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Monitoring of serum 25-(OH)D level in infants and its correlation with bone density and development

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ABSTRACT

Serum 25-hydroxyvitamin D (25(OH)D) is an indicator of nutritional status in the body. Vitamin D (VD) is important for promoting calcium and phosphorus absorption and bone health. This work investigated the correlation between 25(OH)D level and bone density and bone development in infants. the bone density in 150 infants aged 0 to 3 years was measured by ultrasound. Based on the values of bone density, the infants were grouped into a normal (N) group (n = 95) and an abnormal (ABN) group (n = 55). At the same time, serum 25(OH)D, calcium, phosphorus, alkaline phosphatase (ALP), and parathyroid hormone (PTH) levels were detected to analyze their correlations. 25(OH)D, calcium, and phosphorus levels in the ABN group were greatly decreased, while ALP and PTH levels were increased obviously, all presenting remarkable differences with those in the N group (P<0.05). 25(OH)D was positively linked with bone density (r=0.918, P<0.01), calcium level (r=0.316, P<0.05) and phosphorus level (r=0.209, P<0.05) but showed negative associations with ALP level (r=-0.428, P<0.01) and PTH level (r=-0.327, P<0.05). elevating 25(OH)D was crucial in reducing the incidence of abnormal bone density, bettering bone metabolism, and improving the bone health of infants.

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Introduction

Vitamin D (VD) is an important nutrient necessary for humans. It can also play its role through receptors and is a hormone-like substance with a hormone-like mechanism (1). VD importantly participates in maintaining children's growth and development, bone health, and bone metabolism (2). In addition, it regulates calcium and phosphorus metabolism, promoting calcium absorption and calcium salt deposition (3). VD deficiency will elevate the danger of rickets in children and also lead to the occurrence of immune function impairment, autoimmune diseases, metabolic diseases, and other diseases in children (4,5). Therefore, early monitoring of vitamin D nutritional status in children is very important. 25-hydroxyvitamin D is an important indicator to evaluate the status of vitamin D (6).

When vitamin D is deficient or insufficient, less calcium and phosphorus are absorbed in the intestinal tract of the body, and the decrease of blood calcium and phosphorus levels will lead to the elevation of parathyroid hormone (PTH), accelerate the absorption of old bone, promote the release of calcium and phosphorus into extracellular fluid, and thus maintain the normal level of plasma calcium (7). Alkaline phosphatase (ALP) is mainly synthesized by osteoblasts. When vitamin D is deficient or insufficient, the level of bone calcification is decreased, and after the metabolic proliferation of osteoblasts, the activity and concentration of ALP in the blood are increased (8). VD is very important in promoting calcium and phosphorus absorption and maintaining bone health. bone density is a measure of bone mineralization.

Infants nutritional profile of vitamin D has been a focus of pediatric research in China. We investigated the association of infants (OH) D with levels of bone density, calcium, phosphorus, ALP, and PTH in infants aged 0 to 3 years. The objective of this work is to provide a reference for formulating intervention therapy for infants with abnormal bone density index and maintaining their vitamin D nutritional status.

Materials and Methods

General data

Children aged 0 to 3 years who were admitted to Tianjin Medical University General Hospital and subjected to bone density examination from January 2022 to March 2023 were enrolled. They had to satisfy the following conditions: ① examining bone density and bone development by ultrasound after admission; ② no serious deformity; and ③ no vitamin D supplements. If any of the following items were found, the child had to be excluded: ① with liver and kidney dysfunction; ② with endocrine metabolism and immune dysfunction; ③ with malformed osteitis and osteogenic dysplasia may affect bone development; ④with chromosomal disease and congenital appearance disease; ⑤ having received parenteral nutrition support therapy; and ⑥ with concomitant congenital thyroid or parathyroid disease. According to the results of the ultrasonic bone density examination, 150 children were rolled into a normal (N) group (n = 95) and an abnormal (ABN) group (n = 55). 56 males and 39 females were mentioned in the N group and they were 0 to 3 years, with a mean of (1.82 ± 0.71) years and an average birth weight of (2.92 ± 0.56) kg. 31 males and 24 females were in the ABN group

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and were 0 to 3 years old (2.07 ± 0.50 in average) and a mean birth weight of (2.83 ± 0.67) kg. Therefore, no visible difference was observed in general information of patients in different groups (P>0.05). The families of the included children have signed informed consent, and the study was approved by the Medical Ethics Committee of our hospital.

Detection of bone density

The middle part of the left tibia of the children was detected by an ultrasonic bone density detector, and the ultrasonic conduction velocity was recorded. The bone density in children was classified as follows: normal (Z value > -1.0), mild (-1.5 < Z value < -1.0), moderate (-2.0 < Z value < -1.5), and severe (Z value > -2.0). Mild, moderate, and severe bone density were all considered abnormal density.

Detection of serological indicators

The venous blood samples of children were taken from 3 mL, and subjected to centrifugation at 3,000 rpm/min for 10 min at 4℃ to take supernatant. Serum 25(OH)D level wasdetermined as insufficient (25(OH)D < 30 ng/mL) or adequate (25(OH)D ≥ 30 ng/mL or excessive (25(OH)D > 100 ng/mL). OCTEIA Intact kit was utilized to detect PTH levels in serum. Furthermore, the serum calcium, phosphorus, and ALP levels were determined by the automatic biochemical analyzer.

Methods for statistics

SPSS 19.0 was used. Data were displayed as frequency or percentage and compared with χ^2 test. Measurement data with normal distribution were given as mean ± standard deviation ($\bar{x} \pm s$) and compared using t-test. Pearson or Spearman test was applied to analyze the correlation among variables with normal or partial normal distribution. When P<0.05, the difference was statistically significant.

Results

Serum 25(OH)D levels in children with normal and abnormal bone density

The difference in serum 25(OH)D levels between normal and abnormal children was compared by ultrasound, as demonstrated in Figure 1. 25(OH)D levels in the N and ABN group were (98.41 ± 10.23) nmol/L and (56.38 ± 8.95) nmol/L, respectively, suggesting that that in the ABN group was greatly lower and exhibited an obvious difference with that in the N group (P<0.01).

Calcium, phosphorus, ALP, and PTH levels in children

As illustrated in Figure 2, the calcium, phosphorus, ALP, and PTH levels in normal and abnormal children in the N group were (3.95 ± 2.16) nmol/L, (1.98 ± 0.21) nmol/L, (135.71 ± 15.23) U/L, and (1.78 ± 0.20) pmol/L, respectively; while those in the ABN group were (2.16 ± 0.28) nmol/L, (1.64 ± 0.19) nmol/L, (157.88 ± 18.65) U/L, and (2.46 ± 0.17) pmol/L, respectively. Based on the conditions in the N group, the calcium and phosphorus in the ABN group presented greatly lowered levels, while the serum ALP and PTH levels were increased, all showing obvious significances with P<0.01.

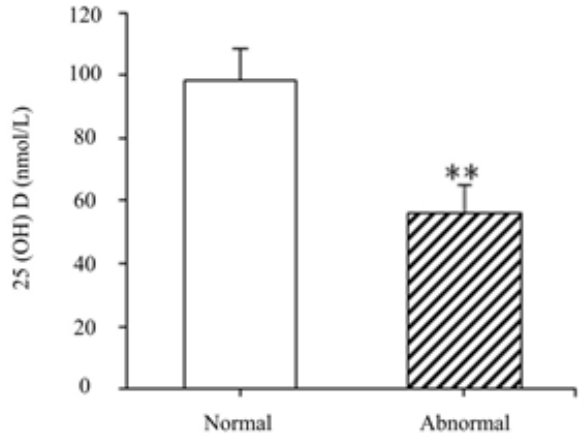

Figure 1. 25(OH)D levels in children. (** suggested a great difference with P<0.05.).

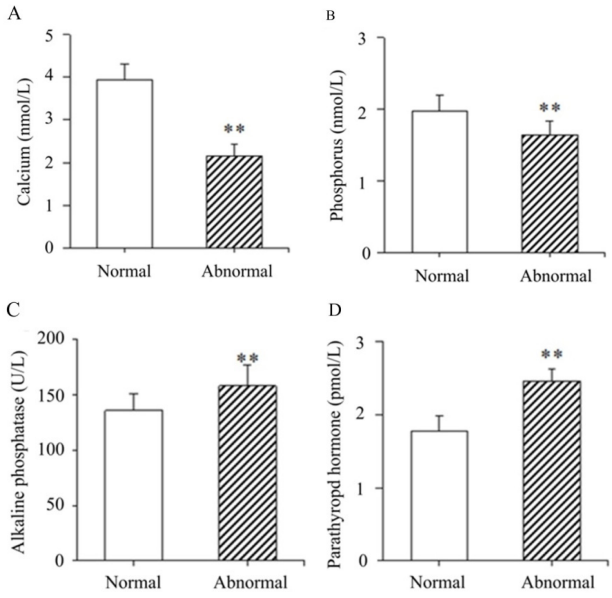

Figure 2. Calcium (A), phosphorus (B), ALP (C), and PTH (D) levels. (** suggested a great difference with P<0.05.).

Correlation between 25(OH)D and bone density

Figure 3 below demonstrates the correlation between 25(OH)D and Z-values of bone density, which revealed that they were positively associated (r=0.918, P<0.01).

Correlations of 25(OH)D to calcium, phosphorus, ALP, and PTH levels

The correlations of 25(OH)D to calcium, phosphorus, ALP, and PTH levels were analyzed, as illustrated in Figure 4 and listed in Table 1. The results suggested that 25(OH)D was positively linked with calcium level (r=0.316, P<0.05), phosphorus level (r=0.209, P<0.05), ALP level (r=-0.428, P<0.01), and PTH level (r=-0.327, P<0.05).

Discussion

Children aged 0 to 3 years are at a critical stage of bone and body growth and development, and factors such as too little exercise, poor nutrition, and abnormal bone density have serious negative effects on infants' growth, and increase the risk of osteomalacia and rickets of infants and

Table 1. Relationship of 25(OH)D to calcium, phosphorus, ALP, and PTH.

Indexes	SD	*r*	*F*	*P*
Calcium	1.902	0.316	4.352	0.031
Phosphorus	2.055	0.209	2.534	0.044
ALP	1.118	-0.428	9.761	0.001
PTH	1.083	-0.327	4.180	0.039

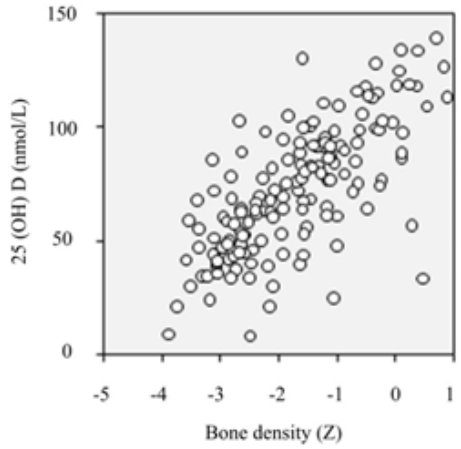

Figure 3. Scatter diagram of 25(OH)D and Z value of bone density.

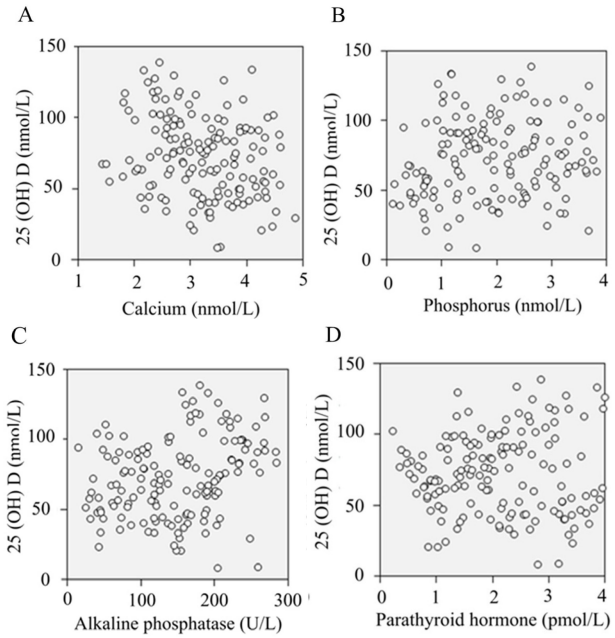

Figure 4. Scatter diagrams of 25(OH)D and calcium (A), phosphorus (B), ALP (C), and PTH (D).

infants (9,10). As an important nutrient for the human body, vitamin D also has hormone-like effects and is crucial in children's growth and development, bone health, and metabolism (11). VD supplements are the primary source of infants and infants in breast milk, infants, mainly obtained from sunlight, but adequate and safe vitamin D exposure to ultraviolet light is highly suspected (12,13). After VD enters the body, it is converted into serum 25(OH)D, which is realized by activating liver 25-hydroxylase, and has the characteristics of stability and high concentration (14). Bone density can reflect the development of human bone. Studies have confirmed that with the increase of age, bone growth and development gradually mature in children, and bone mineral deposition increases, so bone density also increases (15). This work examined differences in 25(OH) D levels of infants in different states of bone density and found that infants and infants with abnormal bone density were sharply lower based on infants in normal states. Active VD greatly affects bone tissue metabolism, which can stimulate osteoblasts to synthesize osteopontin and osteocalcin, thus promoting bone formation (16-18). VD supplements can promote calcium absorption in the body and contribute to enhancing the prevention of osteoporosis (19). 25(OH)D is the best indicator to assess the nutritional status of vitamin D in children. Moreover, 25(OH) D levels of infants were positively correlated with the Z value of ultrasound bone density. The results indicated that the infants bone density increased with the increase of 25(OH)D level. Increased levels of active VD can regulate the metabolism of calcium and phosphorus, and thus affect the state of bone density (20).

Calcium and phosphorus are two kinds of minerals with the highest content in the human body, and their main role is to maintain normal metabolism and physiological functions of the body (21). The serum calcium and phosphorus levels of infants are associated with maternal calcium and phosphorus reserves and autoregulation mechanisms. Results in this work revealed that infants with abnormal bone density were significantly lower in serum calcium and phosphorus levels than infants in normal children, and showed a significant and positive link between infants and infants with abnormal bone density and 25(OH)D levels. VD deficiency or insufficiency can stimulate the increase of kidney 1α-hydroxylase activity, promote the generation of 1,25 (OH) 2D, increase the renal tubule reabsorption of calcium and inhibit the reabsorption of phosphorus, so the blood phosphorus level is reduced (22,23). In addition, the ALP levels of infants reflect the degree of disease and bone metabolism. When the level of ALP increases, the function of osteoblasts increases (24). Bone ALP is mainly synthesized by osteoblasts. When children are in the active stage of rickets, osteoblasts are active, and the level of bone ALP increases (25). PTH is a peptide hormone that works with vitamin D to maintain the stability of calcium and phosphorus in the body. PTH can maintain the serum calcium ion concentration at a normal level by stimulating the renal tubule's calcium reabsorption and bone absorption (26). In addition, the results herein suggested that infants with abnormal bone density were significantly higher than infants in normal infants, and serum ALP and PTH were negatively correlated with serum 25(OH)D levels. PTH can also stimulate bone formation, thereby increasing bone density and improving the microstructure in osteoporosis (27,28). It was suggested that infants and infants of abnormal bone density were provided with early VD supplementation to upregulate 25(OH)D, and to maintain calcium, phosphorus, ALP, and PTH levels in infants and infants.

Conclusion

Serum 25(OH)D reflects the VD nutritional status of

infants. Increasing the 25(OH)D level greatly prevented the infants from abnormal bone density and improved their bone metabolism. Moreover, 25(OH)D was important to reduce the osteomalacia and rickets caused by abnormal bone density in infants and to maintain normal bone growth and development and health of children. However, besides the nutritional status of vitamin D, infants bone metabolism was also affected by age, infection, nutritional diseases, and bone diseases. In the future, more samples should be included to analyze the important factors affecting bone metabolism and bone health in children. In conclusion, the results of this work were intended to offer a reference for improving the bone health status of infants and infants and improving the life quality of children.

References

1. Ahmed Sharif D. The Effectiveness of Vitamin D Supplementation on Oxidative and Inflammatory Markers in Patients Suffering from End-stage Renal Disease, a Randomized Controlled Trial. Cell Mol Biol (Noisy-le-grand) 2022; 68(5): 7-15. https://doi.org/10.14715/cmb/2022.68.5.2
2. Uday S, Manaseki-Holland S, Bowie J, Mughal MZ, Crowe F, Högler W. The effect of vitamin D supplementation and nutritional intake on skeletal maturity and bone health in socio-economically deprived children. Eur J Nutr 2021; 60(6): 3343-3353. https://doi.org/10.1007/s00394-021-02511-5
3. Abbasalizadeh S, Abam F, Mirghafourvand M, Abbasalizadeh F, Taghavi S, Hajizadeh K. Comparing levels of vitamin D, calcium and phosphorus in normotensive pregnant women and pregnant women with preeclampsia. J Obstet Gynaecol 2020; 40(8): 1069-1073. https://doi.org/10.1080/01443615.2019.1678575
4. Zaffanello M, Pietrobelli A, Nosetti L, Piacentini G, Ferrant Ge, Piazza M, Guzzo A, Antoniazzi F. Worldwide interest in vitamin D, negative effects on kidneys, and bone density: analysis of google trends data. J Biol Regulat Homeost Agent 2022; 36(6): 1741-1747. https://doi.org/10.23812/j.biol.regul.homeost.agents.20223606.183
5. Hemamy M, Pahlavani N, Amanollahi A, Islam SMS, McVicar J, Askari G, Malekahmadi M. The effect of vitamin D and magnesium supplementation on the mental health status of attention-deficit hyperactive children: a randomized controlled trial. BMC Pediatr 2021; 21(1): 178. https://doi.org/10.1186/s12887-021-02631-1
6. Żebrowska A, Sadowska-Krępa E, Stanula A, Waśkiewicz Z, Łakomy O, Bezuglov E, Nikolaidis PT, Rosemann T, Knechtle B. The effect of vitamin D supplementation on serum total 25(OH) levels and biochemical markers of skeletal muscles in runners. J Int Soc Sports Nutr 2020; 17(1): 18. https://doi.org/10.1186/s12970-020-00347-8
7. Portales-Castillo I, Simic P. PTH, FGF-23, Klotho and Vitamin D as regulators of calcium and phosphorus: Genetics, epigenetics and beyond. Front Endocrinol (Lausanne) 2022; 13: 992666. https://doi.org/10.3389/fendo.2022.992666
8. Rajab HA. The Effect of Vitamin D Level on Parathyroid Hormone and Alkaline Phosphatase. Diagnostics (Basel) 2022; 12(11): 2828. https://doi.org/10.3390/diagnostics12112828
9. Gupta P, Dabas A, Seth A, Bhatia VL, Khadgawat R, Kumar P, Balasubramanian S, Khadilkar V, Mallikarjuna HB, Godbole T, Krishnamurthy S, Goyal JP, Bhakhri BK, Ahmad A, Angadi K, Basavaraj GV, Parekh BJ, Kurpad A, Marwaha RK, Shah D, Munns C, Sachdev HPS. Indian academy of pediatrics revised (2021) guidelines on prevention and treatment of vitamin D deficiency and rickets. Indian Pediatr 2022; 59(2): 142-158. https://doi.org/10.1007/s13312-022-2448-y
10. Crowe FL, Mughal MZ, Maroof Z, Berry J, Kaleem M, Abburu S, Walraven G, Masher MI, Chandramohan D, Manaseki-Holland S. Vitamin D for Growth and Rickets in Stunted Children: A Randomized Trial. Pediatrics 2021; 147(1): e20200815. https://doi.org/10.1542/peds.2020-0815
11. Cheng HY, Hao JZ, Song YJ, Zhang WH. Effects of vitamin D on glucose and lipid metabolism, endocrine and ovarian morphology and function in rats with polycystic ovary syndrome. Acta Med Mediterr 2022; 3: 2165. https://doi.org/10.19193/0393-6384_2022_3_331
12. Mazahery H, Conlon CA, Beck KL, Mugridge O, Kruger MC, Stonehouse W, Camargo CA Jr, Meyer BJ, Jones B, von Hurst PR. A randomised controlled trial of vitamin D and omega-3 long chain polyunsaturated fatty acids in the treatment of irritability and hyperactivity among children with autism spectrum disorder. J Steroid Biochem Mol Biol 2019; 187: 9-16. https://doi.org/10.1016/j.jsbmb.2018.10.017
13. Khadilkar A, Kajale N, Oza C, Oke R, Gondhalekar K, Patwardhan V, Khadilkar V, Mughal Z, Padidela R. Vitamin D status and determinants in Indian children and adolescents: a multicentre study. Sci Rep 2022; 12(1): 16790. https://doi.org/10.1038/s41598-022-21279-0
14. Hattangdi-Haridas SR, Lanham-New SA, Wong WHS, Ho MHK, Darling AL. Vitamin D Deficiency and Effects of Vitamin D Supplementation on Disease Severity in Patients with Atopic Dermatitis: A Systematic Review and Meta-Analysis in Adults and Children. Nutrients 2019; 11(8): 1854. https://doi.org/10.3390/nu11081854
15. Deodati A, Manco M, Mariani M, Bocchini S, Högler W, Cappa M, Fintini D. Bone density and body composition in small for gestational age children with adequate catch up growth: A preliminary retrospective case control study. Bone 2021; 153: 116114. https://doi.org/10.1016/j.bone.2021.116114
16. Nuszkiewicz J, Czuczejko J, Maruszak M, Pawłowska M, Woźniak A, Małkowski B, Szewczyk-Golec K. Parameters of Oxidative Stress, Vitamin D, Osteopontin, and Melatonin in Patients with Lip, Oral Cavity, and Pharyngeal Cancer. Oxid Med Cell Longev 2021; 2021: 2364931. https://doi.org/10.1155/2021/2364931
17. Wein M, Huelter-Hassler D, Nelson K, Fretwurst T, Nahles S, Finkenzeller G, Altmann B, Steinberg T. Differential osteopontin expression in human osteoblasts derived from iliac crest and alveolar bone and its role in early stages of angiogenesis. J Bone Miner Metab 2019; 37(1): 105-117. https://doi.org/10.1007/s00774-017-0900-1
18. Hill TR, Verlaan S, Biesheuvel E, Eastell R, Bauer JM, Bautmans I, Brandt K, Donini LM, Maggio M, Mets T, Seal CJ, Wijers SL, Sieber C, Cederholm T, Aspray TJ; PROVIDE Consortium. A Vitamin D, Calcium and Leucine-Enriched Whey Protein Nutritional Supplement Improves Measures of Bone Health in Sarcopenic Non-Malnourished Older Adults: The PROVIDE Study. Calcif Tissue Int 2019; 105(4): 383-391. https://doi.org/10.1007/s00223-019-00581-6
19. Chevalley T, Brandi ML, Cashman KD, Cavalier E, Harvey NC, Maggi S, Cooper C, Al-Daghri N, Bock O, Bruyère O, Rosa MM, Cortet B, Cruz-Jentoft AJ, Cherubini A, Dawson-Hughes B, Fielding R, Fuggle N, Halbout P, Kanis JA, Kaufman JM, Lamy O, Laslop A, Yerro MCP, Radermecker R, Thiyagarajan JA, Thomas T, Veronese N, Wit MD, Reginster JY, Rizzoli R. Role of vitamin D supplementation in the management of musculoskeletal diseases: update from an european society of clinical and economical aspects of osteoporosis, osteoarthritis and musculoskeletal diseases (ESCEO) working group. Aging Clin Exp Res 2022; 34(11): 2603-2623. https://doi.org/10.1007/s40520-022-02279-6

20. Miteva MZ, Nonchev BI, Orbetzova MM, Stoencheva SD. Vitamin D and Autoimmune Thyroid Diseases - a Review. Folia Med (Plovdiv) 2020; 62(2): 223-229. https://doi.org/10.3897/folmed.62.e47794
21. Ciosek Ż, Kot K, Kosik-Bogacka D, Łanocha-Arendarczyk N, Rotter I. The Effects of Calcium, Magnesium, Phosphorus, Fluoride, and Lead on Bone Tissue. Biomolecules 2021; 11(4): 506. https://doi.org/10.3390/biom11040506
22. Valentini A, Perrone MA, Cianfarani MA, Tarantino U, Massoud R, Merra G, Bernardini S, Morris HA, Bertoli A. Obesity, vitamin D status and physical activity: 1,25(OH)2D as a potential marker of vitamin D deficiency in obese subjects. Panminerva Med 2020; 62(2): 83-92. https://doi.org/10.23736/S0031-0808.20.03770-2
23. Ciacci C, Bilancio G, Russo I, Iovino P, Cavallo P, Santonicola A, Bucci C, Cirillo M, Zingone F. 25-Hydroxyvitamin D, 1,25-Dihydroxyvitamin D, and peripheral bone densitometry in adults with celiac disease. Nutrients 2020; 12(4): 929. https://doi.org/10.3390/nu12040929
24. Thacher TD, Sempos CT, Durazo-Arvizu RA, Fischer PR, Munns CF, Pettifor JM. The Validity of Serum Alkaline Phosphatase to Identify Nutritional Rickets in Nigerian Children on a Calcium-Deprived Diet. J Clin Endocrinol Metab 2021; 106(9): e3559-e3564. https://doi.org/10.1210/clinem/dgab328
25. Jin H, Cai W, Yu D, Fan J, Liu Q, Yu J. Development of Proliferative Vitreoretinopathy Is Attenuated by Chicken Ovalbumin Upstream Promoter Transcriptional Factor 1 Via Inhibiting Epithelial-Mesenchymal Transition. Discov Med 2022; 34(172): 103-113.
26. Dawale K, Agrawal A. Parathyroid Hormone Secretion and Related Syndromes. Cureus 2022; 14(10): e30251. https://doi.org/10.7759/cureus.30251
27. Zhao LH, Ma S, Sutkeviciute I, Shen DD, Zhou XE, de Waal PW, Li CY, Kang Y, Clark LJ, Jean-Alphonse FG, White AD, Yang D, Dai A, Cai X, Chen J, Li C, Jiang Y, Watanabe T, Gardella TJ, Melcher K, Wang MW, Vilardaga JP, Xu HE, Zhang Y. Structure and dynamics of the active human parathyroid hormone receptor-1. Science 2019; 364(6436): 148-153. https://doi.org/10.1126/science.aav7942
28. Ogunwale AN, Hameed F, Valdez L, des Bordes J, Jamil M, Rianon N. Elevated parathyroid hormone levels in older women treated for osteoporosis using denosumab. Eur Geriatr Med 2022; 13(3): 735-740. https://doi.org/10.1007/s41999-021-00567-4