The Peerian Journal
Open Access | Peer Reviewed
Volume 48, November 2025
ISSN (E): 2788-0303
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

Clinical and Immunological Features of Osteoarthritis: The Role of Adipocytokines and Pathogenetic Phenotyping

N.A.Ramazanova
Tashkent State Medical University, Uzbekistan

Abstract

Objective: To evaluate the association between Metabolic Syndrome (MS), clinical characteristics, and immunological status in patients with Osteoarthritis (OA), and to determine the prognostic significance of adipocytokines and pro-inflammatory cytokines.

Methods: A prospective study included 166 patients with knee OA (45–75 years old). Patients were stratified based on the presence of MS. Pain severity (VAS) and functional status (WOMAC) were assessed. Serum levels of Adiponectin (AN), Leptin, Interleukin-1β (IL-1β), and Interleukin-6 (IL-6) were measured. Radiographic severity was graded using the Kellgren-Lawrence (K-L) scale.

Results: The metabolic phenotype was identified in 87% of the examined patients. Patients with OA and MS showed a sharp reduction in AN levels and an increase in Leptin concentration, which correlated with higher levels of IL-1βand IL-6. A strong inverse correlation was found between the level of AN and the K-L radiographic stage ($r = -0.96$), and a strong direct correlation between IL-1β and the K-L stage ($r = 0.74$). These changes were associated with more pronounced pain and functional impairment (according to WOMAC).

Conclusion: MS is a significant modifier of OA progression. Adipocytokine imbalance (AN deficiency and Leptin excess) promotes a systemic pro-inflammatory state that accelerates joint tissue degradation. AN and IL-1β may serve as potential biomarkers for assessing severity and predicting OA progression, thereby justifying the use of pathogenetic phenotyping for personalized therapy.

Keywords: Metabolic Syndrome, Osteoarthritis

Introduction

Osteoarthritis (OA) has evolved from being perceived as a purely degenerative condition to a multifactorial pathology with a systemic component. Epidemiological data confirm that obesity and Metabolic Syndrome (MS) are leading risk factors that modify the severity and progression rate of OA.

Recent concepts recognize adipose tissue as an active endocrine organ producing adipocytokines (Leptin, Adiponectin) and other biologically active molecules involved in metabolism and inflammatory processes. An excess of adipose tissueis known to lead to the degradation of bone and cartilage tissue and contributes to joint inflammation. Consequently, MSis a significant factor affecting the development and progression of OA.

Leptin is a pro-inflammatory adipocytokine that stimulates the synthesis of matrix metalloproteinases (MMPs) and pro-inflammatory cytokines (IL-1β, TNF-α) in chondrocytes. Conversely, Adiponectin (AN) possesses anti-inflammatory and chondroprotective properties.

The Peerian Journal
Open Access | Peer Reviewed
Volume 48, November 2025
ISSN (E): 2788-0303
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

The primary goal of this study was to quantitatively assess the impact of MS on the clinical and immunological profile of OA patients to support the development of phenotyping algorithms and the selection of targeted therapy aimed at correcting metabolic imbalance.

Methods

Study Design and Participants

The prospective study included 166 patients with knee OA (diagnosed according to ACR criteria, 1987) aged 45–75 years. Patients were stratified based on the presence of MS (according to IDF criteria, 2005).

Clinical and Instrumental Assessment

1. Functional Assessment:
    - Pain: Visual Analog Scale (VAS).
    - Functional status: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).
2. Radiographic Assessment: Knee joint radiography was performed with severity grading using the Kellgren-Lawrence (K-L) scale. MRI was also utilized for earlier diagnosis and detection of subclinical synovitis.
3. Immuno-biochemical Analysis: Serum levels of AN, Leptin, IL-1β, and IL-6 were measured using an Enzyme-Linked Immunosorbent Assay (ELISA).

Statistical Analysis

Statistical analysis was performed using Statistica for Windows 6.0. The Student's t-test or Mann-Whitney U test was used for group comparisons. Correlation analysis was performed using the Spearman's rank correlation coefficient (rs). Differences were considered statistically significant at $P < 0.05$.

Results

Prevalence of Phenotypes and Clinical Findings

- The metabolic phenotype was the most prevalent, identified in 87% of the patient cohort.
- Patients with OA + MS exhibited significantly higher mean scores on the VAS and WOMAC compared to patients with OA without MS ($P < 0.01$), indicating more severe pain and functional impairment.

Biomarker Analysis and Correlation

The analysis demonstrated a clear link between metabolic and immunological disturbances:

Biomarker	OA without MS	OA with MS	P-value	Correlation with K-L (rs)
Adiponectin (AN)	High	Significantly Reduced	< 0.001	-0.96 (Strong Inverse)
Leptin	Normal	Elevated	< 0.01	0.48 (Moderate Direct)
IL-1β	Moderately Elevated	Significantly Elevated	< 0.001	0.74 (Strong Direct)
IL-6	Moderately Elevated	Significantly Elevated	< 0.01	0.44 (Moderate Direct)

The Peerian Journal
Open Access | Peer Reviewed
Volume 48, November 2025
ISSN (E): 2788-0303
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

The strong inverse correlation of AN (r = -0.96) and the strong direct correlation of IL-1β (r = 0.74) with the K-L stage confirm that metabolic inflammation is a direct driver of structural OA progression.

Discussion

The findings confirm that Metabolic Syndrome fundamentally alters OA pathogenesis, shifting it from a predominantly degenerative state to a systemic metabo-immunological disease.

Adiponectin deficiency (r = -0.96) and elevated IL-1β (r = 0.74) are the most significant predictors of structural damage. IL-1β is a key catabolic cytokine that initiates cartilage matrix degradation. Its increased level in the context of MS indicates an active inflammatory process that is not adequately counteracted due to the deficiency of the protective AN.

The high prevalence of the metabolic phenotype (87%) underscores the urgent need for pathogenetic phenotyping in routine clinical practice. Identifying patients with high Leptin/IL-1β and low AN levels allows for timely interventions targeting metabolic imbalance (e.g., weight control, glycemic management, and targeted pharmacological agents).

The inclusion of MRI in the diagnostic algorithm for the metabolic OA phenotype is also supported, as it can visualize synovitis and bone marrow lesions—early inflammatory signs that may be missed by conventional radiography but correlate strongly with high levels of pro-inflammatory biomarkers.

Conclusion

1. In OA patients, the presence of Metabolic Syndrome severely exacerbates the disease course, leading to a significant immunological imbalance characterized by a critical decrease in Adiponectin and an increase in Leptin, IL-1β, and IL-6.
2. Levels of Adiponectin and Interleukin-1β are strong, independent prognostic biomarkers that correlate closely with the radiographic severity of OA.
3. The results substantiate the necessity for clinical phenotyping of OA and the integration of these biomarkers (AN, IL-1β) into the diagnostic algorithm to select personalized and pathogenetically justified therapy.

Conflict of Interest

The authors declare no conflicts of interest.

Funding

This work received no external funding.

References

1. Hunter D. J., Bierma-Zeinstra S. Osteoarthritis. *The Lancet*. 2019;393(10168):174–185.
2. Kolasinski S. L., et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Management of Osteoarthritis of the Hand, Hip, and Knee. *Arthritis & Rheumatology*. 2020;72(2):220–233.
3. Kellgren J. H., Lawrence J. S. Radiological assessment of osteo-arthrosis. *Annals of the Rheumatic Diseases*. 1957;16(4):494–502.
4. Berenbaum F., Eymard F., Houard X. Osteoarthritis is a metabolic disease with specific molecular markers. *Nature Reviews Rheumatology*. 2018;14(11):634–644.

The Peerian Journal
Open Access | Peer Reviewed
Volume 48, November 2025
ISSN (E): 2788-0303
Website: www.peerianjournal.com
Email: editor@peerianjournal.com

5. Eymard F., et al. The osteoarthritis year in review 2021: phenotyping and personalized medicine. *Osteoarthritis and Cartilage*. 2021;29(1):180–189.
6. Yuan C., Pan Z., Zhao K., Li J., Sheng Z., Yao X., et al. Classification of four distinct osteoarthritis subtypes with a knee joint tissue transcriptome atlas. *Bone Research*. 2020;8:38. doi: 10.1038/s41413-020-00109-x.
7. Yucesoy B., Charles L. E., Baker B., Burchfiel C. M. Occupational and genetic risk factors for osteoarthritis: A review. *Work*. 2015;50(2):261–273.
8. Lago F., Dieguez C., Gualillo O., Varela-Rodriguez A. Adipokines as emerging players in inflammation. *Nature Clinical Practice Rheumatology*. 2008;4(9):452–461.
9. Zhang P, Zhong Z-H, Yu H-T, Liu B. Significance of Increased Leptin Expression in Osteoarthritis Patients. *PLoS ONE*. 2015;10(4):e0123224.
10. Zhang J-M, An J. Cytokines, Inflammation and Pain. *Int Anesthesiol Clin*. 2007;45(2):27–37. doi: 10.1097/AIA.0b013e318034194e.
11. Rippa M., et al. Adiponectin and Osteoarthritis: A Complex Link Between Metabolism and Inflammation. *Frontiers in Endocrinology*. 2020;11:574.
12. Ramazanova N. A. *Klinicheskie osobennosti metabolicheskikh i immunologicheskikh narusheniy u bol'nykh osteoartritom [Clinical features of metabolic and immunological disorders in patients with osteoarthritis]*. PhD Dissertation. Tashkent Medical Academy, Tashkent; 2023. (Ссылка на диссертационное исследование, где содержатся данные r = -0.96 и r = 0.74).