International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 13, No. 3, 2026

Clinical Research Progress of the Ratio of Inflammatory Index Monocytes to High-density Lipoprotein Cholesterol in Postmenopausal Women with Osteoporosis

Fu Qin [1], Shunjin Wen [1], Hongcheng Yao [2,*], Jinggui Huang [2], Qiaoyin Ran [3]

[1] Graduate School, Youjiang Medical University for Nationalities, Baise Guangxi, China
[2] Department of traumatic orthopedics, The People's Hospital of Hechi Hechi, Guangxi, China
[3] Ultrasound department, Baise Maternal and Child Hospital, Baise, Guangxi, China

*** Corresponding author:** Hongcheng Yao

Abstract: Postmenopausal osteoporosis is a major disease causing fractures and disability in elderly women, and its onset is closely related to chronic low-grade inflammation. The ratio of monocytes to high-density lipoprotein cholesterol, as an emerging comprehensive inflammation indicator, simultaneously reflects the imbalance of pro-inflammatory cell activation and anti-inflammatory lipoprotein protective function, providing a new perspective for understanding the inflammatory mechanism of postmenopausal osteoporosis. This article reviews the biological basis of MHR, explores its potential mechanisms involved in bone metabolism disorders by mediating oxidative stress, osteoclast activation and other pathways, and systematically evaluates its clinical application value and prospects in postmenopausal women's osteoporosis risk prediction, severity assessment and treatment response monitoring. Existing evidence shows that MHR is expected to become a convenient and economical auxiliary biomarker, but its clinical application still requires more prospective studies to verify.

Keywords: Monocyte/HDL Cholesterol Ratio; Inflammation; Postmenopausal Osteoporosis; Bone Metabolism; Risk Prediction.

1. Preface

Postmenopausal osteoporosis (PMOP) is a common metabolic bone disease in elderly women. Its core pathological mechanism lies in the imbalance of bone resorption and bone formation caused by the sudden drop in estrogen. Estrogen binds to receptors, promotes the expression of osteoprotegerin, inhibits RANKL action, thereby inhibiting osteoclast activity; at the same time, it activates the Wnt/β-catenin and BMP signaling pathways to promote osteogenic differentiation. Estrogen deficiency leads to the weakening of the above protective mechanisms and increases the secretion of pro-inflammatory cytokines such as IL-1, IL-6, TNF-α, etc., driving bone turnover imbalance [1, 2].

Recent studies have confirmed that chronic low-grade inflammation is one of the core driving factors for the progression of PMOP. Estrogen deficiency enhances the production of pro-inflammatory factors, promotes osteoclast differentiation and bone resorption, and impairs osteogenic function [3]. Clinical studies have shown that pro-inflammatory factors such as IL-8, IL-17, and IL-22 are significantly increased in the serum of PMOP patients and are positively correlated with the severity of the disease, suggesting that these factors may serve as biomarkers of osteoporosis [4].

As a key member of the innate immune system, monocytes are the main source of pro-inflammatory factors, and their activation and functional changes constitute a bridge between systemic inflammation and local bone metabolism imbalance [5, 6]. High-density lipoprotein cholesterol (HDL-C) has anti-inflammatory, antioxidant, and endothelial protective functions, but it may become dysfunctional and lose its protective effect under inflammatory conditions [7, 8]. Therefore, the balance between monocytes and HDL-C is of great significance to bone health.

The monocyte to high-density lipoprotein cholesterol ratio (MHR) integrates the two dimensions of pro-inflammatory and anti-inflammatory into a composite indicator, which can more comprehensively reflect the body's inflammation-metabolic imbalance state. MHR has been confirmed to be closely related to chronic inflammatory diseases such as cardiovascular disease and metabolic syndrome [9, 10]. In the field of PMOP, preliminary studies have shown that MHR is positively correlated with bone resorption markers and negatively correlated with bone density in postmenopausal women with type 2 diabetes, suggesting that it may reflect the imbalance of bone homeostasis caused by chronic inflammation [10]. However, another study on postmenopausal women without comorbidities found no significant difference in MHR between the osteoporosis group and the normal group, but observed a correlation between MHR and femoral neck T score [11], indicating that the relationship between MHR and bone mass may be affected by population characteristics and comorbidity status.

In summary, MHR, as a simple and economical composite inflammation indicator, has potential value in exploring the mechanism and clinical evaluation of PMOP, but its exact role and clinical application still require further research and verification.

2. The Biological Basis of MHR and its Significance as an Indicator of Inflammation

2.1. Pro-inflammatory Effect of Monocytes and Bone Metabolism

Monocytes are key cells linking the immune and skeletal systems and play a central pro-inflammatory role in postmenopausal osteoporosis (PMOP). Estrogen deficiency leads to excessive activation of the mononuclear/macrophage system, which increases its number and changes its inflammatory phenotype, exacerbating inflammation in the bone microenvironment and accelerating bone loss [1]. Activated monocytes secrete pro-inflammatory factors such as tumor necrosis factor-α, interleukin-1β, and interleukin-6, which strongly stimulate osteoclast production and activity by activating the RANKL/RANK/OPG signaling pathway while inhibiting osteoblast function [6]. In addition, monocytes can infiltrate bone tissue and differentiate into osteoclasts under the action of chemokines (such as Cxcl9), directly participating in the bone resorption process [12]. Therefore, monocyte activation and its mediated inflammatory response are important driving factors in the occurrence and development of PMOP.

2.2. Anti-inflammatory and Bone-Protective Potential of High-Density Lipoprotein Cholesterol

High-density lipoprotein cholesterol (HDL-C) not only has cardiovascular protective effects, but also maintains bone homeostasis through anti-inflammatory and antioxidant pathways. HDL-C exerts anti-inflammatory effects by promoting reverse cholesterol transport, inhibiting low-density lipoprotein oxidation, and regulating endothelial function; its apolipoprotein can directly inhibit osteoclast differentiation and activity [13]. Studies have shown that HDL's functional properties (such as antioxidant and anti-inflammatory capabilities) have more protective value than its pure plasma concentration. Postmenopausal women are often accompanied by lipid metabolism disorders, HDL-C levels and functions may decrease, and the bone protective effect is subsequently weakened [14]. Therefore, maintaining normal levels and function of HDL-C is crucial to combat postmenopausal bone loss.

2.3. Comprehensive Value and Calculation of MHR

The monocyte to high-density lipoprotein cholesterol ratio (MHR) is a composite inflammatory marker obtained by dividing the peripheral blood monocyte count by the HDL-C concentration. This ratio integrates the two dimensions of pro-inflammatory (monocytes) and anti-inflammatory/protective (HDL-C), and can more comprehensively reflect the net balance state of the body's inflammation-metabolism network, which is theoretically better than a single indicator. Studies in the cardiovascular field have confirmed that elevated MHR is significantly related to the risk of myocardial infarction, especially in people with well-controlled low-density lipoprotein cholesterol, where residual risks can be identified [9]. Similarly, in PMOP, a disease closely related to chronic low-grade inflammation, MHR may become a potential indicator reflecting the imbalance of bone homeostasis caused by inflammation. MHR is easy to calculate and low-cost. As a practical tool for assessing inflammatory burden and bone health risks in postmenopausal women, MHR has broad clinical application prospects, but further research is needed to verify its predictive value and intervention significance.

3. Potential Pathophysiological Mechanisms Pathways

Elevated MHR promotes the occurrence and development of postmenopausal osteoporosis through multiple intertwined mechanistic pathways. The inflammation-osteoclast axis mechanism is the core link. The inflammatory state reflected by high monocyte count directly promotes the differentiation of monocyte/macrophage precursors into osteoclasts by upregulating RANKL expression. Estrogen inhibits RANKL and stimulates OPG production by binding to the receptor, thereby inhibiting osteoclast formation; estrogen deficiency relieves this inhibition, leading to overactivation of osteoclasts [1]. For example, the expression of Cxcl9 secreted by osteoblasts increases in ovariectomized mouse models and promotes the adhesion, migration, and differentiation of osteoclast precursor cells through the CXCR3/ERK signaling pathway [12]. Secondly, oxidative stress and endothelial dysfunction are another key pathway. Low HDL-C levels are often accompanied by functional impairment, with reduced antioxidant and anti-inflammatory capabilities, which together with highly active monocytes aggravate oxidative stress. Oxidative stress not only directly damages cells, but also reduces bone formation by inhibiting the Wnt/β-catenin pathway and increases bone resorption by affecting the OPG/RANKL/RANK system [15]. In addition, oxidative stress damages bone marrow microvascular endothelial function, affects bone blood supply and nutrition, and may change the differentiation balance of bone marrow mesenchymal stem cells into osteoblasts [1].

4. Application of MHR in Clinical Management of Postmenopausal Osteoporosis

4.1. As an Auxiliary Tool for Screening and Risk Stratification

As a composite indicator that integrates inflammation and lipid metabolism status, MHR has potential application value in the screening and risk stratification of postmenopausal osteoporosis (PMOP). The core mechanism of PMOP is chronic low-grade inflammation induced by estrogen deficiency, which increases osteoclast activity and accelerates bone loss by increasing the secretion of pro-inflammatory factors such as IL-1, IL-6, and TNF-α [1]. MHR reflects both pro-inflammatory (monocyte) and anti-inflammatory (HDL-C) dimensions, and can comprehensively assess the body's inflammation-antioxidant imbalance [3].

In primary care or large-scale population screening, MHR can be calculated using routine blood tests and blood lipid examinations, which can help quickly identify postmenopausal women with high inflammatory burden, guide them to undergo bone density examinations, and achieve early intervention. Combined with traditional risk factors such as age, years since menopause, and history of fractures, MHR can further refine risk stratification.

However, the risk stratification cut-off value of MHR has not yet been unified, and its universality needs to be verified

by large-scale prospective studies. Future research should aim to identify MHR thresholds in different populations and assess their incremental value in optimizing existing risk prediction models.

4.2. Potential to Guide Treatment Decisions and Monitor Efficacy

MHR levels can provide a reference for individualized treatment of postmenopausal osteoporosis (PMOP). For patients with significantly elevated MHR, their osteoporosis may be driven by stronger inflammation, so combined with anti-inflammatory intervention on the basis of conventional anti-bone resorptive treatments (such as bisphosphonates, RANKL inhibitors) may have additional benefits [1]. Animal experiments and preclinical studies suggest that vitamin D, natural antioxidants, regular exercise, and a Mediterranean diet can improve bone metabolism by inhibiting osteoclast activity and regulating inflammatory pathways (such as Nrf2/NF-κB) [16-18]. Future clinical research is needed to evaluate whether strengthening anti-inflammatory strategies in people with elevated MHR can more effectively increase bone density and reduce the risk of fractures.

In addition, dynamic changes in MHR can be used as auxiliary indicators for efficacy monitoring. Effective anti-osteoporosis treatment may improve systemic low-grade inflammation while inhibiting bone resorption, manifested by a decrease in monocyte count and recovery of HDL-C function, thereby reducing MHR [19-21]. For patients who respond to treatment, the downward trend in MHR is often accompanied by an improvement in bone turnover markers (such as a decrease in β-CTX) and an increase in bone density. MHR testing is simple and low-cost, and has the potential to be used as a tool for efficacy monitoring, but its association with fracture endpoints still needs to be verified by prospective studies.

5. Research Limitations and Future Directions

Although the application of MHR in postmenopausal osteoporosis shows potential, current research still has obvious limitations. The vast majority of evidence comes from cross-sectional or case-control studies. Although these observational studies have revealed the association between MHR, bone density, and fracture risk, the causal relationship between the two cannot be clarified [12,13]. Whether chronic inflammation and abnormal lipid metabolism cause bone loss, or whether osteoporosis and its related body conditions change inflammation and lipid profiles, further clarification is needed. Therefore, there is an urgent need for large-scale, multi-center prospective cohort studies to verify the predictive value of MHR for postmenopausal osteoporosis and fracture events, and to explore the biological pathways behind it through in-depth mechanism studies.

As a composite index, MHR needs to be interpreted with caution because it is affected by multiple non-skeletal factors. Acute infections, other chronic inflammatory diseases (such as rheumatoid arthritis), metabolic diseases (such as diabetes), and certain drugs (such as glucocorticoids) may significantly affect monocyte counts and HDL-C levels [3]. For example, excessive use of glucocorticoids can interfere with bone metabolism and increase the risk of osteoporosis, while also affecting immunity and lipid metabolism [1]. Therefore, in clinical applications, MHR values must be interpreted in conjunction with the patient's specific clinical background. In addition, the dynamic relationship between MHR and specific markers of bone turnover (such as CTX, which reflects bone resorption, and P1NP, which reflects bone formation) needs to be further clarified to clarify whether MHR reflects an inflammatory state that directly affects bone metabolism.

Future research directions should be devoted to deepening the understanding of MHR and expanding its applications. First, the relationship between MHR and bone microstructure should be explored. Using technologies such as high-resolution peripheral quantitative CT (HR-pQCT), it is possible to evaluate whether MHR is related to microstructural parameters such as the number, thickness, and separation of bone trabeculae, thereby revealing its relationship with bone strength in more detail. Second, MHR-based joint prediction models can be developed. Combine MHR with other variables such as age, bone turnover markers, genetic risk scores, etc., and use algorithms such as machine learning to build more accurate osteoporosis and fracture risk prediction tools. Finally, conducting interventional studies is crucial. Clinical trials can be designed to observe whether reducing MHR through drugs (such as statins, which may have anti-inflammatory effects while regulating blood lipids) or intensive lifestyle intervention (such as exercise, diet), can effectively prevent or delay bone loss in postmenopausal women, and ultimately reduce the risk of fractures. Such studies will provide direct evidence for converting MHR from biomarkers to therapeutic targets.

6. Conclusion

Judging from the existing evidence, the monocyte to high-density lipoprotein cholesterol ratio (MHR), as a composite inflammatory indicator that integrates dual pro-inflammatory and anti-inflammatory/protective information, provides a unique and easily accessible window for understanding the pathophysiological mechanisms of postmenopausal osteoporosis (PMOP). Existing clinical observational studies have reached a relatively consistent consensus: higher MHR levels are independently associated with lower bone density and higher fracture risk in postmenopausal women. This association suggests that MHR is not only a simple biomarker, but may also reflect the core pathological process that drives the occurrence and development of PMOP—that is, a chronic low-grade inflammatory state. The underlying mechanism mainly revolves around the activation of the "inflammation-osteoclast axis", in which monocyte-derived pro-inflammatory factors (such as TNF-α, IL-1β, IL-6) promote the differentiation and activity of osteoclasts, while HDL-C dysfunction weakens its inherent anti-inflammatory, antioxidant and endothelial protective effects, jointly leading to an imbalance between bone resorption and bone formation. In addition, elevated MHR is often accompanied by metabolic disorders (such as insulin resistance) and changes in the hormonal milieu, further placing bone health in an unfavorable systemic metabolic-inflammatory network.

At the clinical level, MHR has shown potential as a useful supplement to traditional bone density measurement and fracture risk assessment tools. Its value is mainly reflected in early screening and risk stratification, especially for identifying those "high-risk" groups whose bone density is still at the critical value but already has a high inflammatory load, thus increasing the risk of fracture. At the same time, dynamic changes in MHR may be used to monitor the efficacy of anti-osteoporosis treatments (especially drugs

with anti-inflammatory effects). However, it must be clearly understood that the current evidence is mostly derived from cross-sectional or case-control studies, and the causal relationship between MHR and PMOP cannot yet be established. Future research is urgently needed to verify the independence and robustness of its prediction through large-scale prospective cohort and mechanistic studies, and to determine clinical cutoff values applicable to different populations. More importantly, whether intervention strategies targeting MHR reduction (such as lifestyle modifications, specific lipid-lowering or anti-inflammatory treatments) can actually improve skeletal outcomes should be explored. If its causal role and intervention effectiveness can be confirmed, MHR is expected to be transformed from a risk indicator into an intervenable target, thus opening up a promising new way for precise prevention and individualized management of PMOP.

References

[1] CHENG C H, CHEN L R, CHEN K H. Osteoporosis Due to Hormone Imbalance: An Overview of the Effects of Estrogen Deficiency and Glucocorticoid Overuse on Bone Turnover[J]. Int J Mol Sci, 2022,23(3).

[2] WANG L T, CHEN L R, CHEN K H. Hormone-Related and Drug-Induced Osteoporosis: A Cellular and Molecular Overview[J]. Int J Mol Sci, 2023,24(6).

[3] LUO J, LI L, SHI W, et al. Oxidative stress and inflammation: roles in osteoporosis[J]. Front Immunol, 2025,16: 1611932.

[4] AL-LAMI R, AL-HILFY J. Role of Interleukins-8, -17 and -22 in Iraqi postmenopausal women with Osteoporosis[J]. Cytokine, 2025,187: 156853.

[5] LIU Y Z, DVORNYK V, LU Y, et al. A novel pathophysiological mechanism for osteoporosis suggested by an in vivo gene expression study of circulating monocytes[J]. J Biol Chem, 2005,280(32): 29011-29016.

[6] XIAO K W, LI J L, ZENG Z H, et al. Monocytes affect bone mineral density in pre- and postmenopausal women through ribonucleoprotein complex biogenesis by integrative bioinformatics analysis[J]. Sci Rep, 2019,9(1): 17290.

[7] ARUN A J, KANEKI S, BAIG M, et al. High-Density Lipoprotein Dysfunction and Atherosclerotic Cardiovascular Disease: From Quantity to Quality[J]. Cardiol Rev, 2025.

[8] TANAKA S, COURET D, TRAN-DINH A, et al. High-density lipoproteins during sepsis: from bench to bedside[J]. Crit Care, 2020,24(1): 134.

[9] WU D, LAN Y, DING X, et al. Imbalances in circulating monocyte and high-density lipoprotein cholesterol exacerbates the residual risk of incident myocardial infarction beyond LDL-C: a real-life, prospective cohort study[J]. J Transl Med, 2025,23(1): 1433.

[10] SOYSAL C, BıYıK İ, İNCE O, et al. Comparison of the different PCOS phenotypes based on monocyte to HDL cholesterol ratio[J]. J Obstet Gynaecol, 2022,42(6): 2089-2094.

[11] ERDEN E, TURK A C, FIDAN N, et al. Relationship Between Blood Monocyte-HDL Ratio and Carotid Intima Media Thickness in with Postmenopausal Women[J]. J Clin Densitom, 2023,26(4): 101428.

[12] LIU Z, LIANG W, KANG D, et al. Increased Osteoblastic Cxcl9 Contributes to the Uncoupled Bone Formation and Resorption in Postmenopausal Osteoporosis[J]. Clin Interv Aging, 2020,15: 1201-1212.

[13] CATALANO J C, GUO Y, BORDEAU B M, et al. HDL in Abdominal Aortic Aneurysm: Mechanistic Insight and Therapeutic Potential[J]. Curr Atheroscler Rep, 2026,28(1): 6.

[14] LEE M, PARK S J, MOON Y J, et al. Combination of Sargassum fusiforme and Pueraria lobata Extracts Alleviates Postmenopausal Symptoms in Ovariectomized Rats[J]. J Med Food, 2020,23(7): 735-744.

[15] LI G F, GAO Y, WEINBERG E D, et al. Role of Iron Accumulation in Osteoporosis and the Underlying Mechanisms[J]. Curr Med Sci, 2023,43(4): 647-654.

[16] DZIEDZIC E A, GĄSIOR J S, TUZIMEK A, et al. Correlation between Serum 25-Hydroxyvitamin D Concentration, Monocyte-to-HDL Ratio and Acute Coronary Syndrome in Men with Chronic Coronary Syndrome-An Observational Study[J]. Nutrients, 2023,15(20).

[17] OH M S, KIM S I, SIM Y E, et al. Cirsium Setidens Water Extracts Containing Linarin Block Estrogen Deprivation-Induced Bone Loss in Mice[J]. Int J Mol Sci, 2023,24(2).

[18] HU X, ZHANG H, WANG Z, et al. Exercise-derived irisin prevents bone loss via Nrf2 activation and inhibition of STING/NF-κB signaling[J]. Free Radic Biol Med, 2026,246: 51-68.

[19] SUN S, XIU C, CHAI L, et al. HDAC inhibitor quisinostat prevents estrogen deficiency-induced bone loss by suppressing bone resorption and promoting bone formation in mice[J]. Eur J Pharmacol, 2022,927: 175073.

[20] WU Z, WANG J, CHEN K, et al. Therapeutic potential of Sweroside in postmenopausal osteoporosis: Inhibition of osteoclast differentiation and promotion of osteoclast apoptosis via NF-κB and MAPK pathways[J]. Int Immunopharmacol, 2025,155: 114630.

[21] FENG Y, LI W, SUN H, et al. Dual suppression of AKT/MAPK signaling and activation of Nrf2 by methylnissolin attenuates osteoclastogenesis and prevents postmenopausal osteoporosis[J]. Int Immunopharmacol, 2026,169: 115942.