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INTERRELATION BETWEEN VITAMIN D DEFICIENCY AND SOMATIC COMPLICATIONS IN CHRONIC PANCREATITIS
(review article)

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Abstract: Chronic pancreatitis (CP) represents a progressive inflammatory disease of the pancreas, characterized by irreversible morphological changes and persistent impairment of its exocrine and endocrine functions. One of the critical metabolic disturbances associated with CP is malabsorption of essential nutrients, particularly fat-soluble vitamins such as vitamin D. Owing to the exocrine insufficiency of the pancreas, patients with CP frequently develop vitamin D deficiency, which significantly exceeds that observed in the general population. This deficiency contributes to a range of systemic complications, including disorders of calcium-phosphorus metabolism, osteopenia, osteoporosis, muscle weakness, cardiovascular dysfunction, and increased susceptibility to infectious diseases.
The present review provides an in-depth analysis of the pathophysiological mechanisms linking vitamin D deficiency to chronic pancreatitis, emphasizing its role in inflammation modulation, immune regulation, and bone metabolism. Special attention is given to current laboratory diagnostic methods for assessing vitamin D status, including the measurement of serum 25(OH)D concentrations, and the interpretation of these findings within the context of somatic comorbidities. Furthermore, the review highlights the clinical importance of early detection, monitoring, and correction of vitamin D deficiency as a preventive and therapeutic strategy aimed at reducing disease burden, improving musculoskeletal and metabolic outcomes, and enhancing the overall quality of life in patients with chronic pancreatitis.
Keywords: chronic pancreatitis, vitamin D, vitamin D deficiency, pathogenesis, laboratory diagnostics, somatic risks, osteoporosis, inflammation, metabolic disorders.

According to experts from the World Health Organization (WHO), the development of a unified international strategy is essential for the effective prevention of osteoporosis (OP) and control of its prevalence [22; p. 287, 7; pp. 834–841]. Expert assessments indicate that osteoporosis ranks fourth in prevalence among chronic non-communicable diseases, following cardiovascular diseases, oncological disorders, and diabetes mellitus. The severe complications associated with OP have a considerable impact on both the healthcare system and the social sphere [30; p. 176, 8; p. 534, 11; pp. 1282–1291.e3].
In this regard, the WHO identifies three priority areas in addressing osteoporosis: early diagnosis, prevention, and treatment. The preventive aspect of this strategy focuses on improving early detection methods, identifying and minimizing risk factors, strengthening bone tissue, slowing the loss of bone mass, and preventing pathological fractures.
The global prevalence of vitamin D deficiency and the resulting damage to various organs and tissues highlight the need for a comprehensive, interdisciplinary approach to this problem. Moreover, the increasing incidence of diseases directly associated with vitamin D deficiency has drawn significant scientific attention. At present, the pathogenetic role of vitamin D deficiency in the development of several gastrointestinal disorders, as well as other somatic pathologies, has

been established [34; p. 151, 6; pp. 1151–1154, 16; pp. 1911–1930, 26; pp. 493–496, 27; pp. 15–18].

Alimentary (nutritional) vitamin D deficiency, which leads to the development of rickets in children and osteomalacia in adults, has been thoroughly studied [46; pp. 528–531, 32; pp. 75–79]. At the same time, the pathogenetic mechanisms and clinical manifestations of vitamin D and calcium deficiency observed in chronic renal failure, hypoparathyroidism, and malabsorption syndrome have been well described [41; pp. 20–27, 29; pp. 258–261, 40; pp. 69–75].

Experimental and clinical studies have confirmed the important role of vitamin D in reducing the risk of various diseases, including arterial hypertension, atherosclerosis, neoplastic processes, autoimmune and chronic inflammatory diseases, as well as reproductive system disorders [33; p. 151, 41; pp. 20–27, 7; p. 75, 17; pp. 800–806].

The chemical structure of the “vitamin D” group includes the steroid compounds ergocalciferol (D2) and cholecalciferol (D3), both of which possess biological activity. The main sources of ergocalciferol are dietary products such as grains, fish oil, butter, milk and dairy products, and egg yolk. Cholecalciferol is synthesized in the body under the influence of sunlight: ultraviolet rays convert cholesterol in subcutaneous fat into vitamin D [16; pp. 1911–1930].

Exposure to sunlight causing slight skin reddening leads to the synthesis of approximately 150 ng/mL of 25(OH)D; however, after the age of 65, the efficiency of this process decreases about fourfold [16; pp. 1911–1930]. About 90% of circulating vitamin D in the blood is cholecalciferol synthesized in subcutaneous tissue, while only about 10% comes from dietary intake [39; pp. 46–51, 14; pp. 2946–2957].

In the blood, vitamin D is bound to lipoproteins or a binding protein, but these forms are inactive. Activation occurs in the liver via microsomal cytochrome P450 2R1 (Cyp2R1) and mitochondrial cytochrome P450 (Cyp27A1) 25-hydroxylases, forming 25-(OH) vitamin D. Subsequently, in the kidneys, mitochondrial 1α,25-hydroxylase Cyp27B1 converts it into the metabolically active form, 1α,25(OH)2D3 (calcitriol).

This renal process is regulated by negative feedback based on blood calcium concentration and parathyroid hormone levels. The primary targets of 1α,25(OH)2D3 are enterocytes, cells of the loop of Henle, and osteoblasts. Active vitamin D increases blood calcium levels by enhancing intestinal absorption and renal reabsorption of calcium, while also lowering parathyroid hormone levels.

Vitamin D also activates cellular immunity and promotes cell growth and differentiation by influencing myeloblasts, promyelocytes, and osteoblasts [44; p. 560].

The mechanism of action of calcitriol is associated with the formation of a hormone-receptor complex through binding to a nuclear receptor—transcription activator, heterodimerization with the retinoid X receptor, and subsequent binding to vitamin D-responsive elements in DNA. Calcitriol’s effects on target cells can also be mediated through non-genomic signaling pathways. The impact of vitamin D on vascular smooth muscle cells, endothelial cells, and cardiomyocytes occurs at the gene level [38; pp. 5–14, 4; p. 1392]. Calcitriol can also act on target cells via paracrine, autocrine, and intracrine mechanisms. This regulation influences the production of numerous cytokines involved in inflammation and fibrosis, as well as the activity of the immune response and the renin-angiotensin-aldosterone system (RAAS) [3; pp. 207–221].

Regulation of bone remodeling by vitamin D occurs through both direct and indirect mechanisms. It is known that bone tissue lacks receptors for this vitamin, so osteoclastogenesis is controlled indirectly [41; pp. 31–37]. In contrast, osteoblasts possess vitamin D receptors, allowing the vitamin to act indirectly by enhancing the synthesis of biologically active peptide factors in bone tissue and promoting osteoblast differentiation.

Notably, 1α,25(OH)2D3 activates the differentiation and proliferation of striated muscle and regulates calcium-dependent muscle contraction mechanisms. Increased plasma levels of 1α,25(OH)2D3 also influence lymphocytes, monocytes, and macrophages.

Vitamin D and its metabolites are involved in regulating the activity of over 100 genes, most of which control the cell cycle.

1α,25(OH)2D3 binds to its specific nuclear receptor (VDR), functioning as a transcription factor and regulating the expression of numerous genes. According to some authors, vitamin D receptors are present in more than 40 tissues and regulate 3–5% of the human genome [32; p. 75, 16; pp. 1911–1930, 46; pp. 70–74]. However, researchers note that erythrocytes, the myometrium, and Purkinje cells of the brain do not contain VDR.

The absence or reduced activity of VDR impairs the action of 1,25(OH)2D3, including decreased calcium absorption in the intestine and reduced renal tubular reabsorption. This often leads to vitamin D-resistant conditions, hypocalcemia, and secondary hyperparathyroidism.

Vitamin D exhibits suppressive effects on inflammatory processes, primarily by inhibiting the synthesis of pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α, which are produced by monocytes and T-lymphocytes. Studies by Eghshatyan L.V. et al. (2014) demonstrated vitamin D deficiency in patients with inflammatory bowel diseases and severe tuberculosis [33; pp. 27–30].

Under bacterial influence, toll-like receptors (TLRs) in macrophages are activated, leading to the expression of VDR and CYP27B1 genes, stimulation of cathelicidin synthesis with antimicrobial activity, and pathogen elimination. Additionally, vitamin D strengthens intestinal epithelial membranes and regulates gut microbiota. According to researchers, vitamin D controls immune responses and influences immune tolerance to intestinal microbiota. The presence of VDR in the gut suppresses bacteria-induced activation of nuclear factor kappa B (NF-κB) [33; pp. 27–30, 47; pp. 84–92].

Calcidiol and calcitriol inhibit NF-κB activity in smooth muscle cells, reduce the expression of metalloproteinases, and inhibit vascular growth factors. Some researchers associate the anti-atherosclerotic effect of calcitriol with an increased number of Foxp3+ T-lymphocytes, suppression of dendritic cell maturation in atherosclerotic plaques, and elevated osteopontin levels, which prevent vascular calcification.

Studies by Zittermann A., Schleithoff S.S., and Koerfer R. (2005) demonstrated that prostacyclin synthesis is activated in vascular smooth muscle cells, which, according to the authors, prevents thrombosis, cell adhesion, and smooth muscle cell proliferation, as well as reduces the expression of plasminogen activator inhibitor-1 [2; pp. 1555–1560].

Research by Mackawy A. et al. (2014) revealed a direct correlation between vitamin D levels and increased tissue sensitivity to insulin. The authors suggest that this is related to enhanced expression of insulin receptors and decreased phosphorylation of their substrates.

According to the clinical guidelines of the Russian Association of Endocrinologists (2015), mass population screening for vitamin D deficiency is not required. Screening is recommended only for patients with risk factors [35; pp. 528–531, 32; pp. 75, 43; pp. 60–84].

To assess vitamin D status in the body, its stable serum form—25(OH)D (calcidiol)—is measured according to international standards (DEQAS, NIST). Expert recommendations classify vitamin D status as follows [32; pp. 75, 43; pp. 60–84]:

- Normal level: 25(OH)D in plasma >30 ng/mL (75 nmol/L)
- Vitamin D insufficiency: 25–30 ng/mL (50–75 nmol/L)
- Vitamin D deficiency: <20 ng/mL (50 nmol/L)

According to expert recommendations, during vitamin D treatment, blood levels should rise to 30–60 ng/mL (75–150 nmol/L) [32; pp. 75, 43; pp. 60–84]. The plasma concentration of

25(OH)D should be re-measured three days after the end of the treatment course using the same method [32; pp. 75, 49; pp. 32–38].

For congenital and acquired disorders of vitamin D metabolism, it is recommended to simultaneously measure plasma levels of 1,25(OH)2D and 25(OH)D.

Epidemiological studies among postmenopausal women have shown that most of them have vitamin D deficiency, with 25(OH)D levels below 20 ng/mL [23; pp. 11–17]. Reduced vitamin D synthesis leads to impaired calcium-dependent processes, disrupted impulse transmission from motor neurons to striated muscles, neuromuscular dysfunction, and decreased muscle contractions. As a result, elderly individuals experience slower motor activity, poorer coordination, and an increased risk of falls [10; pp. 1533–1538, 5; pp. 12–16].

Studies by Belarusian researchers have shown that women with type 2 diabetes have lower plasma vitamin D levels compared to healthy women of the same age [48; pp. 11–17].

According to the clinical guidelines of the Russian Association of Endocrinologists (2015), "Vitamin D Deficiency in Adults: Diagnosis, Treatment, and Prevention," cholecalciferol (D3) and ergocalciferol (D2) are recommended for prevention [32; pp. 75, 43; pp. 60–84].

According to the recommendations of the U.S. Institute of Medicine, the daily preventive dose of vitamin D for healthy individuals aged 18–50 years should be at least 600 IU. For those over 50 years of age, the dose should be at least 800–1000 IU, and for pregnant and breastfeeding women, at least 800–1200 IU. Patients with gastrointestinal malabsorption should receive 2–3 times the standard daily dose [32; pp. 75, 43; pp. 60–84, 18; pp. 402–409].

According to the literature, patients with chronic pancreatitis (CP) develop exocrine pancreatic insufficiency, leading to impaired absorption of dietary fats and fat-soluble vitamins. Compared to the general population, CP patients more frequently exhibit vitamin D deficiency (57.6%; 95% CI 43.9–70.4) [13; pp. 172, 15; pp. 57–61].

Clinical data indicate that approximately 40% of patients with acute or chronic pancreatitis have severe vitamin D deficiency, and this figure can reach 60% in patients with CP [36; pp. 156–160, 25; p. 5779]. This increases the risk of osteoporosis [40; pp. 219–228], muscle weakness, infectious diseases [33; pp. 27–30], cardiovascular disorders [38; pp. 5–14], and reproductive dysfunction [34; pp. 151].

According to the study by Bideev T.V. et al. (2019), vitamin D supplementation in patients with CP resulted in normalization of plasma vitamin D levels [6; pp. 156–160]. European and Russian pancreatology guidelines indicate that in patients with CP and impaired exocrine pancreatic function, clinical, laboratory, and coprological diagnostics allow for accurate selection of enzyme replacement therapy, which positively affects vitamin D deficiency [37; pp. 70–97].

However, it should be noted that the conversion of 25(OH)D3 to 1,25(OH)2D3 occurs via activated macrophages in tissues and may increase the risk of inflammation [15; pp. 172, 20; pp. 541–553]. According to the authors, the reduction of 25(OH)D3 and 1,25(OH)2D3 levels in patients with pancreatitis may represent a protective response of the body aimed at preventing hypercalcemia. The body decreases the production and secretion of 1,25(OH)2D3 and parathyroid hormone by inhibiting the activity of the CYP27B1 enzyme in the kidneys [15; pp. 172, 19; pp. 13–31, 21; pp. 1109–1114].

In addition to the kidneys, the CYP27B1 enzyme is synthesized in the colon, adrenal glands, prostate, mammary glands, brain, and placenta, providing local formation of 1,25(OH)2D3 [23; pp. 327–331]. It should be noted that extrarenal synthesis of 1,25(OH)2D3 is not regulated by parathyroid hormone and does not participate in maintaining blood calcium homeostasis [1; pp. 95–102], acting instead via autocrine and paracrine mechanisms.

According to some authors, extrarenal synthesis of 1,25(OH)2D3 may have negative effects, including contributing to the development of acute pancreatitis [12; pp. 157–163, 25; pp.

1623–1636]. In this case, an increase in calcium concentration in the cytoplasm of calcium-sensitive pancreatic acinar cells activates proteases and leads to their necrosis [12; pp. 157–163].

U.C. Bang et al. (2011) established a correlation between decreased plasma 25(OH)D3 levels in patients with acute pancreatitis and increased C-reactive protein concentrations [28; pp. 135–141]. Many studies have shown that patients with chronic pancreatitis often have plasma 25(OH)D3 levels below 20 ng/mL [24; pp. 1558–1561]. According to the authors, 1,25(OH)2D3 levels in patients with chronic pancreatitis are 40–60% lower than in healthy individuals.

Literature data regarding hypercalcemia and the development of acute pancreatitis are contradictory, requiring a deeper analysis of the pathogenesis of hypercalcemia and chronic pancreatitis. If a negative correlation between them does exist, clinicians face a dilemma in treating chronic pancreatitis, as more than 60% of patients develop osteopenia and osteoporosis. In such cases, vitamin D supplementation may increase the risk of adverse outcomes.

Conclusion. Thus, chronic pancreatitis (CP) is one of the widely prevalent diseases, characterized by a recurrent course, resistance to therapy, reduced working capacity, and the potential development of disability. In CP, there is insufficiency of the exocrine function of the pancreas, which is accompanied by impaired breakdown and absorption of nutrients, particularly leading to a deficiency of fat-soluble vitamins.

A rational collection of medical history, correct analysis of clinical manifestations, assessment of pancreatic functional status, and proper implementation of a diagnostic program allow for adequate therapy of CP and the formulation of justified prognoses regarding disease progression, as well as contribute to a reduction in patient disability. Analysis of disease risk factors and results from large-scale scientific studies confirm that CP represents a significant medical and social problem on a global scale.

At the same time, analysis of CP pathogenesis, evaluation of inflammatory processes involving vitamin D, and determination of whether vitamin D deficiency is a cause or consequence of the disease remain relevant challenges in modern pancreatology. Addressing these issues is important, as assessing vitamin D levels in patients with CP and correcting its deficiency when necessary can improve patients' quality of life, restore digestive processes, and, importantly, prevent the development of osteopenia and osteoporosis.

From this perspective, research focused on the course of the disease in CP patients with vitamin D deficiency, the identification of complications, and the development of principles for correcting vitamin D levels is currently highly relevant.

References.

1. Adams J.S., Hewison M. Extrarenal expression of the 25-hydroxyvitamin D-1-hydroxylase. // Arch Biochem Biophys. 2012; 523: 95-102.
2. Al-Badr W., Martin K.J. Vitamin D and kidney disease // Clin. J. Am. Soc. Nephrol. 2008; 3: 1555-1560.
3. Artaza J.N., Norris K.C. Vitamin D reduces the expression of collagen and key profibrotic factors by inducing an antifibrotic phenotype in mesenchymalmultipotent cells // J. Endocrinol. 2009; 200: 207-221.
4. Bang, Novovic S, Andersen AM, Fenger M, Hansen MB, et al. Variations in serum 25-hydroxyvitamin D during acute pancreatitis: an exploratory longitudinal study. // Endocr Res. 2011; 36: 135-141.
5. Choi HS. Vitamin D Status in Korea. //Endocrinol Metab (Seoul). 2013; 28: 12–16.

6. Dawson-Hughes B. et al. IOF position statement: vitamin D recommendations for older adults // Osteoporos. Int. 2010; 21: 1151-1154.
7. D'Haese JG, Ceyhan GO, Demir IE, et al. Pancreatic enzyme replacement therapy in patients with exocrine pancreatic insufficiency due to chronic pancreatitis: a 1-year disease management study on symptom control and quality of life. //Pancreas. 2014; 43: 834–41.
8. Domínguez-Muñoz JE, Nieto-Garcia L, López-Díaz J, et al. Impact of the treatment of pancreatic exocrine insufficiency on survival of patients with unresectable pancreatic cancer: a retrospective analysis. //BMC Cancer. 2018; 18: 534.
9. Duggan S.N., Smyth N.D., Murphy A. et al. High prevalence of osteoporosis in patients with chronic pancreatitis: a systematic review and meta-analysis. // Clin. Gastroenterol. Hepatol. 2014; 12: 219-228.
10. Flicker L.et al. Serum vitamin D and falls in older women in residential care in Australia // J. Am. Geriatr. Soc. 2003; 51: 1533-1538.
11. Frick T.W. Herole of calcium in acute pancreatitis. // Surgery. 2012; 152: 157-163.
12. Forsmark C.E. Chronic Pancreatitis. //In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. /Edited by M. Feldman, L.S. Friedman, L.J. Brandt. 10th ed. 2015.
13. Gromova O.A., Torshin I.Yu., Pronin A.V., Rudakov K.V. Systematic analysis of neurological roles and prospects for the use of vitamin D for the prevention and treatment of cerebrovascular and demyelinating diseases // Neurology and psychiatry named after S.S. Korsakov. 2014; 12: 57-61.
14. Guía-Galipienso De La., Martínez-Ferran F., Vallecillo M., Lavie N., Sanchis-Gomar C. J., and Pareja-Galeano F., (2021). Vitamin D and Cardiovascular Health. //Clin. Nutr. 2021; 40 (5): 2946–2957.
15. Han Z., Margulies S.L., Kurian D., Elliott M.S. Vitamin D Deficiency in Patients with Pancreatitis: Is Vitamin D Replacement Required? // Pancreat Disord Ther. 2016. 172 (6).
16. Holick M.F. et al. Endocrine Society. Evaluation, treatment and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline // J. Clin. Endocrinol. Metab. 2011; 96(7): 1911-1930.
17. Hoogenboom, SA, Lekkerkerker, SJ, Fockens, P., Boermeester, MA, and van Hooft, JE. Systematic review and meta-analysis of the prevalence of vitamin D deficiency in patients with chronic pancreatitis // Pancreatology. 2016; 16(5):800–806.
18. Hummel, D., Aggarwal, A., Borka, K., et al. Vitamin D System Impaired in Pancreatic Diseases //J Steroid Biochem Mol Biol. 2014; 144 (Pt B): 402–409.
19. Jones G., Prosser D.E., Kaufmann M. Cytochrome P450-mediated metabolism of vitamin D. // J Lipid Res. 2014; 55: 13-31.
20. Kahn, Z.S., Wang, K., Han, H.L., Du, J.J., Lee, Y.Y., & Zhang, K. Design, synthesis, and biological evaluation of a non-secosteridal ligand of the vitamin D receptor carrying a double side chain for the treatment of chronic pancreatitis // 2018; 146: 541-553.
21. Kanakis A, Vipperla K, Papachristou GI, Brand RE, Slivka A,Whitcomb DC, et al. Bone health assessment in clinical practice is infrequenty performed in patients with chronic pancreatitis. //Pancreatology. 2020; 20(6): 1109-1114.
22. Kanis J.A. //On behalf of the World Health Organization Scientific Group. Assessment of osteoporosis at the primary health care level. Technical Report. //World Health Organization Collaborating Center for Metabolic Bone Diseases, University of Sheffield, UK. – Printed by the University of Sheffield, 2007. 287 p.
23. Kaur, P., Mishra, S.K., Mithal, A. Vitamin D toxicity as a result of over-correction of vitamin D deficiency. //ClinEndocrinol. 2015 (Oxf); 83: 327-331.

24. Khamraev A.A. , Inoyatova F.Kh., Aripova N.N Content Of 25(Oh)D In The Blood Serum Of Tashkent City Residents // journal of Pharmaceutical Negative Results. 2022; 13 (8): 1558-1561.
25. Kordes M, Larsson L, Engstrand L, et al. Pancreatic cancer cachexia: three dimensions of a complex syndrome. //Br J Cancer. 2021; 124: 1623–1636.
26. 26. Aripova N.N., Inoyatova F.Kh., Khamraev A.A. The influence of vitamin D on carpology parameters in patients with chronic pancreatitis // Tibbiyotda yangi kun. - 2022. - No. 11 (49). - P. 493-496.
27. 27. Aripova N.N., Khamraev A.A., Sobirova G.N. Vitamin D deficiency and exocrine pancreatic insufficiency: issues of therapeutic correction // Therapeutic Bulletin of Uzbekistan. - 2023. - No. 11. - P. 15-18.
28. 28. Aripova N.N., Khamraev A.A., Sobirova G.N. A Mathematical Model for Predicting the Efficiency of Treatment of Patients with Chronic Pancreatitis with Exocrine Pancreatic Insufficiency and Vitamin D Deficiency //MEDUNION. – 2023. – Vol. 2, No. 3. – P. 75-79.
29. 29. Aripova N.N., Khamraeva A.A. The Importance of Vitamin D in the Development of Pancreatitis // Therapeutic Bulletin of Uzbekistan (TMA). - 2022. - No. 2. – P. 258-261.
30. 30. Benevolenskoy L.I., Lesnyak O.M. Clinical Guidelines. Osteoporosis. Diagnostics, Prevention, and Treatment. / Under the general editorship. GEOTAR-Media, 2005. – P. 176.
31. 31. Bideeva T.V., Andreev D.N., Kucheryavy Yu.A., Maev I.V. Dynamics of vitamin D levels in patients with chronic pancreatitis during enzyme replacement therapy // Medical Council. - 2019. - No. 3. – P. 156-160.
32. 32. Dedov I.I., Melnichenko G.A. Clinical guidelines. Vitamin D deficiency in adults: diagnosis, treatment and prevention. - M., 2015. – 75 p.
33. 33. Egshatyan L.V., Dudinskaya E.N., Tkacheva O.N., Kashtanova D.A. The role of vitamin D in the pathogenesis of chronic non-communicable diseases. // Osteoporosis and osteopathy. - 2014. - Vol. 17, No. 3. - P. 27-30.
34. 34. Zazerskaya I.E. et al. Vitamin D and women's reproductive health. // St. Petersburg: OOO ‘Eco-Vector’, 2017.- 151 p.
35. 35. Zakharova I.N. et al. Vitamin D deficiency in adolescents: results of year-round screening in Moscow // Pediatric pharmacology. - 2015. - Vol. 12, No. 5. - P. 528-531.
36. 36. Ivanov Yu.V., Alekhnovich A.V., Pastukhov A.I. New approaches to the complex treatment of biliary pancreatitis: scientific publication // Annals of surgery. - Moscow, 2005. - No. 4. - P. 43-46.
37. 37. Ivashkin V. T., Maev I. V., Okhlobystin A. V., et al. Recommendations of the Russian Gastroenterological Association for the Diagnosis and Treatment of Chronic Pancreatitis. // Russ. J. Gastroenterol., Hepatol., Coloproctol. - 2014. - Vol. 24, No. 4. - P. 70–97.
38. 38. Kulikov V. A., Grebennikov I. N. The Role of Vitamins D and K in the Development of Vascular Calcification and Atherosclerosis // Vestnik of VSMU. - 2012. - Vol. 11, No. 4. - P. 5–14.
39. 39. Lashkova Yu. S. Prevention and Treatment of Vitamin D Deficiency: A Modern View of the Problem // Pediatric Pharmacology. - 2015. - Vol. 12, No. 1. - P. 46-51.
40. 40. Lutsenko A.S., Rozhinskaya L.Ya., Toroptsova N.V., Belaya Zh.E. The role and place of calcium and vitamin D preparations for the prevention and treatment of osteoporosis. // Osteoporosis and osteopathy. - 2017. - Vol. 20, No. 2. - P. 69-75.

41. 41. Naumov A.V. Hormone D3 as a vitamin for comorbid conditions: who, when and how? // Difficult patient. - 2018. - Vol. 16, No. 3. - P. 20–27.
42. 42. Pigarova E.A., Dzeranova L.K., Yatsenko D.A. Vitamin D: issues of absorption and metabolism in normal and diseased gastrointestinal tract // Obesity and Metabolism. - 2022. - Vol. 19, No. 1. - Pp. 123-133
43. 43. Pigarova E.A., Rozhinskaya L.Ya., Belaya Zh.E. et al. Clinical guidelines of the Russian Association of Endocrinologists for the diagnosis, treatment, and prevention of vitamin D deficiency in adults // Probl. endocr. - 2016. - Vol. 62, No. 4. - Pp. 60–84.
44. 44. Riggs B.L., Melton L.J. Osteoporosis. Etiology, diagnosis, treatment. // Translated from English. Moscow - St. Petersburg: ZAO Izdatelstvo BINOM, Nevsky Dialect, 2000. - 560 p.
45. 45. Sergeev, I. N. Vitamin D status and vitamin D-dependent apoptosis in obesity. // Nutrients. - 2020. - Vol. 12, No. 5. - P. 1392.
46. 46. Sobirova, G. N., Aripova, N. N. The role of vitamin D in pancreatic function and its dependence on obesity // Journal of Nutrition. - 2022. - No. 11 (49). - P. 70-74.
47. 47. Suplotova, L. A., Avdeeva, V. A., Pigarova, E. A., Rozhinskaya, L. Ya., Troshina, E. A. Vitamin D deficiency in Russia: first results of a registry-based non-interventional study of the incidence of vitamin D deficiency and insufficiency in different geographic regions of the country. // Problems of Endocrinology. - 2021. - Vol. 67, No. 2. - Pp. 84-92.
48. 48. Shepelkevich A.P. Modern approaches to the prevention and treatment of vitamin D deficiency // Medical news. - 2016. - No. 6. - Pp. 11-17.
49. 49. Shugurova I.M., Shtuchnyy I.V., Vitamin D. Mechanisms of action and therapeutic potential // Journal "Zemsky Vrach" Almanac. - 2021. - Pp. 32-38.