SpA, Genoa, Italy) using 4.0-13.0 MHz linear probe. All ultrasonographic assessment was done by the same experienced radiologist who was blind to all data but hypertension. Standard procedure was supine position, taking many longitudinal and transverse planes of carotid arteries till getting the best image. The measurement of common carotid artery and internal carotid artery was done 10 mm proximal and 10 mm distal to the bifurcation free of plaque respectively. The distance from the media-adventitia interface to lumen-intima was measured. The arithmetic mean value of right and left measurements was denoted as mean IMT. Atherosclerotic plaque was defined as intima-media thickening over 1 mm or doubles that of the adjacent vascular segment [12].

The study protocol was approved by local ethics committee and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Statistics

SPSS version 10.0 was used for statistical analysis. All parametric variables showing normal distribution excluding diabetes duration, hypertension duration, fasting glucose, TSH, 25 OH vitamin D, HDL, CIMT were evaluated with Student's t test using. The other variables not showing normal distribution were evaluated with Mann Whitney U test. Correlation analysis between CIMT and other variables was done using Pearson correlation analysis. The parametric values were given as mean and standard deviation. Chi square test was done for nonparametric variables. P below 0.05 was considered statistically significant.

Results

Eighty seven patients (49%) had plaques. There was not a side predilection for plaque formation (25 on the right side, 30 on the left, and 32 bilateral). The laboratory data and characteristics of plaque +ve and –ve patients are summarized in Table 1.

Table 1. *Demographic data and laboratory values of patients classified according to the presence of plaques.*

	Plaque (+)	Plaque (-)	P
Age (years)	62.07 ± 7.69	55.17 ± 7.99	0.0001
Gender (F/M)	81/6	80/9	0.44
Duration of HT (years)	9.16 ± 7.22	6.51 ± 5.84	0.008
DM (n)	31	23	0.15
Duration of DM (years)	7.41 ± 6.73	6.17 ± 5.04	0.46
History of smoking (n)	13	26	0.04
BMI (kg/m^2)	32.31 ± 5.10	33.12 ± 6.84	0.37
Obesity (BMI ≥ 30 kg/m^2) (n)	58	54	0.46
Fasting glucose (mg/dL)	117.87 ± 57.04	114.84 ± 69.49	0.89
HbA1c (%) (n=35)	7.67 ± 1.83	7.88 ± 2.29	0.63
Cr (mg/dL)	0.82 ± 0.21	0.78 ± 0.17	0.13
K (meq/L)	4.66 ± 0.46	4.50 ± 0.33	0.04
Corrected Ca (mg/dL)	9.37 ± 0.31	9.38 ± 0.33	0.90
P (mg/dL)	3.49 ± 0.44	3.51 ± 0.54	0.94

ALP (U/L)	82.23 ± 22.25	86.01 ± 33.76	0.35
TSH (mU/L)	4.14 ± 10.05	1.92 ± 1.56	0.04
TSH (mU/L)*	2.74 ± 3.40	1.92 ± 1.56	0.05
PTH (pg/mL)	72.15 ± 34.57	78.62 ± 35.10	0.30
25 OH D vit (ng/mL)	13.34 ± 6.87	14.07 ± 7.10	0.41
LDL (mg/dL)	128.20 ± 34.45	123.52 ± 34.90	0.60
HDL (mg/dL)	51.49 ± 11.58	50.49 ± 10.01	0.51
Triglyceride (mg/dL)	163.92 ± 64.47	159.59 ± 74.36	0.74
Vit D sufficiency** (n)	13	15	0.72
MDRD (mL/min)	79.61 ± 20.03	87.84 ± 24.44	0.01
Mean IMT (mm)	0.73 ± 0.14	0.64 ± 0.11	0.0001

*Extreme values were deleted **25 OH D vit>20 ng/mL.

DM: Diabetes Mellitus; HT: Hypertension; BMI: Body Mass Index; HbA1c: Haemoglobin A1c; Cr: Creatinine; K: Potasssium; Ca: Calcium; P: Phosphorus; ALP: Alkaline Phosphatase; TSH: Thyroid Stimulating Hormone; PTH: Parathormone; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; 25 OH D vit: 25 Hydroxy Vitamin D3; MDRD: Glomerular Filtration Rate Calculated According to Modification of Diet in Renal Disease Study; IMT: Intima Media Thickness of Carotid Artery.

Plaque +ve patients were older than plaque –ve ones (p=0.0001). Gender distribution was similar in both groups (female: 81 in plaque +ve and 80 in plaque-ve group; p=0.44). Plaque +ve patients had longer duration of hypertension (p=0.008). The number of patients receiving ACEI/ARB, statin, calcium channel blocker, diuretic, and calcium-vitamin D were not different between plaque +ve and –ve groups.

There was no statistically significant difference between plaque +ve and –ve groups in terms of frequency of DM (p=0.15) and mean duration of DM (p=0.46). Vitamin D levels were similar in both groups (p=0.41). Plaque +ve patients had higher CIMT as expected (p=0.0001).

Mean PTH, 25 OH D vitamin, ALP, calcium corrected for albumin, phosphorus, fasting glucose, haemoglobin A1c, LDL, HDL, and triglyceride levels were similar between plaque +ve and –ve groups. Although mean creatinine was similar between two groups (p=0.13), MDRD was significantly lower in plaque +ve group (p=0.01).Plaque +ve patients had higher TSH level (p=0.04) even when extreme values were deleted and comparative statistics were redone (p=0.05).

Sixty six patients had GFR above 90 ml/min, 88 had between 60-89 ml/min, and 22 had between 31- 59 ml/min. IMT and vitamin D level was similar between MDRD stages.

IMT was positively correlated with age (r=0.399, p=0.0001), fasting glucose (r=0.165, p=0.036), HbA1c (r=0.384, p=0.002), and negatively correlated with MDRD (r=-0.148, p=0.05) (Table 2). There was no correlation between vitamin D level (p=0.75) and LDL (p=0.581).

Table 2. *Correlation analysis between IMT and daemographic and laboratory data.*

	Mean IMT (mm)	
	R	P
Age (years)	0.399	0.0001
Duration of HT (years)	0.650	0.411
Duration of DM (years)	0.153	0.279
BMI (kg/m^2)	0.006	0.938
Fasting glucose(mg/dL)	0.165	0.036
HbA1c (%)	0.384	0.002
Cr (mg/dL)	0.118	0.133
Na(meq/L)	-0.068	0.390
K (meq/L)	0.105	0.188
Albumin(g/dL)	-0.037	0.638
Corrected Ca(mg/dL)	-0.037	0.641
P (mg/dL)	0.137	0.081
HDL (mg/dL)	0.060	0.469
LDL (mg/dL)	-0.046	0.581
Triglyceride (mg/dL)	0.160	0.055
ALP (U/L)	0.112	0.195
TSH (mU/L)	0.061	0.441
PTH (pg/mL)	-0.076	0.334
25 OH D vit (ng/mL)	0.025	0.750
MDRD (mL/min)	-0.148	0.050

*Extreme values were deleted **25 OH D vit>20 ng/mL.

DM: Diabetes Mellitus; HT: Hypertension; BMI: Body Mass Index; HbA1c: Haemoglobin A1c; Cr: Creatinine; K: Potasssium; Ca: Calcium; P: Phosphorus; ALP: Alkaline Phosphatase; TSH: Thyroid Stimulating Hormone; PTH: Parathormone; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; 25 OH D vit: 25 Hydroxy Vitamin D3; MDRD: Glomerular Filtration Rate Calculated According to Modification of Diet in Renal Disease Study; IMT: Intima Media Thickness of Carotid Artery.

Eighty patients (45.4%) had severe vitamin D deficiency defined as level below 10 ng/ml and 68(38.6%) had insufficiency, (10-20 ng/ml). Twenty eight (16%) patients were vitamin D competent although only 8 (4.5%) had optimal level. IMT did not differ significantly according to D vitamin status (p=0.99). Vitamin D deficient patients had significantly higher A1c level when compared to vitamin D competent ones (p=0.04). Vitamin D competent patients had lower BMI compared to Vitamin D deficient ones (p=0.028). Albumin levels were significantly lower in Vitamin D deficient patients in comparison to Vitamin D insufficient (p=0.039) and vitamin D competent ones (p=0.022). But total calcium level corrected for albumin showed no difference between D vitamin groups.

Discussion

Subclinical atherosclerosis documented by increased IMT predicts future cardiovascular events [3]. Hypertension, smoking, high LDL cholesterol, and impaired glucose

metabolism are conventional cardiovascular risk factors. IMT increases with age [13,14].

In our study IMT was positively correlated with age and plaque +ve patients were older than plaque-ve ones. The plaque +ve subjects had longer duration of hypertension (p=0.008). Our data supports the literature showing positive relation between duration of hypertension in years and increased IMT [15-17].

High LDL and triglyceride and low HDL contribute to plaque formation. In ARIC study it was shown that IMT was strongly associated with atherogenic lipids, smoking, and hypertension [14].

In our study lipid fraction levels were similar between plaque +ve and –ve groups. The number of patients on statin therapy was not different between plaque +ve and –ve groups (n=0.26). Neither IMT was correlated with LDL level (p=0.581). This may indicate that there are factors other than lipid levels (residual risk factors) and statin usage affecting plaque formation. There was no correlation between vitamin D level (p=0.75) and LDL (p=0.581).

Smoking is a well-established contributing factor in atherosclerotic vascular disease. In our study both current and past smokers constituted 22% of subjects. Plaque +ve patients had lower frequency smoking (both current and past smoking). This finding is also contradictory to ARIC study [14].

IMT also increases in diabetes mellitus [18]. In our study IMT was positively correlated with fasting glucose (r=0.165, p=0.036) and HbA1c (r=0.384, p=0.002) (Table 2). But plaque +ve and –ve groups were not different in terms of presence and duration of DM (p=0.15 and p=0.46, respectively). We also failed to find statistically significant difference in terms of fasting glucose and A1c (p=0.63 and p=0.89, respectively). Although DM is a contributing factor in plaque formation, we did not find any relation between DM and plaque formation.

Even extreme TSH values were extracted plaque +ve patients had higher TSH values. IMT may decrease with LT4 replacement in subclinical hypothyroidism defined as normal TSH level with normal free T4 and T3 levels [19].

The decrement was observed in patients with no established cardiovascular risk factors under age 55 and accompanied improvement of lipid profile. On the other hand, vascular smooth muscle cells express iodo thyronine deiodinase type II. Effect of TSH may be beyond improvement of the lipid profile. The increase in IMT reaches significant values at TSH levels above 10 mIU/l [20].

Impaired lipid profile increased blood pressure accompanies subclinical hypothyroidism and may be responsible for increased IMT [20].

Vitamin D deficiency is defined as levels below 20 ng/ml though optimal level is over 30-32 ng/ml for many of the physiologic functions [21]. We detected high frequency of vitamin D deficiency. Only 20.5% of the patients were vitamin D competent (>20 ng/ml). In most of the cohort studies the frequency of vitamin D deficiency is 52-77% when the cut off level is 30 ng/ml [10]. The prevalence of vitamin D deficiency is about 44-60% in Turkey (Vitamin D status and bone mineral density of veiled and unveiled Turkish women [22-24].

In a study done in 254 patients in South part of Turkey showing low socioeconomic status, the frequency of vitamin d deficiency was 94% when 20 ng/ml was taken as cut off level (unpublished data, poster presentation in Turkish Endocrinology and Metabolic Diseases Congress, 2010, Antalya). Also a large scale (n=9560) study evaluating vitamin D status in Turkey, high prevalence (93%) of vitamin D deficiency (<20 ng/ml) was compatible with our results [25].

Mean BMI was over 30 kg/m^2 in plaque +ve and –ve groups. Vit D competent patients had lower BMI compared to Vitamin D deficient ones (p=0.028). Published data indicate vitamin D is lower in obese patients. It is suggested that lipid soluble vitamin D is deposited in adipose tissue. The reason of low vitamin D levels in obese patients may be beyond this simple explanation. Gap junctional communications between osteoblastic progenitors may cause mesenchymal switch to adipogenesis [26]. Animal studies show vitamin D inhibits adipogenesis and induces osteoblastogenesis [26].

In the literature both high and low levels of 25 OH vitamin D are associated with coronary artery disease [6]. Vitamin D may suppress vascular smooth muscle cell proliferation by inhibiting cyclin-dependent kinase-2 activity [6]. High vitamin D level is blamed for arterial calcification. We did not find any relation neither between vitamin D level and IMT nor between vitamin D and plaque formation in hypertensive subjects. The lack of significance may be due to high prevalence of vitamin D deficiency. In a paper published from Turkey, no relation was detected between vitamin D level and plaque type or IMT in hypertensive patients. But vitamin D levels were much higher than ours [27]. In another study an inverse relation was found between vitamin D level and IMT in hypertensive subjects. The modest but significant effect of vitamin D on systolic blood pressure was mediated by increased intima media thickness and endothelial dysfunction [28].

In conclusion we suggest that increased IMT and plaque formation may differ regarding pathogenesis. Only age and decreased MDRD are common risk factors for both increased IMT and plaque formation. While duration of hypertensive injury and smoking facilitates plaque formation, impaired glucose metabolism adversely affects IMT. Serum vitamin D levels do not appear to play a role in subclinical atherosclerosis.

References

1. World Health Report 2002. Reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organization 2002.
2. Kaplan NM. Clinical hypertension Williams & Wilkins, Baltimore (USA), 1998.
3. Lorenz MW, Lorenz MW, von Kegler S, Steinmetz H, Markus HS, Sitzer M. Carotid intima-media thickening indicates a higher vascular risk across a wide age range:

prospective data from the Carotid Atherosclerosis Progression Study (CAPS) Stroke 2006; 37: 87-92.

4. Spence JD. Measurement of intima-media thickness vs. carotid plaque: uses in patient care, genetic research and evaluation of new therapies. Int J Stroke2006; 1: 216-221.
5. Spence J. Technology insight: ultrasound measurement of carotid plaque—patient management, genetic research, and therapy evaluation. Nat Clin Pract Neurol 2006; 12: 611-619.
6. Lim S, Shin H, Kim MJ; Ahn HY, Kang SM, Yoon JW, Choi SH, Kim KW, Song JH, Choi SI, Chun EJ, Shin CS, Park KS, Jang HC. Vitamin D effects endothelium in terms of calcium deposition and increased coronary artery calcification score. J Clin Endocrinol Metab 2012; 97: 169-178.
7. Kilkkinen A, Knekt P, Aro A, Rissanen H, Marniemi J, Heliövaara M, Impivaara O, Reunanen A. Vitamin D status and the risk of cardiovascular disease death. Am J Epidemiol 2009; 170: 1032-1039.
8. Elamin MB, Abu Elnour NO, Elamin KB, Fatourechi MM, Alkatib AA, Almandoz JP, Liu H, Lane MA, Mullan RJ, Hazem A, Erwin PJ, Hensrud DD, Murad MH, Montori VM. Vitamin D and cardiovascular outcomes: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2011; 96: 1931-1942.
9. Reynolds JA, Haque S, Berry JL, Pemberton P, Teh LS, Ho P, Gorodkin R, Bruce Ian N. 25-hydroxyvitamin D deficiency is associated with increased aortic stiffness in patients with systemic lupus erythematosus. Rheumatology 2012; 51: 544-551.
10. Forman JP, Giovannucci E, Homes D, Bischoff-Ferrari HA, Tworoger SS, Willett WC, Curhan GC. Plasma 25-hydroxyvitamin D levels and risk of incident hypertension. Hypertension 2007; 49: 1063–1069.
11. Modification of Diet in Renal Disease Study Group. A more accurate accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Ann Intern Med 1999; 130: 461-470.
12. Mutluay R, Deger SM, Bahadir E, Durmaz AO, Citil R, Sindel S. Uric acid is an important predictor for hypertensive early atherosclerosis. Adv Ther 2012; 29: 276-286.
13. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: The Muscatine Study. Circulation. 2001; 104: 2815-2819.
14. Howard G, Sharrett AR, Heiss G, Evans GW, Chambless LE, Riley WA, Burke GL. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. Stroke 1993; 24: 1297-1304.
15. Su TC, Lee YT, Chou S, Hwang WT, Chen CF, Wang JD. Twenty-four-hour ambulatory blood pressure and duration of hypertension as major determinants for intima-media thickness and atherosclerosis of carotid arteries. Atherosclerosis 2006; 184: 151-156.
16. Zanchetti A, Bond MG, Hennig M, Neiss A, Mancia G, Dal Palù C, Hansson L, Magnani B, Rahn KH, Reid J, Rodicio J, Safar M, Eckes L, Ravinetto R. Risk factors associated with alterations in carotid intima-media thickness in hypertension: baseline data from the European Lacidipine Study on Atherosclerosis J Hypertens 1998; 16: 949-961.
17. Catena C, Colussi G, Brosolo G, Sechi LA. A prothrombotic state is associated with early arterial damage in hypertensive patients. J Atherosler Thromb 2012; 19: 471-478.
18. Folsom AR, Eckfeldt JH, Weitzman S, Ma J, Chambless LE, Barnes RW, Cram KB, Hutchinson RG. Relation of carotid artery wall thickness to diabetes mellitus, fasting glucose and insulin, body size, and physical activity. Atherosclerosis Risk in Communities (ARIC) Study Investigators. Stroke 1994; 25: 66-73.
19. Monzani F, Caraccio N, Kozàkowà M, Dardano A, Vittone F, Virdis A, Taddei S, Palombo C, Ferrannini E. Effect of levothyroxine replacement on lipid profile and intima-media thickness in subclinical hypothyroidism: a double-blind, placebo- controlled study. J Clin Endocrinol Metab. 2004; 89: 2099-2106.
20. Gao N, Zhang W, Zhang YZ, Yang Q, Chen SH. Carotid intima-media thickness in patients with subclinical hypothyroidism: a meta-analysis.Atherosclerosis. 2013; 227: 18-25.
21. Binkley N, Ramamurthy R, Krueger D. Endocrinol Metab Clin N Am 2010; 39: 287–301.
22. Guzel R, Kozanoglu E, Guler-Uysal F, Soyupak S, Sarpel T. Vitamin D status and bone mineral density of veiled and unveiled J Womens Health Gend Based Med 2001; 10: 765-770.
23. Basaran S, Guzel R, Coskun-Benlidayi I, Guler-Uysal F. Vitamin D status: effects on quality of life in osteoporosis among Turkish women. Qual Life Res 2007; 16: 1491-1499.
24. Güler T, Sivas F, Başkan BM, Günesen O, Alemdaroğlu E, Ozoran K. The effect of outfitting style on bone mineral density Rheumatol Int 2007; 27: 723-727.
25. Satman I, Ozbey NC, Boztepe H, Kalaca S, Omer B, Tanakol R, Genc S, Alagol F, on behalf of the TURDEP-II Study Group. Prevalence and of vitamin D deficiency and associated factors in Turkey. Endocrine Abstracts 2013: P135.
26. Bartl R, Frisch B. Osteoporosis. In: Bartl R, Frisch B (eds). Calcium and vitamin D. 2nd edition.Berlin Heidelberg: Springer Verlag; 2009: 111-117.
27. Satilmis C, Celik O, Biyik I, Ozturk D, Celik K, Akin F, Ayca B, Yalcin B, Dagdelen S. Associaiton between serum vitamin D levels and subclinical coronary atherosclerosis and plaque burden/composition in yound adult population. Bosn J Basic Med Sci 2015; 15: 67-72.
28. Puldowski P, Jaworski M, Niemirska A, Litwin M, Szalecki M, Karcmarewicz E, Michalkiewicz J. Vitamin D status, body composition and hypertensive target organ damage in

primary hypertension. J Steroid Biochem Mol Biol 2014; 144: 180-184.

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