AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 63, Issue 01, January 2023

ASSESSMENT OF VITAMIN D3, OSTEOCALCIN, CALCIUM, AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA OR OSTEOPOROSIS

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Abstract

Vitamin D3 and calcium deficiency are influential factors in the development of osteoporosis. Also, osteocalcin is considered to be one of the markers for osteoporosis as it is produced primarily by osteoblasts during bone formation. The aim of this study is to assess the serum levels of vitamin D3, osteocalcin, and calcium with bone mineral density to differentiate between osteopenic and osteoporotic postmenopausal women. A case control study that included 120 postmenopausal Iraqi women divided into three groups [40 postmenopausal women with osteoporosis, 40 postmenopausal women with osteopenia, and 40 post-menopausal women free from osteoporosis and osteopenia as control group. The results obtained showed that vitamin D3 was significantly lower in both osteoporosis and osteopenia groups when compared to the control group. The average levels of osteocalcin were significantly lower in osteoporosis and osteopenia groups when compared to the control. Also, the average levels of serum calcium were significantly lower in osteoporosis and osteopenia groups when compared to the control group. The results of ROC curve analysis demonstrated excellent ability of the included tests variables with AUC= 0.912, 1.00, 0.91 and 1.00 for osteocalcin, vitamin D3, calcium, and T-score, respectively that can classify osteoporosis from control groups, and the cut-off values of these parameters could be used for this differentiation. Also, the results demonstrated excellent ability of all the included tests with the AUC = 0.902, 1.00, 0.912, 1.00 for osteocalcin, vitamin D3, calcium, and T-score, respectively that can classify osteopenia from control groups with the cut-off values. While, the results showed that only T-score (AUC= 1.00) is the best parameter used to differentiate osteoporosis from osteopenia. In conclusion, levels of vitamin D3, osteocalcin and calcium could be used to give an indication of bone mineral density status in osteopenic or osteoporotic postmenopausal women without the use of a DEXA analysis. But, the differentiation between osteopenia and osteoporosis was only obtained by the DEXA analysis method.

Key words: Osteopenia, Osteoporosis, Vitamin D3, Osteocalcin, Calcium

Introduction

Postmenopausal osteoporosis (PMOP), the most prevalent kind of the condition, is characterized

by decreased bone mineral density, skeletal microstructure disintegration, increased bone fragility, and increased fracture risk [1]. This may be due to hormonal changes (estrogen decline) in postmenopausal women lead to accelerated bone loss and osteoporosis [2]. 90% of the calcium in the human body is found in the bones and teeth, making it the most prevalent inorganic salt component. The type I collagen matrix of bones becomes deposited with calcium crystals called hydroxyapatite, which strengthens the bones. Getting insufficient calcium can cause osteoporosis and fractures [3]. Vitamin D, which is obtained through sunlight, food, and other dietary supplements, is another vitamin that is vital to the mineralization of the skeleton.

However, vitamin D deficiency still exists in many regions of the world owing to dietary deficiencies, sun avoidance, and sunscreen use [4]. It is well recognized that the majority of the circulating vitamin D comes from cutaneous production and should be seen as a hormone rather than a vitamin. Due to its participation in several physiological systems, vitamin D insufficiency (50 nmol/L) is an epidemic that affects people all over the world and has numerous effects on human health. Numerous studies have demonstrated a reduction in the frequency of non-vertebral and hip fractures with greater blood 25-hydroxy vitamin D levels [5-7].

Osteocalcin (OC), the main and best-researched non-collagenous protein in bone extracellular matrix, has been maintained in bone. The amount and activity of osteoblasts are indicated by the serum concentration of total OC, which has been used as a biochemical indicator of osteogenesis [8]. It is essential for the mineralization of the matrix and has a great affinity for calcium [9, 10].

Bone strength, which is determined by a number of skeletal characteristics including its composition, microarchitecture, size, and shape [11], is a measure of a bone's resistance to breaking. The most used method for calculating bone mineral density (BMD), assessing bone strength, and diagnosing osteoporosis is dual-energy X-ray absorptiometry [12]. There are several drawbacks of dual-energy X-ray absorptiometry [13, 14]. Due to the limitations of the DEXA scan as well as the limitations of its accessibility and availability, the goal of this study is to evaluate serum levels of vitamin D3, osteocalcin, and calcium as well as bone mineral density to distinguish between osteopenic and osteoporotic postmenopausal women.

Methods

A case-control research that involved 120 postmenopausal Iraqi women aged 45 to 65 who attended AL-Imamain AL-Kadimain Hospital and Baghdad Teaching Hospital in the Medical City Complex, Iraq, from February to May 2022. The College of Medicine at Al-Nahrain University in Baghdad, Iraq, institutional review board gave the study its approval.

The subjects were split into three groups based on the T-score for bone mineral density obtained from the DEXA scan: (G1) 40 postmenopausal women with osteoporosis (T-score-2.5 or more below), (G2) 40 postmenopausal women with osteopenia (T score between-1 and -2.5), and (G3) 40 post-menopausal women free from osteoporosis or osteopenia (T score -1 and above).

Exclusion Criteria:

Women with oligomenorrhea, amenorrhea, or early menopause before the age of 40, hyperparathyroidism, corticosteroid therapy applied for more than three months, hormonal

therapy, liver and kidney dysfunction, rheumatoid arthritis, malignant tumors, hematologic diseases, previous pathological fractures, or myocardial infarction were excluded from this study.

Methods used

Vitamin D3 and osteocalcin were measured using ELISA technique (My biosourse/USA kits), while calcium was measured by spectrophotometric technique using Cromatest- linear –spain kit.

Statistical Analysis

The data for qualitative variables were provided in terms of the number of instances (n) and percentages, whilst the data for continuous variables were presented in terms of mean and standard deviation. The results were compared using an ANOVA. Comparing categorical variables was done using the Fisher's exact test, also known as the chi-square test. The normal distribution of the data was examined using the Kolmogorov-Smirnov test. Quantitative variables were compared for associations using Pearson's correlation coefficient. Cohen's criterion was applied to determine the connections' strength. As a result, coefficients between 0.10 and 0.29 are regarded as having a modest impact size, 0.30 to 0.49 as having a moderate effect size, and coefficients over 0.50 as having a big effect size [15]. For each test, the statistical significance level for an alpha value was set at 0.05. Both GraphPad Prism version 8.0.0 for Windows (GraphPad Software, San Diego,California,USA;www.graphpad.com) and SPSS, Version 26 for Windows (SPSS, Inc., Chicago, IL, USA) were used for all of the analyses.

Results

Vitamin D3

There were significant differences in Vitamin D3 by group as indicated by ANOVA analysis, $F(2,117) = 140.10$, $p < .001$. The R2 was 0.71 indicating group explains approximately 71% of the variance in Vitamin D3. The mean of Vitamin D3 for Osteoporosis (52.21± 9.54 ng/ml) was significantly smaller than for Control group (184.05± 69.78 ng/ml), $p < .001$. the mean of Vitamin D3 for Osteopenia (50.74± 7.65 ng/ml) was significantly smaller than for Control group (184.05± 69.78 ng/ml), $p < .001$. No other significant effects were found. The means and standard deviations are presented in Table-1 and Figure-1.

Osteocalcin

The results of the ANOVA showed that there were significant differences in Osteocalcin across the groups. The $F(2, 117)$ value was 42.34, and the p value <.001. The R2 value was 0.42, which indicates that group explains roughly 42% of the variation in Osteocalcin. The average level of osteocalcin in patients with osteoporosis coming in at (34.92± 5.39 ng/ml) which was significantly lower than in the control group (46.31± 6.93 ng/ml) ($p< .001$).

A p value < .001 indicates that the average level of osteocalcin in patients with osteopenia (34.08± 7.43 ng/ml) was significantly lower than that of the control group (46.31± 6.93 ng/ml). There were

no more significant effects discovered. The mean values and standard deviations are shown in Table-1 and Figure-1

Calcium

Calcium levels differed significantly between groups as indicated by ANOVA analysis, F(2, 117) = 37.85, p< .001. The R2 value was 0.39, this finding indicate that groups explain approximately 39% of the variance in Ca. The mean Ca for osteoporosis (5.97 ±1.95 mg/dL) and osteopenia (5.60± 2.13 mg/dL) were both significantly lower than the mean Ca for control (8.85± 1.30 mg/dL), p< 0.001. There were no further significant findings. The means and standard deviations are shown in Table-1; Figure -2.

T-SCORE

There were significant differences in T-SCORE by group, F(2, 117) = 298.28, p < .001. The R2 was 0.84 indicating group explains approximately 84% of the variance in T-Score. The mean of T-Score for Osteoporosis (-3.21± 0.47) was significantly smaller than for Osteopenia group (-1.84± 0.42), p < .001. the mean of T-Score for Osteoporosis (-3.21± 0.47) was significantly smaller than for Control group (-0.28± 0.68), p < .001., the mean of T-Score for Osteopenia group (-1.84± 0.42) was significantly smaller than for Control group (-0.28± 0.68), p < .001. The means and standard deviations are presented in Table-1 and Figure-2.

Table-1: Comparison of mean values and standard deviation of Osteocalcin, Vitamin D3, and Ca using ANOVA test

	Variable	*Mean ± SD*	SE_M	*Median*	*F*	*p*	R^2
Osteocalcin ng/ml	Osteoporosis	34.92± 5.39	0.85	33.78	42.34	< .001	0.42
	Osteopenia	34.08± 7.43	1.18	32.52			
	Control	46.31± 6.93	1.10	47.07			
Vit D3 ng/ml	Osteoporosis	52.21± 9.54	1.51	48.94	140.10	< .001	0.71
	Osteopenia	50.74± 7.65	1.21	48.67			
	Control	184.05± 69.78	11.03	162.66			
Ca mg/dL	Osteoporosis	5.97± 1.95	0.31	5.40	37.85	< .001	0.39
	Osteopenia	5.60± 2.13	0.34	4.97			
	Control	8.85± 1.30	0.21	8.91			
T_SCORE	Osteoporosis	-3.21± 0.47	0.07	-3.20	298.28	< .001	0.84
	Osteopenia	-1.84± 0.42	0.07	-1.90			
	Control	-0.28± 0.68	0.11	-0.50			

Results for Significance Testing against the groups using *F*-Tests SE_M, *Standard error of mean;* R^2, goodness of fit

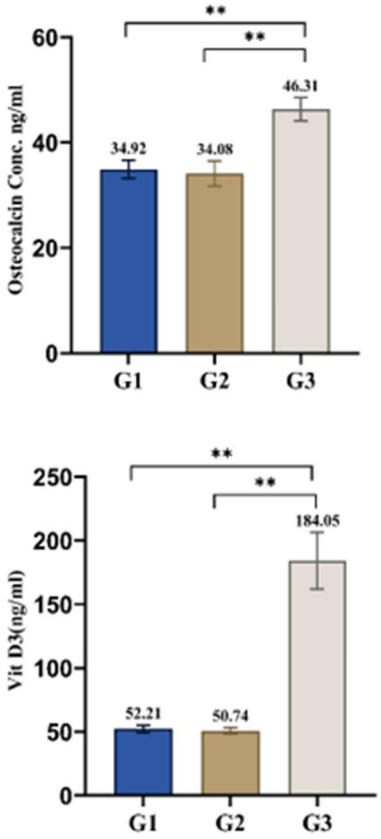

Figure-1: Means of Osteocalcin and Vit D3 by group with 95.00% CI Error Bars, ** = P value < 0.001

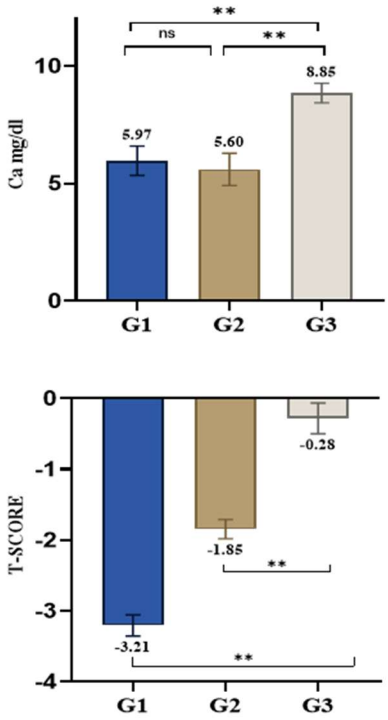

Figure-2: Means of Ca and T-Score by group with 95.00% CI Error Bars, ** = P< .001

The results of Receiver Operator Curve (ROC) analysis showed the area under the curve (AUC), cut-off values and sensitivity and specifity for each parameter in this study as shown in Table-2.

Combination	Variable	AUC	SE	95% CI	Cutoff	Sensitivity	Specificity
Osteoporosis vs Control	Osteocalcin	0.912	0.0366	0.827 to 0.964	≤36.71	80.00	97.50
	Vit. D3	1.000	0.000	0.955 to 1.000	≤83.341	100.00	100.00
	Ca	0.910	0.0392	0.824 to 0.962	≤6.49	82.50	100.00
	T-SCORE	1.000	0.000	0.955 to 1.000	≤-2.6	100.00	100.00
Osteopenia vs Control	Osteocalcin	0.902	0.0411	0.814 to 0.957	≤40.18	87.50	95.00
	Vit D3	1.000	0.000	0.955 to 1.000	≤80.701	100.00	100.0
	Ca	0.912	0.0396	0.828 to 0.964	≤6.49	82.50	100.00
	T-SCORE	1.000	0.000	0.955 to 1.000	≤-1.1	100	100
Osteoporosis vs Osteopenia	Osteocalcin	0.595	0.0645	0.479 to 0.703	>31.01	82.50	40.00
	Vit. D3	0.515	0.0662	0.401 to 0.628	>56.477	22.50	92.50
	Ca	0.585	0.0659	0.470 to 0.694	>4.48	92.50	35.00
	T-SCORE	1.000	0.000	0.955 to 1.000	≤-2.6	100	100

Discussion

In this study, individuals with osteoporosis and osteopenia had average osteocalcin levels that were considerably lower than those of the control group. There was no discernible change in serum OC between osteoporotic patients and controls according to Biver et almeta-analysis's investigation of multiple bone turnover indicators [16]. According to all currently available and relevant research, a different study's analysis found no discernible difference in the blood OC level between PMO patients and controls. The circulation of OC molecules is highly diverse, and the metabolism of glucose can have an impact. Consequently, serum OC is not a reliable predictor of the high bone turnover state in PMO at this time [17]. Additionally, a research found that postmenopausal women with diabetes in Thi-Qar Province, Iraq, had significantly lower blood levels of osteopontin and

OC as well as lower bone mineral density. They discovered that OC and glucose metabolism may interact, with PMO females exhibiting certain energy metabolism abnormalities [18]. The much lower mean level of OC in PMO women in this study likely be ascribed to the high percentage of diabetic individuals. Another possibility is that OC exists in two states depending on the degree of carboxylation: completely carboxylated OC (cOC) and undercarboxylated OC (ucOC), which is missing carboxylation at one or more sites [19, 20]. 40% to 60% of the OC that is now in circulation is ucOC. In observational and randomized controlled trial (RCT) investigations, it was shown that poor vitamin K consumption, low levels of vitamin K in the blood, high levels of ucOC, or low levels of total OC were all linked to an increased risk of bone fractures [21]. A study showed the profile of serum ucOC levels by gender and age in a Chinese population and showed links between ucOC and BMD and BTMs as well as the risk of osteopenia or osteoporosis being common. These results provide a hint as to how ucOC functions in bone metabolism [22]. Therefore, it may be crucial for future research to consider the usefulness of ucOC.

The osteoporosis and osteopenia groups in this study had considerably lower mean vitamin D3 levels than the control group. This finding was consistent with earlier research; Chidre and Shaikh observed a high frequency of vitamin D insufficiency with low 25 OHD levels and came to the conclusion that vitamin D deficiency is significantly undertreated in women with osteoporosis. These women, especially those who are at a high risk for fragility fractures, must receive vitamin D supplements [23]. Another study found that osteopenic and osteoporotic individuals had a greater frequency of vitamin D insufficiency than healthy participants.

Additionally, vitamin D supplementation enhanced bone density measurements and decreased the prevalence of osteoporosis. They advised using vitamin D supplements continuously and often, especially for women and the elderly, to treat and even reverse osteoporosis [24]. According to a study, vitamin D insufficiency is rather common among post-menopausal women with probable osteoporosis. Since vitamin D cannot be obtained from food sources or sunshine, supplementation is necessary to treat vitamin D deficiency and prevent fractures. In order to make the best judgments about whether to start taking vitamin D supplements, it was advised that postmenopausal women undergo routine vitamin D testing [25]. The mean blood calcium levels for both osteoporosis and osteopenia in this research were considerably lower than those for the control group.The majority of research connects a calcium deficit to osteoporosis, and some advocate routine calcium testing to track the development of the condition [26, 27, 28]. Other studies found serum calcium levels to increase the risk of bone loss [29, 30, 31]. Despite the fact that new osteoporosis risk variables emerged with hormonal changes following the loss of the estrogen action in postmenopausal women, the link between serum calcium and bone loss was diminished [31].

In this study Receiver Operator Curve (ROC) analysis demonstrated excellent ability of the included tests variables with AUC= 0.912, 1.00, 0.91 and 1.00 for osteocalcin, vitamin D3, calcium, and T-score, respectively that can classify osteoporosis from control groups, and the cut-off values of these parameters could be used for this differentiation (≤ 36.71 ng/ml, ≤ 83.341 ng/ml, ≤ 6.49 mg/dL, and ≤ -2.6 respectively). Also, the results demonstrated excellent ability of all the

included tests with the AUC = 0.902, 1.00, 0.912, 1.00 for osteocalcin, vitamin D3, calcium, and T-score, respectively that can classify osteopenia from control groups with the cut-off values (≤ 40.18ng/ml, ≤ 80.701 ng/ml, ≤ 6.49 mg/dL, and ≤ -1.1respectively).While, the results showed that only T-score (AUC= 1.00) is the best parameter used to differentiate osteoporosis from osteopenia. While the results showed that only T-score (AUC= 1.00) is the best parameter used to differentiate osteoporosis from osteopenia. This may be due to the fact that there were no significant differences between the other parameters between osteopenia and osteoporosis groups.

Conclusion:

Decrease in serum vitamin D3, osteocalcin, and calcium in osteopenia or osteoporosis in post-menopausal women are affected by decrease in bone density. Levels of vitamin D3, osteocalcin and calcium could be used to give an indication of bone mineral density status in osteopenic or osteoporotic postmenopausal women without the use of a DEXA analysis. While, the differentiation between osteopenia and osteoporosis can only be obtained by a DEXA analysis, this may be due to the fact that there were no significant differences of the measured parameters between osteopenia and osteoporosis groups.

Conflict of interest

There were no conflicts of interest with the publishing of this work, according to the authors.

References

1. Pouillès, J.-M., et al., TBS in early postmenopausal women with severe vertebral osteoporosis. Bone, 2021. 142: p. 115698.
2. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis, 2016. Endocr Pract 22, Suppl. 4, 1–42.
3. Seeman E, Delmas PD. Bone quality—the material and structural basis of bone strength and fragility. N Engl J Med. 2006;354(21):2250–61.
4. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? Br J Nutr. 2003;89:552- 72.
5. Calleja-Agius, J. and M.P. Brincat, The urogenital system and the menopause. Climacteric, 2015. 18(sup1): p. 18-22.
6. Brincat, M., et al., *The role of vitamin D in osteoporosis.* Maturitas, 2015. **80**(3): p. 329-332.
7. Geddawy, A., et al., Response regarding the importance of vitamin D and calcium among undergraduate health sciences students in Al Kharj, Saudi Arabia. Archives of Osteoporosis, 2020. 15(1): p. 1-7.
8. Diaz Franco MC, De Leon RFD, Villafan Bernal JR. Osteocalcin-GPRC6A: an update of its clinical and biological multi-organic interactions (review). Mol Med Rep 2019;19:15–22. 13.
9. Macias I, Alcorta Sevillano N, Rodriguez CI, Rodriguez CI, Arantza Infante A. Osteoporosis and the potential of cell-based therapeutic strategies. Int J Mol Sci 2020;21:1653. 14.

10. Carvalho MS, Poundarik AA, Cabral JMS, da Silva CL, Vashishth D. Biomimetic matrices for rapidly forming mineralized bone tissue based on stem cell-mediated osteogenesis. Sci Rep 2018;8:14388.
11. Diez Perez A, Brandi ML, Al-Daghri N, Branco JC, Bruyere O, Cavalli L, et al. Radiofrequency echographic multispectrometry for the in vivo assessment of bone strength: state of the art-outcomes of an expert consensus meeting organized by the European society for clinical and economic aspects of osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO). Aging Clin Exp Res 2019;31:1375–89.
12. Marushchak M, Krynytska I. Pharmacological treatment of osteoporosis in patients with coronary heart disease complicated plicated by chronic heart failure. Asian J Pharm Clin Res 2019;12:443-6.
13. Jain RK, Vokes T. Dual-energy X-ray absorptiometry. J Clin Densitom 2017;20:291–303.
14. Krugh M, Langaker MD. Dual-energy X-ray absorptiometry (DEXA). In: Stat pearls. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519042/. [Last accessed on 24 Apr 2020].
15. Cohen, J. (1988). Statistical Power Analysis for the Behavioral Sciences (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates, Publishers.
16. Biver E, Chopin F, Coiffier G, Brentano TF, Bouvard B, Garnero P, Cortet B. Bone turnover markers for osteoporotic status assessment? A systematic review of their diagnosis value at baseline in osteoporosis. Joint Bone Spine. 2012; 79(1):20-5.
17. Liu Z, Chen R, Jiang Y, Yang Y, He L, Luo C, Dong J, and Rong L. A meta-analysis of serum osteocalcin level in postmenopausal osteoporotic women compared to controls. BMC Musculoskeletal Disorders, 2019; 20:532 https://doi.org/10.1186/s12891-019-2863-y
18. Roomi A B, Salih A M, Noori S D, Nori W, and Tariq S. Evaluation of Bone Mineral Density, Serum Osteocalcin, and Osteopontin Levels in Postmenopausal Women with Type 2 Diabetes Mellitus, with/without Osteoporosis. Hindawi, Journal of Osteoporosis. Volume 2022, Article ID 1437061, 5 pages https://doi.org/10.1155/2022/1437061
19. Gundberg CM, Nieman SD, Abrams S, Rosen H. Vitamin K Status and Bone Health: An Analysis of Methods for Determination of Undercarboxylated Osteocalcin. J Clin Endocrinol Metab (1998) 83(9):3258–66. doi: 10.1210/jcem.83.9.5126
20. Hauschka PV, Carr SA. Calcium-Dependent Alpha-Helical Structure in Osteocalcin. Biochemistry (1982) 21(10):2538–47. doi: 10.1021/bi00539a038
21. Fusaro M, Cianciolo G, Brandi ML, Ferrari S, Nickolas TL, Tripepi G, Plebani M, Zaninotto M, Iervasi G, La Manna G, Gallieni M, Vettor R, Aghi A, Gasperoni L, Giannini S, Sella S, M Cheung A. Vitamin K and Osteoporosis. Nutrients. 2020 Nov 25;12(12):3625. doi: 10.3390/nu12123625. PMID: 33255760; PMCID: PMC7760385.
22. Xu Y, Shen L, Liu L, Zhang Z and Hu W. Undercarboxylated Osteocalcin and Its Associations With Bone Mineral Density, Bone Turnover Markers, and Prevalence of Osteopenia and Osteoporosis in Chinese Population: A Cross-Sectional Study. Front. Endocrinol. (2022) 13:843912. doi: 10.3389/fendo.2022.843912

23. Chidre YV, Shaikh AB. Association of vitamin d and osteocalcin levels in post-menopausal women with osteoporosis. Int J Reprod Contracept Obstet Gynecol 2017;6:1244-8.
24. Shahnazari B, Moghimi J, Foroutan M, Mirmohammadkhani M and Ghorbani A. "Comparison of the effect of vitamin D on osteoporosis and osteoporotic patients with healthy individuals referred to the Bone Density Measurement Center" Biomolecular Concepts, vol. 10, no. 1, 2019, pp. 44-50. https://doi.org/10.1515/bmc-2019-0005
25. Suganthan N, Kumanan T, Kesavan V, Aravinthan M, Rajeshkannan N. Vitamin D status among postmenopausal osteoporotic women: a hospital based cross-sectional study from Northern Sri Lanka. BMC Nutr. 2020 Mar 18;6:15. doi: 10.1186/s40795-020-00341-y. PMID: 32206326; PMCID: PMC7081545.
26. ADLER, R. A. 2012. Laboratory testing for secondary osteoporosis evaluation. Clinical biochemistry, 45, 894-900.
27. MUIR, J. M. 2012. The Effect of Physical Activity on Bone Mineral Density and Fracture Rate in Very Old Post-menopausal Women.
28. LEE, J. & VASIKARAN, S. 2012. Current recommendations for laboratory testing and use of bone turnover markers in management of osteoporosis. Annals of laboratory medicine, 32, 105-112.
29. Dalemo S., Eggertsen R., Hjerpe P., Almqvist E.G., Bostrom K.B. Bone mineral density in primary care patients related to serum calcium concentrations: A longitudinal cohort study from Sweden. Scand. J. Prim. Health Care. 2018;36:198–206. doi: 10.1080/02813432.2018.1459430.
30. Liu M., Yao X., Zhu Z. Associations between serum calcium, 25(OH)D level and bone mineral density in older adults. J. Orthop. Surg. Res. 2019;14:458. doi: 10.1186/s13018-019-1517-y.
31. Park HS, Kim GY, Lo JA, Kim JS, Ahn SY, Ko GJ, Kwon YJ, Kim JE. Urine and Serum Electrolytes and Biochemical Values Associated with Osteoporosis in Premenopausal and Postmenopausal Women: A Longitudinal and Cross-Sectional Study Using Korean Genome and Epidemiology Study (KoGES) Cohort. J Clin Med. 2021 May 17;10(10):2155. doi: 10.3390/jcm10102155.