



**MODERN VIEWS OF THE DEVELOPMENT OF OSTEOPOROSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE
(LITERATURE REVIEW AND OWN DATA)**

Yuldosheva D. Kh.

Akhmedov Sh. J.

Bukhara State Medical Institute. Bukhara City, Uzbekistan

Abstract

Nonalcoholic fatty liver disease (NAFLD) is associated with metabolic disorders - central nervous system obesity, dyslipidemia, hypertension, hyperglycemia, and persistent liver dysfunction. From the studied literature, it is shown that the stages of the disease in NAFLD increase, steatosis, steatohepatitis increase the risk of inflammation in the liver, the inflammatory cytokines increase, the amount of TNF- α and IL-1 in the blood increases, and the development of osteoporosis increases [1,3,7,9,11,12,14].

A number of studies show that BMD may be a risk factor for the development of osteoporosis [7,21-24]. One study conducted by Chinese researchers found a link between NAFLD and osteoporosis in middle-aged and elderly men [2,6]. However, other studies have debated the effect of osteoporosis on NAFLD [2,4,6,8,9]

Osteoporosis is a group of bone diseases caused by various causes, including common factors related to aging, obesity, and sex steroid hormone deficiency, as well as specific risk factors such as glucocorticoid use, decreased bone quality, and impaired microarchitectural integrity [1,3,6,7,9,12,14,17,18]. In most cases, osteoporosis is caused by loss of bone tissue, primarily due to increased bone resorption. Osteoporosis is characterized by low bone mineral density (BMD), bone pain, and easy fractures. Osteoporosis is an insidious disease that may not show symptoms until there are fractures in the bones, and can lead to serious problems and even death when the bones are damaged. Osteoporosis is scientifically proven to occur in 9-38% of women and 1-8% of men over the age of 50 in developed countries. It follows that osteoporosis is not only dangerous for health, but also increases the financial burden of these countries [1,2,4,5,7,8,17].

Many studies have shown that NAFLD is associated with BMD and osteoporosis. The liver is a source of many proteins, a regulator of bone metabolism and several pathways. Among them, one of the important functions of the liver is the metabolism of vitamin D, which is important in the origin of the relationship between NAFLD and osteoporosis [1,2,3,5,6,9,18].





In addition to its role in calcium and bone metabolism, vitamin D interacts in many tissues. Serum vitamin D levels were found to be significantly lower in patients with NAFLD compared to controls [2,4,6,8,18].

Osteoporosis is associated with many physical diseases or somatic diseases such as estrogen deficiency, endocrine disorders, hypertension and smoking [2,6,8].

Interestingly, patients with NAFLD have a comorbid clinical feature with a clinical presentation similar to osteoporosis. For example, NAFLD is associated with hypertension, dyslipidemia, insulin resistance, and diabetes. Studies have shown that low bone mineral density can be caused by a variety of diseases, including obesity, depression, nephropathy, and heart failure. [1,4,5,7,9,12]. As Duarte and colleagues found, increased inflammation is important in the pathogenesis of NAFLD. High secretion of tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6) in patients with NAFLD; Kupffer cell phagocytosis disorders are important in the development of the disease. Increased production of TNF- α produced by hepatocytes and non-parenchymal cells in patients with NAFLD has been reported in several studies [3,5,9,11,13,15]. Osteopontin, a T-helper, promotes inflammation in several chronic inflammatory diseases, including NAFLD [5,17,18]. Many risk factors: Systemic inflammatory diseases increase the risk of bone loss and osteoporosis. Inflammatory cytokines TNF- α , IL-1 are associated with osteoporosis, and these pro-inflammatory cytokines are important in the development of osteoporosis [1,3,6,9]. Inflammatory cytokines (TNF- α , IL-1, IL-6) are associated with bone resorption by osteoclasts. Osteopontin has both osteoblastic and osteoclastic functions to inhibit bone mineral growth. Detection of high levels of osteopontin in blood serum, menopause increases the development of osteoporosis [1,2,4,6,8,17]. These tests confirm the risk of bone metabolism and the development of osteoporosis. Vitamin D deficiency increases the risk of osteoporosis. One group of studies found that vitamin D deficiency increases the risk of NAFLD [3,7]. Chinese researchers have studied the relationship between NAFLD and vitamin D. In NAFLD, vitamin D deficiency increases the risk of osteomalacia, bone fractures, and osteoporosis. NAFLD may be a risk factor for osteoporosis due to insulin resistance and increased leptin levels. Other researchers have found that elderly patients with diabetes have an increased risk of developing osteoporosis [1,4,6,11,16]. Serum osteocalcin increases osteoblast expression and insulin secretion. The amount of osteocalcin in patients with NAFLD decreases. Thus, it can be concluded that the risk of developing osteoporosis may increase in NAFLD with insulin resistance. Dyslipidemia is considered a potential risk factor for the subsequent development of osteoporosis in patients with NAFLD. In the program in Taiwan, almost all patients diagnosed with dyslipidemia were widely treated with





statins. A meta-analysis shows that men treated with statins had higher bone mineral density at the hip joint and lumbar spine [2,4,6,8,11,12]. It can be concluded that statins may also play an important role in gender differences.

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Thus, based on the literature review and personal data, the following conclusion can be drawn: the association between nonalcoholic fatty liver disease and osteoporosis depends on body mass index and vitamin D status, patient comorbidities, and gender. Also, the relationship between non-alcoholic fatty liver disease and osteoporosis has not been fully studied in different countries.

References

1. Cao L, An Y, Liu H, Jiang J, Liu W, Zhou Y, Shi M, Dai W, Lu Y, Zhao Y, Lu Y, Chen L, Xia Y. Global epidemiology of type 2 diabetes mellitus in patients with NAFLD or MAFLD: a systematic review and meta-analysis. *BMC Med.* 2024 Mar 6; 22(1):101. doi: 10.1186/s12916-024-03315-0. PMID: 38448943
2. Cui A, Xiao., Fan Z, Lei J, Han S, Zhang D, Wei S, Wang., Zhuang Y. Causal association of NAFLD with osteoporosis, fracture and falls risk: a bidirectional Mendelian randomization study. *Anterior Endocrinol (Lausanne).* 2023 Aug 9;14:1215790. DOI: 10.3389/fendo.2023.1215790. Collection 2023. PMID: 37621646
3. Hansen SG, Wernberg KW, Grønkjær LL, Jacobsen BG, Caterino TD, Krag A, Juhl KB, Lauridsen MM, Shanbhog VV. Are nonalcoholic fatty liver disease and bone mineral density associated? - A cross-sectional study using liver biopsy and dual-energy X-ray absorptiometry. *JBMR Plus.* 2023 Jan 11; 7(3):e10714. DOI: 10.1002/jbm4.10714. Collection 2023 Mar. PMID: 36936359
4. Hassan AM, Haridi MA, Shoair MZ, Abdel-Aziz TM, Kura MK, Kenawy EM, Mansour TM, Salaheldin Elsayed S, Ali WE, Abdelmeguid MM, Abdel-Gawad M. Non-alcoholic fatty liver disease is associated with decreased bone mineral density in Upper Egyptian patients. *Sci Rep.* 2023 Mar 16; 13(1):4353. DOI: 10.1038/s41598-023-31256-w. PMID: 36928441
5. Pan B, Cai J, Zhao, Liu J, Fu S, Jing G, Niu Q, Li Q. Relationship between prevalence and risk of osteoporosis or osteoporotic fracture in non-alcoholic fatty liver disease: a





- systematic review and meta-analysis. *Osteoporos Int.* 2022 Nov; 33(11):2275–2286. DOI: 10.1007/s00198-022-06459-y. Epub 2022 Jun 28. PMID: 35764892 Review.
- 6.Roderburg K, Krieg S, Krieg A, Demir M, Ludde T, Kostev K, Liesen SH Eur J Non-alcoholic fatty liver disease (NAFLD) is associated with increased incidence of chronic kidney disease (CKD). *Med Res.* 2023 Apr 17;28(1):153. doi: 10.1186/s40001-023-01114-6. PMID: 37062837
- 7.Roderburg K, Losen S, Kostev K, Demir M, Jordens MS, Ludde T. Non-alcoholic fatty liver disease is associated with a higher incidence of celiac disease. *Eur J Gastroenterol Hepatol.* 2022 Mar 01;34(3):328-331. doi: 10.1097/MEG.0000000000002234. PMID: 34138765
- 8.Vachliotis ID, Anastasilakis AD, Goulas A, Goulis DG, Polizos SA. Non-alcoholic fatty liver disease and osteoporosis: potential link to treatment implications. *Diabetes Obesity Metab.* 2022 Sep; 24(9):1702–1720.
- 9.Xamrayev A.A., Yuldosheva D.X., Zokirov V.Z., Muxammedova Z.R. Clinical-laboratory markers of progression of non-alcoholic fatty liver disease // *American Journal of Medicine and Medical Sciences.* – USA, 2021, 11(5). – P. 419-425.
- 10.Xamrayev A.A., Yuldosheva D.X., Шамсиева Т.Т., Хайдаров Д.Б. Diagnostic significance of molecular-genetic markers in the development of non-alcoholic fatty liver disease // *Тиббиётда янги кун журнали.* – Тошкент, 2022. – № 9(47) – С. 374-381.
- 11.Yuldasheva D.H. Shadjanova N.S., Oltiboyev R.O. Non-alcoholic fatty liver disease and modern medicine // *Academica an international multidisciplinary research journal* // Vol.10. Issue 11. Nov.2020. – P. 1931 – 1937.
- 12.Yuldasheva D.H., Zokirov V.Z., G`ulomova Sh.Q. Non-alcoholic fatty liver disease: Modern view of the problem // *A Multidisciplinary Peer Reviewed Journal.* Vol.6. Issue 12. Dec.2020. – P. 286 – 292.
- 13.Yuldosheva D.X. Diagnostic significance of laboratory markers, inflammatory and anti – inflammatory cytokines in the development of non-alcoholic fatty liver disease steatosis and steatohepatitis // *British Medical Journal*, 2022. – № 3. – P. 26-35.
- 14.Yuldosheva D.X. Prevalence of non- alcoholic fatty liver disease, clinical and laboratory markers // *Eurasian journal of medical and natural sciences.* Tashkent. 2022, – P. 94-100.
- 15.Yuldosheva D.X. Relationship to the refluxate type of the effectiveness of treatment degree of gastroesophageal reflux disease // *European Journal of Research.* Austria, Vienna. – 2019. – № 2. – С. 110-114.



16. Yuldosheva D.X., Zokirov V.Z., Gulomova Sh.Q. Non-alcoholic fatty liver: modern view of the problem // Multidisciplinary Peer reviewed journal. India. Vol.6, Issue 12, 2020. – P.286-292.

17. Zhai T, Chen Q, Xu J, Jia S, Xia. Prevalence and trends of low bone density, osteopenia, and osteoporosis in US adults with nonalcoholic fatty liver disease, 2005–2014. *Anterior Endocrinol (Lausanne)*. 2022 Jan 19;12:825448. DOI: 10.3389/fendo.2021.825448. eCollection 2021. PMID: 35126317

18. Zhang G, Zhao Y, Wang S, Gong Q, Li HJ. Association between non-alcoholic fatty liver disease and bone mineral density in elderly Chinese. *Orthop Surg Res*. 2023 Sep 13; 18(1):679. DOI: 10.1186/s13018-023-04168-8. PMID: 37705028

