e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 569-573

Original Research Article

Role of Metabolic Syndrome in Early Onset Knee Osteoarthritis

Vibhu Amrutiya[1], Yunus Shahab[2], Yusuf Shahab[3], Prabha Joshi[4], Srishti Dutta[5], Tithi Neeraj Pandya[6]

[1]MBBS, GMERS Medical College, Valsad, Gujarat, India
[2]MBBS, GMERS Medical College, Valsad, Gujarat, India
[3]MBBS, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India
[4]MBBS, DMRD Resident (PGY-1), Hayat Hospital, Guwahati, Assam, India
[5]MBBS, DNB Surgery (PGY-2), Downtown Hospital, Guwahati, Assam, India
[6]MBBS Student (3rd Year – Part 1), GMERS Medical College, Valsad, Gujarat, India

Received: 15-07-2025 / Revised: 14-08-2025 / Accepted: 15-09-2025
Corresponding Author: Tithi Neeraj Pandya
Conflict of interest: Nil

Abstract:

Background: Osteoarthritis (OA) is a common chronic joint disorder with knee OA (OAK) being the most prevalent form. Metabolic syndrome (MetS) has been suggested to contribute to OA progression through systemic inflammation and metabolic abnormalities. Understanding the association between MetS and OAK severity may aid early intervention.

Materials and Methods: A case-control study took place at a tertiary care hospital over one year, including 216 participants aged ≥50 years with primary knee OA. Cases (n=108) were scheduled for total knee replacement, while controls (n=108) had OA not requiring surgery. Anthropometric measurements, blood pressure, and laboratory tests for MetS components were recorded. Radiographs were graded using the Kellgren-Lawrence (KL) system, and statistical analyses were performed using Chi-square tests, t-tests, and odds ratios.

Results: Gender distribution was similar between groups (P=0.372). MetS was more common in cases (68.5%) than controls (37%), with an odds ratio of 3.6. Patients with MetS had higher KL grades, greater BMI, waist circumference, and lower HDL levels compared to controls. Blood pressure, fasting glucose, and triglycerides were comparable between groups.

Conclusion: Metabolic syndrome is strongly correlated with enhanced severity of OAK, highlighting the need for early metabolic evaluation and management.

Keywords: Knee Osteoarthritis, Metabolic Syndrome, Total Knee Replacement, Obesity, Kellgren-Lawrence Grading.

Introduction

Osteoarthritis (OA) is the most common chronic joint disease worldwide that represents a leading cause of pain and functional impairment [1]. While OA primarily affects the hip, knee, and hand joints, the knee joint is particularly susceptible, accounting for nearly 80% of the global OA burden [2]. In India, OA has a prevalence ranging from 22% to 39% [3,4]. Clinically, OA manifests as stiffness of joints, pain, and limitations in daily activities, significantly reducing quality of life despite not directly causing mortality [5]. Mechanical stress, aging, obesity, and female sex are well-recognized risk factors, highlighting the multifactorial nature of OA [2,6].

The rise in sedentary lifestyles and increased dietary fat intake has contributed to the growing prevalence of metabolic disturbances, including obesity, dyslipidaemia, hypertension, hypercholesterolemia, and diabetes, collectively referred to as metabolic syndrome (MetS) [6,7]. According to the National Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) guidelines, the presence of any three of these parameters defines MetS [8]. Recent evidence suggests a potential link between MetS and osteoarthritis of the knee (OAK), as systemic inflammation associated with insulin resistance and dyslipidaemia may exacerbate joint inflammation and accelerate cartilage degeneration [9–11]. Low-grade tissue inflammation and oxidative stress have been proposed as common pathogenic mechanisms connecting MetS and OA, which may contribute to cartilage, bone, and synovial tissue damage independent of obesity [12–14].

Despite emerging evidence, significant gaps remain regarding whether MetS or its individual components specifically increase the risk of early

onset or advanced OAK requiring total knee replacement (TKA). Genetic and neuroendocrine factors may further modulate the pathophysiology of OAK, emphasizing the complex interplay of systemic and local factors [15]. This study investigates the association between MetS and osteoarthritis severity and examines whether MetS or its components contribute to early-onset knee osteoarthritis.

Methodology

Study Design, Place, and Duration: This case-control study took place at a tertiary care hospital from August 2022 to August 2023.

Study Population and Sample Size: A total of 216 participants were enrolled, including cases and controls. Cases (patients with primary knee OA scheduled for total knee replacement, TKA) and controls (patients with primary knee OA not requiring TKA) were included. Exclusion criteria comprised secondary arthritis, neutral or valgus knee alignment, neurological disorders, ongoing medications for metabolic disorders, unfitness for surgery, metabolic bone diseases, other arthropathies, and neoplasms. Participants aged 50 years or older with knee pain were evaluated clinically for OA.

Clinical and laboratory investigations: Socio-demographic, anthropometric, and health data were collected through a structured questionnaire, including measurements of weight, height, BMI, waist circumference, and blood pressure, alongside knee examinations by trained clinicians. Venous blood samples were analyzed for fasting blood sugar, triglycerides, total cholesterol, LDL, and HDL, with MetS diagnosed per Modified NCEP ATP III criteria. Bilateral weight-bearing AP and lateral knee radiographs were obtained and graded independently by two blinded orthopedic surgeons using the Kellgren-Lawrence (KL) system, with discrepancies resolved by consensus. Radiographic OA was defined as KL grade ≥2 in at least one knee.

Statistical Analysis: Statistical analyses were performed using SPSS v28. Categorical variables were compared with Chi-square tests, continuous variables with unpaired t-tests, and odds ratios calculated, with $p<0.05$ considered significant.

Results

The study included 216 participants, equally divided into 108 cases and 108 controls. Among the cases, 50 (46.3%) were male and 58 (53.7%) were female, while in the control group, 52 (48.1%) were male and 56 (51.9%) were female (Table 1).

Table 1: Distribution of Study Participants as per gender (n=216)

Cohort	Male	Female	Total	P
Controls (n=108)	52 (48.1%)	56 (51.9%)	108	0.372
Cases (n=108)	50 (46.3%)	58 (53.7%)	108	
Total	102 (47.2%)	114 (52.8%)	216	

Metabolic syndrome was observed in 74 of 108 cases (68.5%), compared to 40 of 108 controls (37%). The difference was statistically significant ($P<0.001$), with an odds ratio of 3.6, suggesting that patients with advanced knee osteoarthritis requiring total knee replacement were more than three times as likely to have MetS as those with milder OA not requiring surgery (Table 2).

Table 2: Prevalence of MetS in Cases and Controls

MetS Status	Controls (n=108)	Cases (n=108)	Total	P
Positive	40 (37%)	74 (68.5%)	114	<0.001
Negative	68 (63%)	34 (31.5%)	102	
Total	108	108	216	

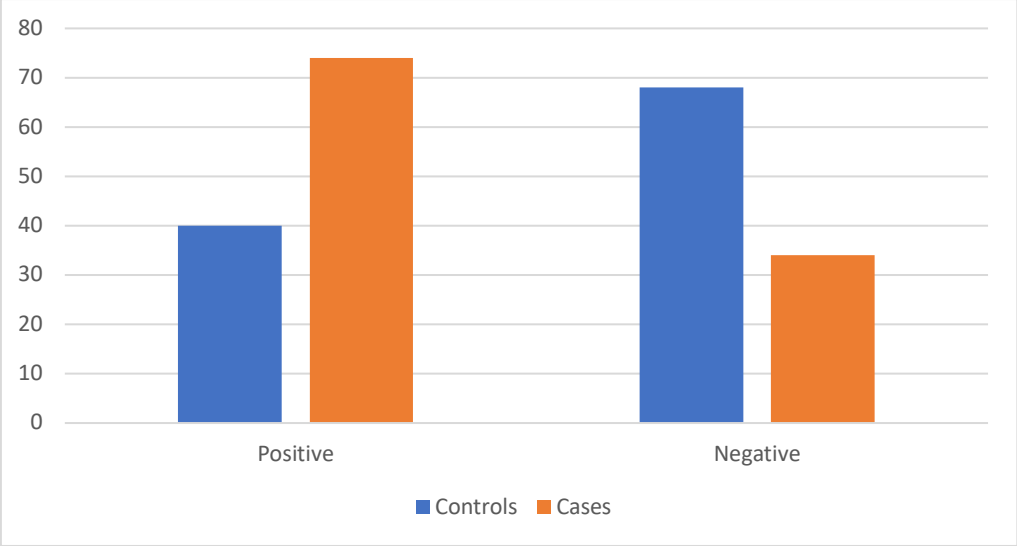

Figure 1: Prevalence of MetS in Cases and Controls

Analysis of Kellgren-Lawrence (KL) radiographic grades revealed that patients with MetS were more likely to present with higher OA severity. Among MetS-positive participants, 64 (56.1%) had KL grade 4, 36 (31.6%) had grade 3, 12 (10.5%) had grade 2, and only 2 (1.8%) had grade 1. In contrast, MetS-negative participants showed a lower proportion with KL grade 4 (35.3%) and a higher proportion with grades 2 and 3. The association between MetS and higher KL grades was statistically significant (P=0.026) (Table 3).

Table 3: KL Grading of OA and Metabolic Syndrome

KL Grade	MetS Positive	MetS Negative	Total	P
1	2 (1.8%)	6 (5.9%)	8	0.026
2	12 (10.5%)	28 (27.5%)	40	
3	36 (31.6%)	32 (31.4%)	68	
4	64 (56.1%)	36 (35.3%)	100	
Total	114	102	216	

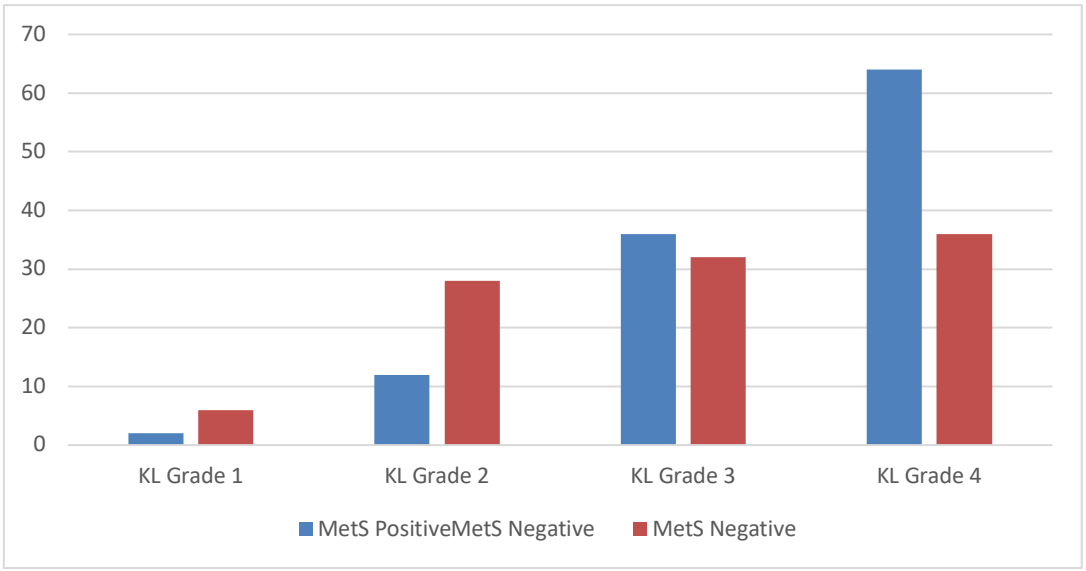

Figure 2: KL Grading of OA and Metabolic Syndrome

Comparing cases and controls, patients with advanced OA had higher mean weight (71.5 ± 13.2 kg vs. 66.2 ± 10.1 kg), BMI (28.0 ± 5.3 kg/m² vs. 24.4 ± 3.2 kg/m²), and waist circumference (92.1 ± 13.5 cm vs. 83.7 ± 12.8 cm), indicating a greater prevalence of obesity-related parameters. Fasting blood sugar and triglyceride levels were slightly higher in cases, while HDL cholesterol was notably

lower (48.2 ± 13.8 mg/dl vs. 55.6 ± 15.0 mg/dl), reflecting a more adverse metabolic profile. Blood pressure values were similar between the two groups (Table 4).

Table 4: Anthropometric and Metabolic Parameters in Cases and Controls

Parameter	Controls (n=108)	Cases (n=108)
Weight (kg)	66.2 ± 10.1	71.5 ± 13.2
Height (cm)	164.8 ± 8.1	160.2 ± 9.4
BMI (kg/m²)	24.4 ± 3.2	28.0 ± 5.3
Waist Circumference (cm)	83.7 ± 12.8	92.1 ± 13.5
Systolic BP (mmHg)	129.2 ± 17.1	128.4 ± 18.2
Diastolic BP (mmHg)	82.3 ± 11.0	84.1 ± 10.3
Fasting Blood Sugar (mg/dl)	114.5 ± 42.1	107.6 ± 28.7
Triglycerides (mg/dl)	165.3 ± 72.4	168.7 ± 65.2
HDL Cholesterol (mg/dl)	55.6 ± 15.0	48.2 ± 13.8

Discussion

The gender distribution in the present study of 216 participants was similar across cases and controls, with 53% females in cases and 50% in controls, showing no statistically significant difference. This indicates that gender did not act as a confounding factor in our analysis. While several studies have reported that osteoarthritis of the knee (OAK) is more prevalent in women in contrast to men, particularly in the geriatric groups [16], the present study's findings suggest that, in this cohort, both genders were evenly represented, supporting the relevance of metabolic factors over gender in disease progression.

Metabolic syndrome (MetS) was significantly more prevalent among cases (68.5%) compared to controls (37%) in the present study, with an odds ratio of 3.6 (P<0.001). A strong association was observed between MetS and the severity of OAK, as indicated by higher Kellgren-Lawrence (KL) grades and the need for TKA. These findings align with the hypothesis that systemic metabolic factors contribute to the pathophysiology of OA [17]. Previous research, including meta-analyses by Liu SY et al., [18] has reported bidirectional relationships between MetS and OA, with higher OA prevalence in participants with baseline MetS. Our results extend this evidence by demonstrating not only increased OA prevalence but also greater severity among patients with MetS.

Obesity-related parameters, including BMI and WC, were significantly larger in cases in contrast to controls (BMI: 28.0 vs 24.4 kg/m²; WC: 92.1 vs 83.7 cm). This supports prior findings that components of MetS, such as obesity and dyslipidemia, exacerbate joint degeneration by promoting systemic inflammation and cartilage degradation [14,19,20]. While fasting blood sugar, triglycerides, and HDL cholesterol showed differences, blood pressure did not differ significantly between cases and controls, consistent with mixed findings in the literature [21,22]. These variations may reflect differences in age, ethnicity, and diagnostic criteria for OA and MetS across studies.

The pro-inflammatory state associated with MetS, characterized by elevated cytokines, may accelerate the progression of OA, contributing to increased KL grades and higher likelihood of TKA in patients with MetS [23,24]. This underscores the importance of early identification and management of MetS in OA patients. Interventions targeting lifestyle factors, including diet, physical activity, and metabolic control, may help mitigate OA progression and reduce the need for surgical intervention [18]. Overall, the present findings suggest that addressing metabolic abnormalities may not only improve systemic health but also slow the advancement of knee OA, highlighting the clinical importance of integrating metabolic evaluation into OA management.

Conclusion

In the present investigation, metabolic syndrome was significantly more prevalent among individuals with advanced knee osteoarthritis requiring total knee replacement and was strongly associated with higher Kellgren-Lawrence grades. Obesity-related parameters, including BMI and WC, were notably higher in cases, highlighting the contribution of metabolic abnormalities to disease severity. These findings suggest that MetS not only elevates the incidence rate of developing knee OA but may also accelerate its progression, emphasizing the importance of early identification and management of metabolic risk factors. Integrating metabolic evaluation and lifestyle interventions into the care of OA patients may help mitigate disease progression and reduce the need for surgical intervention.

References

1. Briggs AM, Cross MJ, Hoy DG, Sànchez-Riera L, Blyth FM, Woolf AD, et al. Musculoskeletal health conditions represent a global threat to healthy aging: A report for the 2015 World Health Organization world report on aging and

health. Gerontologist. 2016;56:S243–55. doi: 10.1093/geront/gnw002.
2. World Health Organisation. Chronic rheumatic conditions. WHO. Available from: https://www.who.int/news-room/fact-sheets/detail/rheumatoid-arthritis
3. Silman AJ, Hochberg MC. Epidemiology of the Rheumatic Diseases. 2nd ed. Oxford: Oxford University Press; 2001.
4. Symmons D, Mathers C, Pfleger B. Global Burden of Osteoarthritis in Year 2000: Global Burden of Disease 2000 Study. Version 2.;World Health Report. 2002 5 Available from: https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=b8a9097eb0f2007d53def02dd7c265e206f84707
5. Glyn-Jones S, Palmer AJ, Agricola R, Price AJ, Vincent TL, Weinans H, et al. Osteoarthritis. Lancet. 2015;386:376–87. doi: 10.1016/S0140-6736(14)60802-3.
6. Kluzek S, Newton JL, Arden NK. Is osteoarthritis a metabolic disorder? Br Med Bull. 2015;115:111–121. doi: 10.1093/bmb/ldv028.
7. Farnaghi S, Crawford R, Xiao Y, Prasadam I. Cholesterol metabolism in the pathogenesis of osteoarthritis disease. Int J Rheum Dis. 2017;20:131–40. doi: 10.1111/1756-185X.13061.
8. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of The National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult treatment panel III) JAMA. 2001;285:2486–97. doi: 10.1001/jama.285.19.2486.
9. Zhuo Q, Yang W, Chen J, Wang Y. Metabolic syndrome meets osteoarthritis. Nat Rev Rheumatol. 2012;8:729–37. doi: 10.1038/nrrheum.2012.135.
10. Le Clanche S, Bonnefont-Rousselot D, Sari-Ali E, Rannou F, Borderie D. Inter-relations between osteoarthritis and metabolic syndrome: A common link? Biochimie. 2016;121:238–52. doi: 10.1016/j.biochi.2015.12.008.
11. Courties A, Sellam J, Berenbaum F. Metabolic syndrome-associated osteoarthritis. Curr Opin Rheumatol. 2017;29:214–22. doi: 10.1097/BOR.0000000000000373.
12. Carnevale Schianca GP, Fra GP, Steffanini M, Pogliani G, Marconi C, Bigliocca M, et al. Impaired glucose metabolism in hypertensive patients with/without the metabolic syndrome. Eur J Intern Med. 2014;25:477–81. doi: 10.1016/j.ejim.2014.04.006.
13. Sun AR, Friis T, Sekar S, Crawford R, Xiao Y, Prasadam I. Is synovial macrophage activation the inflammatory link between obesity and osteoarthritis? Curr Rheumatol Rep. 2016;18:57. doi: 10.1007/s11926-016-0605-9.
14. Schett G, Kleyer A, Perricone C, Sahinbegovic E, Iagnocco A, Zwerina J, et al. Diabetes is an independent predictor for severe osteoarthritis: Results from a longitudinal cohort study. Diabetes Care. 2013;36:403–9. doi: 10.2337/dc12-0924.
15. Iannone F, Lapadula G. Obesity and inflammation--targets for OA therapy. Curr Drug Targets. 2010;11:586–98. doi: 10.2174/138945010791011857.
16. Lee BJ, Yang S, Kwon S, Choi KH, Kim W. Association between metabolic syndrome and knee osteoarthritis: A cross-sectional nationwide survey study. J Rehabil Med. 2019;51:464–70. doi: 10.2340/16501977-2561.
17. Audrey HX, Abd Razak HR, Andrew TH. The truth behind subchondral cysts in osteoarthritis of the knee. Open Orthop J. 2014;8:7–10. doi: 10.2174/1874325001408010007.
18. Liu SY, Zhu WT, Chen BW, Chen YH, Ni GX. Bidirectional association between metabolic syndrome and osteoarthritis: A meta-analysis of observational studies. Diabetol Metab Syndr. 2020;12:38. doi: 10.1186/s13098-020-00547-x.
19. Dahaghin S, Bierma-Zeinstra SM, Koes BW, Hazes JM, Pols HA. Do metabolic factors add to the effect of overweight on hand osteoarthritis?The Rotterdam study. Ann Rheum Dis. 2007;66:916–20. doi: 10.1136/ard.2005.045724.
20. Puenpatom RA, Victor TW. Increased prevalence of metabolic syndrome in individuals with osteoarthritis: an analysis of NHANES III data. Postgrad Med. 2009;121:9–20. doi: 10.3810/pgm.2009.11.2073.
21. Shin D. Association between metabolic syndrome, radiographic knee osteoarthritis, and intensity of knee pain: results of a national survey. J Clin Endocrinol Metab. 2014;99:3177–83. doi: 10.1210/jc.2014-1043.
22. Zhang YM, Wang J, Liu XG. Association between hypertension and risk of knee osteoarthritis: A meta-analysis of observational studies. Medicine (Baltimore) 2017;96:e7584. doi: 10.1097/MD.0000000000007584.
23. Yusuf E, Nelissen RG, Ioan-Facsinay A, Stojanovic-Susulic V, DeGroot J, et al. Association between weight or body mass index and hand osteoarthritis: A systematic review. Ann Rheum Dis. 2010;69:761–5. doi: 10.1136/ard.2008.106930.
24. Berenbaum F, Griffin TM, Liu-Bryan R. Metabolic regulation of inflammation in osteoarthritis. Arthritis Rheum. 2017;69:9–21. doi: 10.1002/art.39842.