









Journal Homepage: http://mjtu.tu.edu.iq



## Effect of Adiposity on Vitamin D level

#### Sura Khairialdeen Mohialdeen

University of Mosul College of Medicine Department. of Biochemistry skm@uomosul.edu.iq ORCID 0000-0002-1305-0950

Received: 17/01/2025 **Revising:** 18/01/2025 **Proofreading:** 13/02/2025 Accepted: 11/04/2025

#### **KEY WORDS:**

Vitamin D,

Obesity, adipose tissue

#### **ABSTRACT**

**Background**: Adiposity is a serious health problem worldwide and is described as having excessive amount of body fat. It is generally known that vitamin D deficiency is very common in obese people and is most likely brought on by volumetric dilution into the higher amounts of fat, serum, liver, and muscle. However, other mechanisms might also be working at the same time, so they cannot be completely ruled out. Low vitamin D could not yet be ruled out as a cause of obesity because of its impact on adipose tissue's vitamin D receptors. Even though research has yielded conflicting findings and taking vitamin D is still not proven to be advantageous.

**Aim**: This review aims to find the frequently documented link between low vitamin D levels and obesity, taking into account potential underlying mechanisms.

Methods: match the word "vitamin D" with several other terms, such as "obesity," "weight loss," and "fatty tissue inflammation."

**Results and conclusion**: Obesity and 25-hydroxyvitamin D levels are often shown to be inversely correlated in observational research's. Vitamin D supplementation in obese individuals suggests that it may have a protective effect on the development of obesity. Weight loss may improve vitamin D state. There was a negative correlation between vitamin D levels and some of adipokines.

**Keywords:** Vitamin D, Obesity, adipose tissue

DOI: http://doi.org/10.25130/mjotu.30.1.1



© 0 2024. This is an open access article under the CC by licenses http://creativecommons.org/licenses/by/4.0

#### **INTRODUCTION:**

It is commonly known that vitamin D is essential for maintaining calcium and phosphate balance as well as bone and muscle health [1]. The human body contains its receptors throughout, which indicate that it has a variety of activities. As a result of endogenous synthesis being the primary source of body vitamin D, the term "vitamin" in the strict sense is now more frequently used to describe hormones. The active form of vitamin D" dihydroxyvitamin D (1,25(OH)2D)", has extra skeletal functions as well [2]. Some studies claim that up to 70% to 90% of the vitamin D supply comes from endogenous synthesis, whereas only 10% to 25% comes from external sources.. Endogenous vitamin D production is still being debated. Vitamin D is known to improve immune function, differentiation, and muscular cell function.[3]. Vitamin D deficiency, "indicated by serum 25(OH)D a concentration below 20 ng /mL" [4, 5], has been linked to a wide range of illnesses, including metabolic syndrome and its related effects, such as type 2 diabetes, heart disease, myocardial infarction, and stroke [ 6,7,8,9,10,111.

Adipose tissue is a crucial organ for metabolism in maintaining glucose equilibrium and energy balance. It is where vitamin D is primarily stored [12]. Additionally, it produces vitamin receptors vitamin D [13]. Vitamin D has recently been shown to be functional in adipocytes. It engages in interactions with phosphatases, nuclear co-regulator proteins, adaptor molecules, and membrane receptors. As a result, it takes role in regulating both cell signaling and gene expression [14].

Recent investigations discovered an association between obesity and low "1,25 hydroxyvitamin D" concentrations, high PTH concentrations, and reduced "25

hydroxy vitamin D" concentrations [15, 16]. Additionally, it has been noted that body fat percentage and serum "25 hydroxy vitamin D" concentration are inversely correlated, and that this correlation is larger than that of "25 hydroxyvitamin D" with BMI [17,18]. According to a bi-directional genetic analysis that minimizes confounding, higher associated with lower hydroxyvitamin D, with the effects of lower "25 hydroxy vitamin D" on BMI expected to be minimal. Therefore, it is generally known that decreased "25 hydroxyvitamin D" concentrations are associated with obesity, even though the reasons are unclear[19].

#### **MATERIAL**

The review's foundation is a methodical examination of peer-reviewed literature, clinical trials, and meta-analyses that were obtained from sources including Google Scholar, PubMed, and Scopus. The study's focus was on research published between 2000 and 2023 that examined the connection between vitamin D levels and obesity. Included were research that looked at vitamin D metabolism, bioavailability, and how it affects the health of overweight and obese people. Studies with limited sample sizes or those lacking sufficient control groups were among the exclusion criteria. Match the word "vitamin D" with several other terms, such as "obesity," "weight loss," and "fatty tissue inflammation."

## RESULTS AND DISCUSSION Low vitamin D in Obese Patients: Causes:

#### 1. Adipose Tissue storage

According to a recent studies, plasma 25(OH)D levels are lower in obese individuals than in normal-weight individuals [20,21,22,23,24]. Serum levels of 1,25(OH)2D and 25(OH)D are inversely correlated with BMI [25,26]. Obesity induced isoprenaline-mediated lipolysis may be the cause of this decreased

elimination of 1,25(OH)2D from subcutaneous adipose tissue [27].

#### 2. Theory of the Dilution Effect

According to several researches the most likely reason for the negative correlation between vitamin D levels and BMI is volume dilution of vitamin D [28]. Vitamin D levels in lean and obese persons are similar, but in overweight people, the vitamin is dispersed over a larger volume, which lowers serum concentrations. In particular, the increased liver, fat, muscle, and serum compartments contain the majority of 25(OH)D In addition, Drincic et al. [27]. Obese people merely diluted 25(OH)D in a larger volume, confirming the volumetric dilution theory [29,30]. Low plasma 25(OH)D concentrations may arise from the prolonged storage site for 25(OH)D provided by increased adipose tissue seen in obesity [31]. According to a recent study, older obese people's vitamin D levels may be impacted by the same set of possible which include lower variables, hydroxylation, increased catabolism of vitamin D in adipose tissue, and reduced sun exposure [32]. Additionally, a different study found that the increase in serum 25(OH)D following vitamin D supplementation was less in obese individuals than in individuals of normal weight [33]. However, if volumetric dilution is the primary factor contributing to low 25(OH)D in obese individuals, weight loss would likely result in an increase in vitamin D serum levels. However, studies on weight loss provide erratic findings. Some individuals report elevated 25OHD blood levels [34], whereas other individuals report negligible increases in serum levels. In a twelve month regime program that included exercise and reducing calories, Mason et al. studied the effects of weight loss on 25(OH)D blood levels in a negligibly small number of obese postmenopausal individuals However. 25(OH)D

considerably rose 7.7 ng/mL in the group who dropped >15% of weight, which raises the possibility that there is a weight loss threshold [35]. According to the theory that vitamin D is sequestered in adipose tissue, vitamin D supplement had less of an impact on obese patients [37]. According to a study, low plasma 25(OH)D levels may be a predictor of eventual obesity and metabolic syndrome [38] and obesity is highly common in adults, children[39], and older women [40,41].

Hepatic 25-hydroxylation is hindered, which is another potential cause of decreased 25 hydroxyvitamin D. Nonalcoholic fatty liver disease which is very common in obesity, is characterized by poor 25-hydroxylation in patients, according to Targher et al. [42]. Decreases in 25 hydroxyvitamin D serum concentrations were also found to be closely associated with the level of severity of liver steatosis, inflammation, and necrosis as determined by histology. However, because NAFLD is associated strongly with metabolic syndrome and obesity, large randomized, placebo controlled trials are needed to assess the possible advantages of vitamin D supplementation and to validate the association between this condition and low 250HD [43].

## 3. Aspects of Habit and Nutrition

Reduced sun exposure, a diet low in foods high in vitamin D, and sedentary activity are linked to obesity that may result in decreased vitamin D levels. It has been demonstrated that obese men consume less vitamin D than their non-obese [44]. Poor calcium and vitamin D consumption are dditionally linked to obesity in both sex [45]. **Vitamin D and fatty tissue inflammation** Vitamin D's ability to lower inflammation linked to obesity and other chronic illnesses has drawn more attention. It has become increasingly obvious that 1,25 dihydroxy vitamin D has strong regulatory properties

for the immune system. According to Patriota et al. research, There was a negative correlation between vitamin D levels and leptin and a positive relationship with adiponectin [46]. also Gangloff et al., found a negative relationship between leptin and vitamin D levels. The authors also noted a correlation between a rising in plasma vitamin D concentrations and a drop in leptin levels and visceral adipose tissue volume [47]. According to certain research, vitamin D may reduce leptin production and reduce fat tissue inflammation. Overall, these results imply that increasing vitamin D level in obese individuals may reduce fatty tissue inflammation, and might lower the possibility of diseases linked to obesity [48]. The active vitamin D prevents chronic inflammation brought on by obesity in culture. It does this by preventing the proinflammatory cytokines IL 1, IL 6, IL 8, and IL 12 [49]. One meta-analysis that looked at the relationship among vitamin D supplemental funding and systemic inflammation in people with type 2 diabetes showed that dietary cholecalciferol supplementation assists in achieving a major decrease in the degree of inflammation and supported the findings that adequate vitamin D aid in lowering levels of TNF-alpha and C-reactive protein, lower levels of ESR and leptin [50].Data from a Nikitina study evaluating the impact of vitamin D in people who are overweight and obese showed that vitamin D deficiency in these people worsens resistance to insulin and encourages abnormalities in lipid profiles [51].

# Administration of Calcium and Vitamin D:

Because calcium usage depends on vitamin D, taking both of them combined can make it harder to distinguish between their effects. An open label study that looked at weight, visceral fat mass, and visceral fat area changes involved obese undergraduates who were randomly assigned to a calorie

restricted meal with calcium (600)milligram) or without, and vitamin D (one hundred twenty five IU daily) for a period of twelve weeks. While the groups did not differ in changes in weight, The group that took supplements showed considerably larger decreases in visceral fat mass and area [53]. According to the findings of a secondary analysis of data from a population based, double blind, placebo controlled, randomized trial of 1179 postmenopausal women, which examined the influence of vitamin D and calcium on fractures due to osteoporosis, taking calcium supplements for four years improved body composition, but vitamin D had no further effect when calcium intake was high [54].

## Weight loss's effects on vitamin D

There is proof that shedding pounds raises 25 hydroxyvitamin D, which could add to the body's defenses against chronic illness. Results of 383 overweight or obese women who participated in a two year clinical trial of a program for losing weight showed that those who did not lose weight at twenty-four months had an increase in serum 25(OH)D of 1.9 ng/mL. However, 25(OH)D increased by 5 ng/mL for those who lost more than 10 percent of their starting weight and by 2.7 ng/mL for those who lost five percent to ten percent of their starting weight. According to these results, weight loss in overweight or obese women is linked to a higher serum 25 hydroxy vitamin D content. 25 hydroxy vitamin D levels < 20 ng/mL (50 nmol/L) were present in 49% of subjects [55]. Ceglia L et al highlight the likelihood that the concentration of plasma 25OHD rises with weight loss [56]

#### **CONCLUSION**

The association between obesity and decreased "25 hydroxy vitamin D" levels can be adequately explained by a volumetric, dilutional model. To increase low "25 hydroxyvitamin D" level in obese people, greater dosages are required than are

typically recommended for the general population. With the caveat that it might be challenging to separate effects from calcium from effects from vitamin D, There are some experimental data and plausible processes that suggest vitamin D has a part in weight loss. The inadequate quality of study design has contributed to the lack of conclusive results from clinical studies. It may have been shown that vitamin D replete individuals do not experience any further benefits from vitamin D supplementation.

A significant need exists for prospective interventions with sufficient power, baseline assessment of "25 hydroxyvitamin D" concentrations, and adequate doses of vitamin D supplementation. It is currently uncertain how vitamin D doses can prevent obesity until these research are published.

#### **CONFLICT OF INTEREST**

Author declare that there are no any conflicts of interest

#### **ACKNOWLEDGEMENTS**

My profound gratitude is extended to the University of Mosul, College of Medicine, for their assistance in the completion of this review.

#### REFERENCES

- [1] Christakos, S.; Dhawan, P.; Verstuyf, A.; Verlinden, L.; Carmeliet, G. "Vitamin D: Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects". Physiol. Rev. 2016, 96, 365–408. [Google Scholar] [CrossRef] [PubMed]
- [2] Holick, M.F. Vitamin D: A d-lightful solution for health. J. Investig. Med. 2011, 59, 872–880. [Google Scholar] [CrossRef]
- [3] Heaney, R.P.; Armas, L.A.G.; French, C. All-Source Basal Vitamin D Inputs Are Greater Than Previously Thought and Cutaneous Inputs Are Smaller. J. Nutr. 2013, 143, 571–575. [Google Scholar] [CrossRef][Green Version]

- [4] Costa P.R.F., Assis A.M.O., Santos C.A.S.T., Santos D.B., Pereira-Santos M., Pereira-Santos M., Pereira-Santos M. "Obesity and vitamin D deficiency: A systematic review and meta-analysis". Obes. Rev. 2015;16:341–349. [PubMed] [Google Scholar] [Ref list]
- [5] Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, Durazo-Arvizu RA, Christopher Gallagher J, Gallo RL, Jones G, Kovacs CS, Mayne ST, Rosen CJ, SA. "The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know". J Clin Endocrinol Metab. 2011Jan 96 (1):53–58. https://doi.org/10.1210/jc.2010-2704
- [6] Pathania M, Dhar M, Kumar A, Saha S, Malhotra R. "Association of Vitamin D Status With Metabolic Syndrome and Its Individual Risk Factors: A Cross-Sectional Study". Cureus. 2023; Apr 30;15(4):e38344. doi: 10.7759/cureus.38344.
- [7] hiu, KC, Chu, A, Go, VLW, et al. "
  Hypovitaminosis D is associated with insulin resistance and beta cell dysfunction". Am J Clin Nutr.2004; 79, 820–825.CrossRefGoogle ScholarPubMed
- [8] Vrieling, A, Hein, R, Abbas, S, et al. "
  Serum 25-hydroxyvitamin D and postmenopausal breast cancer survival: a prospective patient cohort study ". Breast Cancer Res . 2011; 13, R74.
- [9] Barchetta I, Angelico F, Del Ben M, Baroni MG, Pozzilli P, Morini S, Cavallo MG. "Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes ". BMC Med. 2011 Jul 12;9:85. doi: 10.1186/1741-7015-9-

- 85. PMID: 21749681; PMCID: PMC3148980.
- [10] Osei, K. " 25-OH vitamin D: is it the universal panacea for metabolic syndrome and type 2 diabetes? " J Clin Endocrinol Metab. 2010; 95, 4220–4222.
- [11] Lagunova, Z.; Porojnicu, A.; Lindberg, F.; Hexeberg, S.; Moan, J. " The dependency of vitamin D status on body mass index, gender, age and season ". Anticancer Res. 2009, 29, 3713–3720. [Google Scholar]
- [12] Malmberg P., Karlsson T., Svensson H, Malin Lönn M, Nils-Gunnar Carlsson , A Sandberg A , Jennische E, Osmancevic A, Holm äng A. " A new approach to measuring vitamin D in human adipose tissue using time-of-flight secondary ion mass spectrometry: a pilot study ". J. Photochem. Photobiol. B.2014;138, 5 September: 295-301
- [13] Hewison M., Burke F, Evans KN, David A. Lammas DA, David M. Sansom DM, Liu P, Modlin RL, John S. Adams JS. " Extrarenal 25-hydroxyvitamin D<sub>2</sub>-1 alpha-hydroxylase in human health and disease ". J. Steroid Biochem. Mol. Biol. 2007; 103, Issues 3–5, March 2007: 316-321
- [14] Haussler MR, Jurutka PW, Mizwicki M, Norman AW. "Vitamin D. receptor (VITAMIN DR)-mediated actions of 1α, 25(OH)<sub>2</sub>vitamin D<sub>3</sub>: genomic and nongenomic mechanisms". Best Pract. Res. Clin. Endocrinol. Metab.2011; 25(4): 543-559
- [15] Arunabh, S.; Pollack, S.; Yeh, J.; Aloia, J.F. "Body fat content and 25-hydroxyvitamin D levels in healthy women ". J. Clin. Endocrinol. Metab. 2003, 88, 157–161.
- [16] L Wamberg, T Christiansen, S K Paulsen, S Fisker, P Rask, L

- Rejnmark, B Richelsen & S B Pedersen. "Expression of vitamin D-metabolizing enzymes in human adipose tissue—the effect of obesity and dietinduced weight loss ". International Journal of Obesity. 2013; 37:651–657 (2013)
- [17] Vimeswaran, K.; Berry, D.; Lu, C.; Pilz, S.; Hiraki, L.; Cooper, J.; Dastani, Z.; Li, R.; Houston, D.; Wood, A. "Causal relationship between obesity and vitamin D status: Bi-directional mendelian randomization analysis of multiple cohorts". PLoS Med. 2013;10: 1549–1676.
- [18] Wortsman J, Matsuoka LY, Chen TC, Lu Z, Holick MF. Decreased bioavailability of vitamin D in obesity. Am J Clin Nutr. 2000 Sep;72(3):690-3. doi: 10.1093/ajcn/72.3.690. Erratum in: Am J Clin Nutr. 2003 May;77(5):1342. PMID: 10966885.
- [19] Konradsen, S.; Ag, H.; Lindberg, F.; Hexeberg, S.; Jorde, R. " Serum 1,25-dihydroxy vitamin D is inversely associated with body mass index ". Eur. J. Nutr. 2008, 47, 87–91.
- [20] Pramono, A.; Jocken, J.W.E.; Goossens, G.H.; Blaak, E.E. "Vitamin D release across abdominal adipose tissue in lean and obese men: The effect of β-adrenergic stimulation ". Physiol. Rep. 2019, 7, e14308. [Google Scholar]
- [21] Hyppönen E, Boucher BJ. "Adiposity, vitamin D requirements, and clinical implications for obesity-related metabolic abnormalities ". Nutr Rev. 2018; 76(9):678-692. doi: 10.1093/nutrit/nuy034. PMID: 30020507.
- [22] Marquina C, Mousa A, Scragg R, de Courten B. "Vitamin D and cardiometabolic disorders: a review of current evidence, genetic determinants and pathomechanisms ". Obes Rev. 2019; 20(2):262-277. doi:

- 10.1111/obr.12793. Epub 2018 Nov 18. PMID: 30450683.
- [23] Cheng S, Massaro JM, Fox CS, Larson MG, Keyes MJ, McCabe EL, Robins SJ, O'Donnell CJ, Hoffmann U, Jacques PF, Booth SL, Vasan RS, Wolf M, Wang TJ. "Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study ". Diabetes. 2010; 59(1):242-8. doi: 10.2337/db09-1011. Epub 2009 Oct 15. PMID: 19833894; PMCID: PMC2797928.
- [24] Mai XM, Chen Y, Camargo CA Jr, Langhammer A. " Cross-sectional and prospective cohort study of serum 25-hydroxyvitamin D level and obesity in adults: the HUNT study ". Am J Epidemiol. 2012;175(10):1029-36. doi: 10.1093/aje/kwr456. Epub 2012 Feb 6. PMID: 22312120.
- [25] Konradsen S, Ag H, Lindberg F, Hexeberg S, Jorde R. "Serum 1,25-dihydroxy vitamin D is inversely associated with body mass index ". Eur J Nutr. 2008; 47(2):87-91. doi: 10.1007/s00394-008-0700-4. Epub 2008 Mar 4. PMID: 18320256.
- [26] Walsh J.S., Bowles S., Evans A.L. "Vitamin D in obesity ". Curr. Opin. Endocrinol. Diabetes Obes. 2017;24:389–394. doi: 10.1097/MED.00000000000000371.
- [27] Drincic A.T., Armas L.A., Van Diest E.E., Heaney R.P. "Volumetric Dilution, Rather Than Sequestration Best Explains the Low Vitamin D Status of Obesity ". Obesity. 2012;20:1444–1448. doi: 10.1038/oby.2011.404.
- [28] Pereira-Santos M, Costa PR, Assis AM, Santos CA, Santos DB. Obesity and vitamin D deficiency: a systematic review and meta-analysis. Obes Rev. 2015 ;16(4):341-9. doi: 10.1111/obr.12239. Epub 2015 Feb 17. PMID: 25688659.

- [29] Wortsman J., Matsuoka L.Y., Chen T.C., Lu Z., Holick M.F. "Decreased bioavailability of vitamin D in obesity ". Am. J. Clin. Nutr. 2000;72:690–693. doi: 10.1093/ajcn/72.3.690.
- [30] Perna S. The enigma of vitamin D supplementation in aging with obesity. Minerva Gastroenterol (Torino). 2022 Dec;68(4):459-462. doi: 10.23736/S2724-5985.21.02955-7. Epub 2021 Jul 30. PMID: 34328295.]
- [31] Gallagher J.C., Yalamanchili V., Smith L.M. " The effect of vitamin D supplementation on serum 25(OH)D in thin and obese women ". J. Steroid Biochem. Mol. Biol. 2013;136:195–200. doi: 10.1016/j.jsbmb.2012.12.003.
- [32] Drincic A., Fuller E., Heaney R.P., Armas L.A.G. "25-Hydroxyvitamin D Response to Graded Vitamin D3Supplementation Among Obese Adults ". J. Clin. Endocrinol. Metab. 2013;98:4845–4851. doi: 10.1210/jc.2012-4103.
- [33] Wamberg L., Christiansen T., Paulsen S.K. "Expression of vitamin D-metabolizing enzymes in human adipose tissue—The effect of obesity and dietinduced weight loss ". Int. J. Obes. 2013;37:651–657. doi: 10.1038/ijo.2012.112.
- [34] de Oliveira L.F., de Azevedo L.G., da Mota Santana J., de Sales L.P.C., Pereira-Santos M. " Obesity and overweight decreases the effect of vitamin D supplementation in adults: Systematic review and meta-analysis of randomized controlled trials ". Rev. Endocr. Metab. Disord. 2019;21:67–76. doi: 10.1007/s11154-019-09527-7.
- [35] Mason C, Xiao L, Imayama I, Duggan CR, Bain C, Foster-Schubert KE, Kong A, Campbell KL, Wang CY, Neuhouser ML, Li L, W Jeffery R, Robien K, Alfano CM, Blackburn GL, McTiernan A. " Effects of weight loss on serum

- vitamin D in postmenopausal women ". Am J Clin Nutr. 2011;94(1):95-103. doi: 10.3945/ajcn.111.015552. Epub 2011 May 25. PMID: 21613554; PMCID: PMC3127511.
- [36] Gagnon C., Lu Z.X., Magliano D.J., Dunstan D.W., Shaw J.E., Zimmet P.Z., Sikaris K., Ebeling P.R., Daly R.M. " Low Serum 25-Hydroxyvitamin D Is Associated with Increased Risk of the Development of the Metabolic Syndrome at Five Years: Results from a National, Population-Based Prospective Study (The Australian Diabetes, Obesity and Lifestyle Study: AusDiab) ". J. Clin. Endocrinol. Metab. 2012;97:1953-1961. doi: 10.1210/jc.2011-3187.
- [37] Gilbert-Diamond D., Baylin A., Mora M., Marin C., Arsenault J.E., Hughes M.D., Willett W.C., Villamor E. "Vitamin D deficiency and anthropometric indicators of adiposity in school-age children: A prospective study ". Am. J. Clin. Nutr. 2010;92:1446–1451. doi: 10.3945/ajcn.2010.29746.
- [38] LeBlanc E.S., Rizzo J.H., Pedula K.L., Ensrud K.E., Cauley J., Hochberg M. "Associations Between 25-Hydroxyvitamin D and Weight Gain in Elderly Women ". J. Women's Health. 2012;21:1066–1073. doi: 10.1089/jwh.2012.3506.
- [39] González-Molero I., Rojo-Martínez G., Morcillo S., Gutierrez C., Rubio E., Pérez-Valero V., Esteva I., De Adana M.S.R., Almaraz M.C., Colomo N., et al. "Hypovitaminosis D and incidence of obesity: A prospective study ". Eur. J. Clin. Nutr. 2013;67:680–682. doi: 10.1038/ejcn.2013.48.
- [40] Zhu, W.; Cai, D.; Wang, Y.; Ning, L.; Hu, Q.; Qi, Y.; Ma, S.; Amarasekara, S. " Calcium plus vitamin D3 supplementation facilitated fat loss in overweight and obese college students

- with very-low calcium consumption: A randomized controlled trial ". Nutr. J. 2013, 12, 8–12.
- [41] Zhou, J.; Zhou, L.-J.; Watson, P.; Zhang, Q.; Lappe, J. "The effect of calcium and vitamin D supplementation on obesity in postmenopausal women: Secondary analysis for a large-scale, placebo controlled, double-blind, 4-year longitudinal clinical trial ". Nutr. Metab. 2010, 7, 62.
- [42] Targher G., Bertolini L., Scala L., Cigolini M., Zenari L., Falezza G., Arcaro G. "Associations between serum 25-hydroxyvitamin D3 concentrations and liver histology in patients with non-alcoholic fatty liver disease ". Nutr. Metab. Cardiovasc. Dis. 2007;17:517–524.
  - doi: 10.1016/j.numecd.2006.04.002.
- [43] Mikolasević I., Milic S., Wensveen T.T., Grgic I., Jakopcic I., Štimac D., Wensveen F., Orlic L. "Nonalcoholic fatty liver disease—A multisystem disease? ". World J. Gastroenterol. 2016;22:9488–9505. doi: 10.3748/wjg.v22.i43.9488.
- [44] Kamycheva, E.; Joakimsen, R.M.; Jorde, R. " Intakes of calcium and vitamin D predict body mass index in the population of northern norway ". J. Nutr. 2003, 133, 102–106
- [45] Nimitphong, H., Park, E. & Lee, M. J. "Vitamin D regulation of adipogenesis and adipose tissue functions ". Nutr. Res. Pract. 2020; 14(6): 553–567
- [46] Patriota P, Rezzi S, Guessous I & Marques-Vidal P. " Association between anthropometric markers of adiposity, adipokines and vitamin D levels ". Scientific Reports . 2022; 12, Article number: 15435
- [47] Gangloff A, Bergeron J, Lemieux I, Tremblay A, Poirier P, Alméras N & Després J. " Relationships between circulating 25(OH) vitamin D,

- leptin levels and visceral adipose tissue volume: results from a 1-year lifestyle intervention program in men with visceral obesity ". International Journal of Obesity. 2020; 44: 280–288.
- [48] Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G. "Vitamin D: metabolism, molecular mechanism of action, and pleiotropic effects". Physiol Rev. 2016; 96:365–408. doi: 10.1152/physrev.00014.2015
- [49] Mousa A, Naderpoor N, Teede H, Scragg R, de Courten B. "Vitamin D supplementation for improvement of chronic low-grade inflammation in patients with type 2 diabetes: a systematic review and meta-analysis of randomized controlled trials ". Nutr Rev. 2018; 76:380–94. doi: 10.1093/nutrit/nux077
- [50] Yu Y, Tian L, Xiao Y, Huang G, Zhang M. Effect of Vitamin D Supplementation on Some Inflammatory Biomarkers in Type 2 Diabetes Mellitus Subjects: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Ann Nutr Metab. 2018;73(1):62-73. doi: 10.1159/000490358. Epub 2018 Jun 26. PMID: 29945132.
- [51] Nikitina IL, Todiyeva AM, Karonova TL. " Metabolic risks in children with obesity and deficit of vitamin D ". Practical Med. 2017; 5:48–52.
- [52] Rock, C.L.; Emond, J.A.; Flatt, S.W.; Heath, D.D.; Karanja, N.; Pakiz, B.; Sherwood, N.E.; Thomson, C.A. "Weight loss is associated with increased serum 25-hydroxyvitamin D in overweight or obese women ". Obesity 2012, 20, 2296–2301
- [53] Zakharova IN, Malyavskaya SI, Tvorogova TM, Vasilieva SV, Dmitrieva YA, Pschenichnikova II. " Metabolic syndrome in children and adolescents. Definition. Diagnostic

- criteria ". Medicinskiy Sovet . 2016;16:103–9. doi: 10.21518/2079-701X-2016-16-103-109
- [54] Kamycheva, E.; Sundsfjord, J.; Jorde, R. "Serum parathyroid hormone level is associated with body mass index. The 5th tromso study ". Eur. J. Endocrinol. 2004, 151, 167–172.
- [55] Kamycheva, E.; Joakimsen, R.M.; Jorde, R. Intakes of calcium and vitamin D predict body mass index in the population of northern norway. J. Nutr. **2003**, 133, 102–106.
- [56] Ceglia, L., Nelson, J., Ware, J. et al. "
  Association between body weight and composition and plasma 25-hydroxyvitamin D level in the Diabetes Prevention Program ". Eur J Nutr 56, 161–170 (2017). https://doi.org/10.1007/s00394-015-1066-z