



## THE RELATIONSHIP BETWEEN THE MANDIBULAR BONE QUALITY ASSESSED BY DIGITAL PANORAMIC RADIOGRAPHY AND SERUM BIOLOGICAL PARAMETERS IN PATIENTS PLANNING DENTAL IMPLANT SURGERY

### ABSTRACT

**Objectives:** The aim of this study was to evaluate the bone density of the implant site with panoramic radiomorphometric parameters [mandibular cortical index (MCI), mental index (MI)], and to investigate the relationships between bone density, vitamin D, HDL, and LDL.

**Materials and Methods:** Forty patients with mandibular first molar or second molar tooth deficiency who had undergone implant surgery were included in the study. Blood samples and panoramic MCI and MI parameters were used to evaluate mandibular bone density. Data were analyzed using the Mann-Whitney U and Kruskal-Wallis tests. The relationships between MI and the study variables were assessed by Spearman's correlation coefficient. The Chi-square or Fisher's exact tests were used to determine the relationships between MCI and the study variables.  $p < 0.05$  was considered statistically significant.

**Results:** There were significant weak positive correlations of MI with Vitamin D and LDL ( $r = 0.329$ ,  $p = 0.038$ ;  $r = 0.341$ ,  $p = 0.031$ ). Vitamin D, LDL, and HDL measurements were not statistically different among the MCI groups ( $p=0.100$ ,  $p=0.119$ ,  $p=0.840$ , respectively).

**Conclusions:** Vitamin D level may carry importance in addition to radiographic and clinical parameters; thus, patients should be evaluated in this respect. Further studies involving larger patient groups are needed to conclude the relationship between vitamin D level and bone quality.

**Keywords:** Dental implant, bone remodeling, Vitamin D, HDL cholesterol, LDL cholesterol.

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## INTRODUCTION

Dental implant surgeries are the most common treatments in patients with missing teeth. The quality or density of the available bone is the most critical factor for success in implant surgeries. The bone density in the toothless region, treatment planning, the structure of the implant, surgical approach, healing time, and loading are the criteria that affect the loading process during the prosthetic stage. The alveolar bone structure of the implant drilling site defines the success of anchored endosseous implants. In the presence of a toothless crest, dense or porous cortical bone can be found on the outer surface of the bone, and sometimes the trabecular bone inside the cortical bone, whether the crest is thick or thin. While the cortical bone has the function of withstanding torsional loading and provides higher initial stability, cancellous bone is more abundant in vascular canals and thus, vasculature supplying mesenchymal progenitor cells. Therefore, it is essential to evaluate the bone quality and quantity in potential implant sites.<sup>1</sup> Accurate evaluation of the bone structure and planning of surgery before placement of the implant affect the success and survival rates of the implant.<sup>2</sup> Mandibular radiomorphometric parameters such as the Mandibular Cortical Index (MCI) and the Mental Index (MI) are used to evaluate the bone quality of the mandible.<sup>3,4</sup>

MCI classifies the visibility of the cortical bone at the lower edge of the mandible. MI is the amount of cortical bone thickness measured at the mental foramen region.<sup>5</sup> Although different reference ranges have been reported in various studies, it has been concluded that asymptomatic dental patients with an MI < 3 mm without osteoporosis might be referred for bone mineral density measurement and must be evaluated for osteoporosis risk.<sup>6</sup> These indices play critical roles in the identification and evaluation of patients with osteoporosis or low mineral density.<sup>5,7</sup> Qualitative and quantitative panoramic indices, including MCI, MI, and PMI (Panoramic Mandibular Index), are the measurements developed in order to evaluate the quality and quantity of mandibular bone density on panoramic radiographs and to identify the resorption points. MI is the best predictor of

reduced cortex width under the two mental foramina. Osteopenia can be defined by measuring the cortical thickness at the lower border of the mandible. Thin mandibular cortical width is a finding that shows reduced skeletal bone mineral density (BMD).<sup>7</sup> MCI shows the porosity of the mandible but is also associated with BMD.<sup>8</sup> MCI has been found to be useful in demonstrating osteoporosis.

One of the hypotheses of failure after implant or graft applications in recent years is the presence of underlying biological disorders affecting bone metabolism. There is evidence that LDL (low-density lipoprotein) cholesterol (dyslipidemia) slows bone metabolism or reduces the osseointegration of dental implants. It is also known that Vitamin D is the key to natural and acquired immunity and that both immunities are impaired in vitamin D deficiency. Therefore, vitamin D deficiency slows the osseointegration of the implant or increases the risk of graft infection.<sup>9,10</sup>

Today, the use of dental implants for rehabilitation of missing teeth is increasing day by day. In this parallel, complications of peri-implant tissues and implant failures have become more common. The most important criteria for implant success are the quantity and quality of the available bone. Therefore, it is crucial to evaluate factors that may negatively affect the density, quantity, quality, or metabolism of the bone before the procedure. In the present study, we evaluated the radiographic and biochemical parameters and posterior bone structure of patients who were planned to undergo implant surgery, and we think that this can help to prevent further possible complications. The aim of the study was to evaluate the bone density of the implant site with panoramic radiomorphometric indices and to investigate the relationships between bone density and biochemical parameters.

## MATERIALS AND METHODS

The study was conducted on patients aged 18-49 years who had undergone mandibular molar region implant surgery in the Department of Dentomaxillofacial Radiology of Baskent University Faculty of Dentistry. MCI and MI indexes were measured by three radiologists on digital panoramic radiographs. The study protocol

was conducted in full accordance with the Helsinki Declaration and was approved by Baskent University Institutional Review Board and Ethics Committee (Project no: D-KA18/21). Written informed consent was obtained from all subjects.

Panoramic radiographs were taken with the same device (Veraviewpocs 2D, Morita, Japan) and with the same technical parameters (64–66 kVp; 6–9 mA; 10 s and voxel size 0.08 mm<sup>3</sup>). Klemetti *et al.*<sup>7</sup> defined MCI as C1, C2, C3 according to the visibility of the mandibular cortical bone. Cortical bone thickness was measured at the site of mental foramen using Clearcanvas (Synaptive Medical, Toronto, Canada) program for MI. The standard magnification value of the panoramic device used in MI was 10%.

C1: Normal cortex, cortical bone on both sides regular and continuous,

C2: Moderately eroded cortex, half-moon defects, and stratification in cortical bone,

C3: Severely eroded cortex, extreme irregularity in cortical bone, and significant porosity. It was reported that the C3 category should be evaluated in terms of the risk of osteoporosis.<sup>6</sup>

LDL, HDL (high-density lipoprotein), and vitamin D levels in blood samples were obtained from patients who accepted implant surgery. In serum, the reference value for HDL cholesterol was between 35–55 mg/dL and for LDL cholesterol, <130 mg/dL. For 25-OH-cholecalciferol, reference value between 6.2–45.5 ng/mL was used.

Inclusion criteria for the study were as follows:

- 1) No drug or systemic disease affecting bone metabolism,
- 2) Missing teeth only in the first molar or second molar region of the mandible,
- 3) No periodontal disease,
- 4) No diagnosis of menopause.

### **Statistical Analysis**

Statistical analysis of the data was performed by SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented with mean  $\pm$  standard deviation and median (min-max) for continuous variables in accordance with the data distribution. Categorical variables were expressed as numbers and percentages. The distribution of normality of data for statistical test selection was examined by the Shapiro-Wilk test. Since parametric test assumptions were not met, Mental Index (MI) values in sex and smoking groups and Vitamin D, LDL, and HDL measurements in Mandibular Cortical Index (MCI) groups were compared using the Mann-Whitney U test. Mental index (MI) values were compared with the Kruskal-Wallis test in the tooth-loss year groups. The relationships between MI and tooth-loss year, Vitamin D, HDL, and LDL were investigated with Spearman's correlation coefficient according to data distribution. The relationships between MCI and gender, smoking, tooth-loss year, LDL, and HDL were investigated by Chi-square or Fisher exact test. The statistical significance level was considered as  $p < 0.05$ .

### **RESULTS**

In the present study, there were 14 (35%) females and 26 (65%) males. The mean age of the patients was  $38.8 \pm 5.90$  (23–49) years. The mean age of females was  $36.93 \pm 7.10$  (23–48) years, and the mean age of males was  $39.81 \pm 5$  (29–49) years. The mean ages of male and female patient groups were not statistically different ( $p = 0.143$ ). Eighteen (45%) of the patients reported smoking, while 22 (55%) stated that they did not smoke. Smoking rates of men and women were similar according to gender groups ( $p = 0.257$ ). 57.1% ( $n = 8$ ) of females were smoking and 38.5% ( $n = 10$ ) of males were smoking. The average vitamin D level was found to be  $16.38 \pm 9.69$  ng / mL in the 40 subjects, whereas the average LDL value was  $129.5 \pm 47.91$  mg/dL, and the average HDL value was  $43.5 \pm 9.47$  mg /dL (Table 1).

**Table 1.** Mean Vitamin D, LDL, and HDL levels in study patients

Variables	N	Mean±SD	Median (min-max)
Vitamin D ng / mL	40	16.38±9.69	14.75 (7.1-44,9)
LDL mg / dL	40	129.52±47.91	129 (46-209)
HDL mg / dL	40	43.62±9.74	43.5 (19-63.6)

MCI, C1, and C2 ratios were similar in females and males ( $p = 0.641$ ). There was no statistically significant difference between C1 and C2 rates of smoking groups ( $p = 0.064$ ). There

was no significant difference between C1 and C2 ratios, according to the toothless period ( $p = 0.849$ ) (Table 2).

**Table 2.** Comparison of Mandibular Cortical Index (MCI) by gender, smoking, and period of tooth loss

		MCI		Total N	P-value
		C1 N(%)	C2 N(%)		
Gender	Female	7 (50%)	7 (50%)	14	0.641 <sup>†</sup>
	Male	11 (42.3%)	15 (57.7%)	26	
Smoking	No-smoking	7 (31.8%)	15 (68.2%)	22	0.064 <sup>†</sup>
	Smoking	11 (61.1%)	7 (38.9%)	18	
Period of Tooth Loss	5 years and less	5 (38.5%)	8 (61.5%)	13	0.849 <sup>‡</sup>
	5-10 years	8 (47.1%)	9 (52.9%)	17	
	More than 10 years	5 (50%)	5 (50%)	10	

<sup>†</sup> Chi-square test, <sup>‡</sup> Fisher exact test

MI measurements according to demographic and clinical characteristics of the patients were shown in Table 3. The mean MI did not differ

significantly regarding gender, smoking, and the toothless period ( $p = 0.944$ ,  $p = 0.946$ ,  $p = 0.552$ , respectively).

**Table 3.** Comparison of Mental Index (MI) measurements according to demographic and clinical characteristics of patients

		N	MI		P value
			Mean±SD	Median (min-max)	
Gender	Female	14	5.29±0.72	5 (4-7)	0.944 <sup>¶</sup>
	Male	26	5.42±1.41	5 (4-10)	
Smoking	No-smoking	22	5.45±1.50	5 (4-10)	0.946 <sup>¶</sup>
	Smoking	18	5.28±0.75	5 (4-7)	
Tooth loss time	5 years or less	13	5.15±1.28	5 (4-7)	0.552 <sup>§</sup>
	5-10 years	17	5.65±1.41	5 (4-10)	
	More than 10 years	10	5.20±0.63	5 (4-6)	

<sup>¶</sup> Mann Whitney U test

<sup>§</sup> Kruskal-Wallis test

SD: Standart Deviation:

Vitamin D, LDL, and HDL measurements were not statistically different between the MCI

groups ( $p = 0.100$ ,  $p = 0.119$ ,  $p = 0.840$ , respectively) (Table 4).

**Table 4.** Comparison of Vitamin D, LDL, and HDL levels according to Mandibular Cortical Index (MCI) groups.

	MCI groups	N	Mean±SD	Median (min-max)	p value
Vit D	C1	18	13.61±6.87	10 (7-26)	0.100 <sup>¶</sup>
	C2	22	18.64±11.16	16 (7-45)	
LDL	C1	18	116.5±49.69	107.5 (46-209)	0.119 <sup>¶</sup>
	C2	22	140.23±44.69	141 (74-206)	
HDL	C1	18	42.78±11.52	43.5 (19-64)	0.840 <sup>¶</sup>
	C2	22	44.36±8.28	43.5 (33-60)	

<sup>¶</sup> Mann Whitney U test

SD: Standart deviation

Significant positive weak correlations of MI with VitaminD and LDL were determined to be

present( $r = 0.329$ ,  $p = 0.038$ ;  $r = 0.341$ ,  $p = 0.031$ ) (Table 5).

**Table 5.** Results of correlation analysis between Mental Index (MI) and VitD, HDL and LDL

		<b>VitD</b>	<b>LDL</b>	<b>HDL</b>
<b>MI</b>	R	<b>0.329*</b>	<b>0.341*</b>	0.063
	P	<b>0.038</b>	<b>0.031</b>	0.698
	N	<b>0.038</b>	40	40

\* Spearman's rho correlation statistically significant

## DISCUSSION

Vitamin D is a fat-soluble vitamin derived from endogenous production in the skin following exposure to adequate sunlight (cholecalciferol) or obtained through dietary means (ergocalciferol and cholecalciferol), then converted in the liver to 25-hydroxyvitamin D (25(OH) D). Thereafter, 25(OH)D is converted in the kidney to its active form 1,25-hydroxyvitamin D (1,25(OH)D).<sup>11</sup> Vitamin D is involved in the intestinal absorption and regulation of calcium homeostasis and is crucial for bone and overall health.<sup>12</sup> This vitamin can stimulate osteoblastic bone matrix production, coupling bone resorption to bone formation, and optimizing bone remodeling.<sup>13</sup> It increases calcium absorption in the intestine, leading to a reduction in PTH (parathyroid hormone) secretion and lowers systemic bone resorption with a possible inhibition of osteoclastogenesis. 1, 25-dihydroxyvitamin D<sub>3</sub> can stimulate bone resorption by binding to vitamin D receptors of osteoblasts and by altering the balance between RANKL and osteoprotegerin.<sup>14,15</sup> Although vitamin D has been widely used in the treatment and prevention of osteoporosis in recent years, studies investigating its effects on implant osseointegration are limited.<sup>9,16</sup>

In an animal experiment, Kelly *et al.*<sup>17</sup> observed low bone-implant connection (BIC) in rats with vitamin D deficiency two weeks after implant placement. However, the same study emphasized that the prevalence of vitamin D deficiency might vary in different populations. Recently, the effect of topical application of vitamin D (10%) and melatonin (5%) solutions on the surface of immediate implants placed in dogs was evaluated. Both topical applications improved new bone formation around implants significantly and reduced crestal bone loss at 12 weeks following surgery, indicating the positive correlation between vitamin D and early stages of

osseointegration.<sup>18</sup> Aydın *et al.*<sup>19</sup> reported a significant increase in the amount of vitamin D in propolis groups and stated that the healing of the implanted bone was improved.

A retrospective study with the purpose of investigating a correlation between early implant failure and low serum level of vitamin D showed a higher incidence of the implant failure rate in these patients, but a correlation between the two factors could not be determined.<sup>20</sup>

The results of the current study revealed that vitamin D level was below the threshold of 20 ng/mL in thirty individuals included in the study. The World Health Organization reported that the insufficiency of vitamin D could be considered in levels below 20 ng/mL (50 nmol/L), and the deficiency of vitamin D levels could be considered below 10 ng/mL (25 nmol/L).<sup>21,22</sup> We think that the probability of implant failure in these individuals may be higher in subsequent implant applications. These individuals may be offered vitamin D supplementation before implant surgery, and patients maybe needed to be kept under control for peri-implantitis following implant surgery.

The results showed that there was no relationship between MCI and vitamin D level, whereas there was a weak positive correlation between MI and vitamin D level. This result shows that the vitamin D level may affect bone metabolism and structure.

Animal experiments showed that there were more bone resorption and less bone formation, together with higher levels of bone turnover marker after high cholesterol diets.<sup>23,24</sup> During *et al.*<sup>23</sup> reported that fatty acids and high cholesterol levels may adversely affect the rate of bone formation / bone destruction by down-regulating the Wnt signaling pathway. Wnt pathway balances

mesenchymal cell differentiation by inhibiting adipogenesis and stimulating osteoblasts proliferation, maturation, and differentiation. Although the adverse effects of obesity and increased cholesterol and triglycerides are widely known in the medical field, the effect of hyperlipidemia on osseointegration of dental implants is not fully known.<sup>25</sup> In a study, it was reported decreased bone formation and poor bone-implant attachment after 12 weeks of a high-fat diet.<sup>24</sup> However, in a study conducted by Dündar *et al.*<sup>26</sup>, no change in the status of bone-implant connections after a 3-month high-fat diet was determined in post-implant 12-week evaluations in rabbits.

According to the results of the present study, there were no correlations between the MCI index, HDL, and LDL, whereas there was a weak positive correlation between MI and LDL. As mentioned in the literature, we think that hyperlipidemia may affect bone quality and density, but adverse effects may be speculated in implant osseointegration. In addition, meaningful results may be obtained in studies with more substantial-sized samples.

In this study, no significant relationship was found between the duration of tooth loss and radiomorphometric indices. This can be explained by the presence of the natural teeth at the mesial and distal of the edentulous crest in the patients. In the literature, it has been reported that the presence of natural teeth, partial and total edentulism can be related to these indices.<sup>27</sup>

## CONCLUSIONS

Panoramic radiographs are frequently used before implant surgery. It was concluded that biomarkers such as Vitamin D might be relevant in addition to radiographic and clinical parameters, and patients should be evaluated in this respect.

In addition, the inverse relationship between plasma 25-OH D and serum PTH levels is very well known.<sup>28,29</sup> PTH plays a central role in calcium-phosphorus homeostasis. Thus, a combined evaluation of vitamin D and PTH levels may provide an accurate assessment. The limitation of the current study is the small sample size. However, vitamin D insufficiency was observed in

the majority of the patient group in the study, and the issue of whether vitamin D supplementation would be necessary before implant surgery was raised. Future studies are needed to evaluate vitamin D and PTH together and to evaluate the rate of peri-implantitis in patients with vitamin D deficiency after implant surgery.

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## CONFLICTS OF INTEREST STATEMENT

The author reports no conflicts of interest

### *Dental Implant Cerrahisi Planlanan Hastalarda Dijital Panoramik Radyografi ile Değerlendirilen Mandibular Kemik Kalitesi ile Serum Biyolojik Parametreler Arasındaki İlişki*

#### ÖZ

**Amaç:** Bu çalışmanın amacı, panoramik radyomorfometrik indeksler [mandibular kortikal indeks (MKI), mental indeks (MI)] kullanılarak implant bölgelerinde kemik densitesini değerlendirmek ve kemik densitesi ile D vitamini, HDL ve LDL arasındaki ilişkiyi incelemektir. **Gereç ve Yöntemler:** Çalışmaya mandibular birinci molar veya ikinci molar diş eksikliği olup implant cerrahisi planlanan 40 hasta dahil edilmiştir. Mandibular kemik dansitesini değerlendirmek için kan örnekleri ve panoramik MKI ve MI kullanılmıştır. Veriler Mann-Whitney U ve Kruskal-Wallis testleri kullanılarak analiz edildi. MI ve çalışma değişkenleri arasındaki ilişki Spearman korelasyon katsayısı ile değerlendirildi. MKI ve çalışma değişkenleri arasındaki ilişkiyi belirlemek için Ki-kare veya Fisher exact testleri kullanıldı. p değerinin <0,05 olması anlamlı kabul edildi. **Bulgular:** MI ile D vitamini ve LDL arasında anlamlı zayıf pozitif korelasyon bulunmuştur ( $r=0,329$ ,  $p=0,038$ ;  $r=0,341$ ,  $p=0,031$ ). MKI grupları arasında D vitamini, LDL ve HDL değerleri bakımından istatistiksel olarak fark bulunamamıştır (sırasıyla  $p=0,100$ ,  $p=0,119$ ,  $p=0,840$ ). **Sonuçlar:** D vitamini klinik ve radyolojik parametrelere ek olarak önemli bir faktör olabilmektedir ve hastalar bu açıdan değerlendirilmelidir. D vitamini ile kemik kalitesi arasındaki ilişkiyi araştıran daha çok sayıda hastanın dahil edildiği çalışmalara ihtiyaç vardır. **Anahtar Kelimeler:** diş implantları, kemiğin yeniden şekillendirilmesi, vitamin D, HDL kolesterol, LDL kolesterol.

## REFERENCES

1. Kohn DH. Overview of factors important in implant design. *J Oral Implantol* 1992; 18: 204-219.
2. Jemt T, Lekholm U. Implant treatment in edentulous maxillae: a 5-year follow-up report on patients with different degrees of jaw resorption. *Int J Oral Maxillofac Implants* 1995; 10: 303-311.
3. Zlataric DK, Celebic A. Clinical bone densitometric evaluation of the mandible in removable denture wearers dependent on the morphology of the mandibular cortex. *J Prosthet Dent* 2003; 90: 86-91.
4. Yeler DY, Koraltan M, Hocaoglu TP, Arslan C, Erselcan T, Yeler H. Bone quality and quantity measurement techniques in dentistry. *Cumhuriyet Dent J* 2016; 19: 73-86.
5. Taguchi A, Tsuda M, Ohtsuka M, Kodama I, Sanada M, Nakamoto T, et al. Use of dental panoramic radiographs in identifying younger postmenopausal women with osteoporosis. *Osteoporos Int* 2006; 17: 387-394.
6. Devlin H, Karayianni K, Mitsea A, Jacobs R, Lindh C, van der Stelt P, et al. Diagnosing osteoporosis by using dental panoramic radiographs: the OSTEODENT project. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2007; 104: 821-828.
7. Klemetti E, Kolmakov S, Kroger H. Pantomography in assessment of the osteoporosis risk group. *Scand J Dent Res* 1994; 102: 68-72.
8. Silverstein LH, Melkonian RW, Kurtzman D, Garnick JJ, Lefkove MD. Linear tomography in conjunction with pantomography in the assessment of dental implant recipient sites. *J Oral Implantol* 1994; 20: 111-117.
9. Xiong Y, Zhang Y, Guo Y, Yuan Y, Guo Q, Gong P, et al. 1alpha,25-Dihydroxyvitamin D3 increases implant osseointegration in diabetic mice partly through FoxO1 inactivation in osteoblasts. *Biochem Biophys Res Commun* 2017; 494: 626-633.
10. Insua A, Monje A, Wang HL, Miron RJ. Basis of bone metabolism around dental implants during osseointegration and peri-implant bone loss. *J Biomed Mater Res A* 2017; 105: 2075-2089.
11. Anand N, Chandrasekaran SC, Rajput NS. Vitamin D and periodontal health: Current concepts. *J Indian Soc Periodontol* 2013; 17: 302-308.
12. Vieth R. Vitamin D toxicity, policy, and science. *J Bone Miner Res* 2007; 22 Suppl 2: V64-68.
13. Kogawa M, Findlay DM, Anderson PH, Ormsby R, Vincent C, Morris HA, et al. Osteoclastic metabolism of 25(OH)-vitamin D3: a potential mechanism for optimization of bone resorption. *Endocrinology* 2010; 151: 4613-4625.
14. Leizaola-Cardesa IO, Aguilar-Salvatierra A, Gonzalez-Jaranay M, Moreu G, Sala-Romero MJ, Gomez-Moreno G. Bisphosphonates, vitamin D, parathyroid hormone, and osteonecrosis of the jaw. Could there be a missing link? *Med Oral Patol Oral Cir Bucal* 2016; 21: e236-240.
15. Christakos S, Lieben L, Masuyama R, Carmeliet G. Vitamin D endocrine system and the intestine. *Bonekey Rep* 2014; 3: 496.
16. Zhou C, Li Y, Wang X, Shui X, Hu J. 1,25Dihydroxy vitamin D(3) improves titanium implant osseointegration in osteoporotic rats. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012; 114: S174-178.
17. Kelly J, Lin A, Wang CJ, Park S, Nishimura I. Vitamin D and bone physiology: demonstration of vitamin D deficiency in an implant osseointegration rat model. *J Prosthodont* 2009; 18: 473-478.
18. Salomo-Coll O, de Mate-Sanchez JE, Ramirez-Fernandez MP, Hernandez-Alfaro F, Gargallo-Albiol J, Calvo-Guirado JL. Osseoinductive elements around immediate implants for better osteointegration: a pilot study in foxhound dogs. *Clin Oral Implants Res* 2018; 29: 1061-1069.
19. Aydin E, Hepokur C, Misir S, Yeler H. Effects Of Propolis On Oxidative Stress In Rabbits Undergoing Implant Surgery *Cumhuriyet Dent J* 2018;21: 136-144.
20. Mangano F, Mortellaro C, Mangano N, Mangano C. Is Low Serum Vitamin D Associated with Early Dental Implant Failure? A Retrospective Evaluation on 1625 Implants Placed in 822 Patients. *Mediators Inflamm* 2016; 2016: 5319718.



- 21.** Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. *Mayo Clin Proc* 2010; 85: 752-7; quiz 7-8.
- 22.** Spiro A, Buttriss JL. Vitamin D: An overview of vitamin D status and intake in Europe. *Nutr Bull* 2014; 39: 322-350.
- 23.** During A, Penel G, Hardouin P. Understanding the local actions of lipids in bone physiology. *Prog Lipid Res* 2015; 59: 126-146.
- 24.** Soares EA, Nakagaki WR, Garcia JA, Camilli JA. Effect of hyperlipidemia on femoral biomechanics and morphology in low-density lipoprotein receptor gene knockout mice. *J Bone Miner Metab* 2012; 30: 419-425.
- 25.** Keuroghlian A, Barroso AD, Kirikian G, Bezouglaia O, Tintut Y, Tetradis S, et al. The effects of hyperlipidemia on implant osseointegration in the mouse femur. *J Oral Implantol* 2015; 41: e7-e11.
- 26.** Dundar S, Yaman F, Ozupek MF, Saybak A, Gul M, Asutay F, et al. The effects of high-fat diet on implant osseointegration: an experimental study. *J Korean Assoc Oral Maxillofac Surg* 2016; 42: 187-192.
- 27.** Dutra V, Yang J, Devlin H, Susin C. Radiomorphometric indices and their relation to gender, age, and dental status. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; 99: 479-484.
- 28.** Dawson-Hughes B, Harris SS, Dallal GE. Plasma calcidiol, season, and serum parathyroid hormone concentrations in healthy elderly men and women. *Am J Clin Nutr* 1997; 65: 67-71.
- 29.** Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, et al. Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 1997; 7: 439-443.