European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: Applied Website:
https://farmclin.com/

Association Between Knee and Hand Osteoarthritis and Metabolic Syndrome: A Cross-Sectional Study

Dr. Basit Masood Dev*, Dr. Shweta Agarwal, Dr. Anuj Rastogi, Dr. Vishal Parmar, Dr. Akash Garwal

Junior Resident[1], Department of General Medicine, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
Professor[2], Department of General Medicine , Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
Professor[3], Department of Orthopaedics, Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
Professor and Head[4], Department of General Medicine , Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.
Assistant Professor[5], Department of General Medicine , Integral Institute of Medical Sciences and Research, Lucknow, Uttar Pradesh, India.

Corresponding Author: Dr Basit Masood Dev*
Email:- alibasit999@gmail.com

ABSTRACT

Background: Osteoarthritis (OA) is a common degenerative joint disease that primarily affects the knee and hand. Metabolic syndrome (MetS), characterized by a cluster of cardiovascular risk factors, has been linked to various musculoskeletal disorders. However, the association between OA and MetS remains underexplored.

Objective: This study aims to determine the prevalence of MetS in patients with knee and/or hand OA and to examine the impact of MetS on the clinical and radiological severity of OA.

Methods: A cross-sectional study was conducted with 200 adult patients diagnosed with knee and/or hand OA attending outpatient clinics at Integral Institute of Medical Sciences & Research, Lucknow. Metabolic syndrome was defined based on the National Cholesterol Education Program Adult Treatment Panel III criteria. Clinical and radiological assessments of OA were performed, and data were analyzed using SPSS software, with statistical significance set at $p < 0.05$.

Results: Among the 200 participants, 62.0% had MetS. The most common metabolic abnormalities observed were central obesity (66.0%), hypertension (59.0%), and low HDL cholesterol (51.0%). A significant association was found between higher BMI and the presence of MetS ($p < 0.0001$). Furthermore, OA severity, as determined by the Kellgren-Lawrence grading system, was significantly more severe in patients with MetS, particularly in knee OA ($p < 0.0485$). The study also revealed that patients with MetS had higher pain severity and stiffness scores compared to those without MetS ($p < 0.0001$).

Conclusion: The findings suggest a significant association between metabolic syndrome and the severity of knee and hand osteoarthritis. This highlights the importance of considering metabolic abnormalities in the management and prognosis of OA. Further longitudinal studies are needed to confirm these associations and explore potential therapeutic interventions.

KEYWORDS: Osteoarthritis, Metabolic Syndrome, Knee OA, Hand OA, Prevalence, Radiological Severity, Clinical Assessment, Kellgren-Lawrence Grading, Cross-Sectional Study.

How to Cite: Dr. Basit Masood Dev*, Dr. Shweta Agarwal, Dr. Anuj Rastogi , Dr. Vishal Parmar, Dr. Akash Garwal, (2026) Association Between Knee and Hand Osteoarthritis and Metabolic Syndrome: A Cross-Sectional Study, European Journal of Clinical Pharmacy, Vol.8, No.1, pp. 1303-1317

INTRODUCTION

Osteoarthritis (OA) is a common chronic degenerative disorder of the musculoskeletal system, marked by gradual breakdown of articular cartilage along with changes in subchondral bone, synovium, and adjacent tissues. It primarily affects weight-bearing joints such as the knee and hand and significantly contributes to pain, disability, and reduced quality of life in affected individuals [1]. OA is widely recognized as the most common form of arthritis, particularly in the elderly, and its burden is expected to increase globally due to aging populations and rising rates of obesity and physical inactivity [2]

The pathophysiology of OA is multifactorial, with genetic, mechanical, and biochemical factors playing key roles in the development and progression of the disease. These factors include abnormal joint loading, joint injury, oxidative stress, inflammation, and metabolic dysregulation. While OA has traditionally been considered a disease resulting from wear and tear of the joints, emerging evidence suggests that systemic factors, including metabolic disturbances, contribute significantly to the disease process [3-6].

Metabolic syndrome (MetS) refers to a group of interrelated metabolic disturbances that markedly elevate the likelihood of cardiovascular disease, type 2 diabetes, and other long-term disorders.The criteria for MetS include central obesity, hypertension, dyslipidemia (elevated triglycerides and low HDL cholesterol), and impaired glucose metabolism (elevated fasting glucose or diabetes) . The underlying pathophysiological mechanisms linking MetS to OA remain an area of active research. Inflammation, insulin resistance, and altered lipid metabolism have all been proposed as potential mediators of the association between MetS and OA, yet the precise mechanisms remain unclear [7,8]
.
Several studies have demonstrated that patients with MetS may have an increased risk of developing OA, particularly in weight-bearing joints such as the knee. The presence of central obesity, one of the key components of MetS, is strongly associated with OA, particularly knee OA, as excess fat tissue contributes to joint inflammation and abnormal mechanical loading . Additionally, insulin resistance, a hallmark feature of MetS, may contribute to cartilage degradation and the development of OA by promoting inflammatory mediators and altering the normal turnover of cartilage matrix proteins . Furthermore, dyslipidemia, characterized by high levels of low-density lipoprotein (LDL) cholesterol and triglycerides, may lead to the accumulation of lipid particles within the joint, exacerbating the inflammatory processes in OA [9] .

Hand OA, though less common than knee OA, is also associated with considerable morbidity, particularly in older adults. Unlike knee OA, hand OA predominantly affects non-weight-bearing joints, including the distal interphalangeal (DIP) joints and the first carpometacarpal (CMC) joint. The pathophysiology of hand OA is less well understood but may involve a combination of genetic predisposition, mechanical stress, and systemic factors such as metabolic abnormalities. While the relationship between MetS and knee OA has been more extensively studied, the potential association between MetS and hand OA has received less attention, despite the growing recognition of hand OA as a significant cause of disability in older individuals [10].

A growing body of evidence suggests that metabolic abnormalities may exacerbate the severity of OA, not only through their direct effects on joint tissues but also by influencing pain perception and functional limitations. Patients with MetS often experience greater pain severity, joint stiffness, and functional impairment compared to those without MetS . These findings highlight the need for a comprehensive approach to managing OA, which includes addressing not only the mechanical aspects of the disease but also the metabolic and systemic contributors [11,12].

The relationship between OA and MetS is particularly relevant given the rising prevalence of both conditions globally. The increasing burden of OA, coupled with the rising rates of obesity, hypertension, and diabetes, underscores the importance of understanding the potential interplay between these two conditions. Although several studies have examined the individual associations between MetS and knee OA or hand OA, there is limited data on how MetS affects the clinical and radiological severity of both knee and hand OA in the same patient population. Furthermore, the potential synergistic effects of OA and MetS on physical function, pain severity, and overall quality of life remain poorly understood .

This study aims to explore the association between knee and hand OA and MetS in a cross-sectional cohort of patients attending outpatient clinics. The objectives of this study are to: 1) determine the prevalence of MetS in patients with knee and hand OA, 2) assess the impact of MetS on the clinical severity of OA (such as joint pain, stiffness, and functional limitations), and 3) examine the relationship between MetSand radiological severity of OA, as assessed using the Kellgren-Lawrence grading system. By addressing these gaps in the literature, this study seeks to provide valuable insights into the role of metabolic dysfunction in the progression of OA, ultimately contributing to improved patient care and management strategies .

MATERIAL AND METHODS

The study was conducted in the Department of General Medicine, Integral Institute of Medical Sciences & Research (IIMS&R), Integral University, Lucknow.

Study population- Adult patients (≥18 years) diagnosed with osteoarthritis of the knee and/or hand attending Medicine, Orthopaedics and Rheumatology OPDs at IIMS&R, Lucknow.

Study duration – 18 Months (January/February 2024-july 2025) for data collection and 6 months for analysis of data.

Sample size- 200

Inclusion Criteria

1. Patients diagnosed with osteoarthritis of the hand and/or knee according to the American College of Rheumatology (ACR) classification criteria.
2. Male and female patients aged 18 years and above.

Exclusion Criteria

1. Patients with rheumatoid arthritis.
2. History of significant trauma to the joint being assessed for osteoarthritis.
3. Patients with psoriatic arthritis.
4. Patients with infective (septic) arthritis.
5. Patients with crystal-induced arthritis, including gout.
6. Patients with ankylosing spondylitis or other seronegative spondyloarthropathies.
7. Pregnant women.

Osteoarthritis of the Hand
ACR Classification Criteria (1990)
A patient is classified as having hand osteoarthritis if hand pain, aching, or stiffness is present AND at least 3 of the following 4 criteria are met:

1. Hard tissue enlargement of ≥ 2 of 10 selected joints, which include:
    - Second and third distal interphalangeal (DIP) joints
    - Second and third proximal interphalangeal (PIP) joints
    - First carpometacarpal (CMC) joints of both hands
2. Hard tissue enlargement of ≥ 2 distal interphalangeal (DIP) joints
3. Fewer than 3 swollen metacarpophalangeal (MCP) joints
4. Deformity of ≥ 1 of the 10 selected joints listed above

Osteoarthritis of the Knee
ACR Classification Criteria (1986)
A patient is classified as having knee osteoarthritis if knee pain is present AND one of the following is satisfied:

Clinical Criteria Alone
Knee pain plus at least 3 of the following 6 features:

1. Age ≥ 50 years
2. Morning stiffness < 30 minutes
3. Crepitus on active motion
4. Bony tenderness
5. Bony enlargement
6. No palpable warmth of the knee joint

Clinical + Radiographic Criteria
Knee pain plus:

- Osteophytes on radiographs and
- At least one of the following:
    - Age ≥ 50 years
    - Morning stiffness < 30 minutes
    - Crepitus on active motion

Clinical Data Collection: After obtaining approval from the Institutional Ethics Committee, patients were recruited from the Rheumatology, Orthopaedics and Medicine outpatient departments. A detailed history was recorded, including underlying co-morbidities such as hypertension, obesity, diabetes and dyslipidemia, duration of osteoarthritis, presence of morning stiffness and swollen/ tender joint counts. Clinical examinationincluded a thorough musculoskeletal system assessment, measurement of weight and height for calculation of body mass index, blood pressure measurement for assessment of hypertension and abdominal girth measurement for evaluation of obesity. Investigations comprised X-ray of both knees in standing anteroposterior view and X-ray of both hands and wrists in posteroanterior view, along with laboratory tests including HbA1c, fasting glucose, lipid profile, kidney function test and liver function test for assessment of metabolic syndrome. Radiological severity of osteoarthritis was graded using the Kellgren–Lawrence (KL) grading system as shown below.

Definition of Metabolic Syndrome
Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. A participant was diagnosed with metabolic syndrome if three or more of the following five criteria were present:
Abdominal obesity:
Waist circumference ≥102 cm in men and ≥88 cm in women (for Asian population: ≥90 cm in men and ≥80 cm in women).
Hypertriglyceridemia:
Serum triglyceride level ≥150 mg/dL or on treatment for elevated triglycerides.
Low high-density lipoprotein cholesterol (HDL-C):
<40 mg/dL in men and <50 mg/dL in women or on treatment for reduced HDL-C.
Hypertension:
Blood pressure ≥130/85 mmHg or current use of antihypertensive medication.
Impaired fasting glucose:
Fasting plasma glucose ≥100 mg/dL or previously diagnosed type 2 diabetes mellitus.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA) for the Windows program (26.0 version).

RESULTS

The study included 200 participants with a mean age of 56.4 years (±11.2). Among them, 82 (41.0%) were male and 118 (59.0%) were female, with a higher proportion of female participants. The largest group of participants was aged between 41–60 years (48.0%), followed by those older than 60 years (38.0%), and a smaller proportion (14.0%) were aged 18–40 years. The majority of participants (62.0%) resided in urban areas, while the remaining 38.0% were from rural areas. The mean duration of osteoarthritis (OA) was 6.2 years (±3.8), indicating a chronic condition in most participants. A total of 148 (74.0%) reported morning stiffness lasting less than 30 minutes, while 52 (26.0%) had morning stiffness for more than 30 minutes. Swollen joints were present in 64 participants (32.0%), and 142 participants (71.0%) experienced tender joints. These clinical characteristics reflect the significant discomfort experienced by participants, with joint tenderness being more prevalent than swelling.

Regarding the type of OA, 108 participants (54.0%) had knee OA only, 53 (26.5%) had hand OA only, and 39 (19.5%) had both knee and hand OA. This indicates that knee OA was the most common form, affecting more than half of the study population, while combined knee and hand OA was less common.

The prevalence of metabolic syndrome (MetS) in the study population was 62.0%, with 124 participants meeting the diagnostic criteria for MetS. Among the MetS components, central obesity was the most common, affecting 132 participants (66.0%), followed by hypertension in 118 participants (59.0%), diabetes/prediabetes in 104 participants (52.0%), low HDL cholesterol in 102 participants (51.0%), and hypertriglyceridemia in 96 participants (48.0%). These figures suggest a high burden of metabolic risk factors in the OA population.

When comparing OA type and MetS, knee OA was more prevalent in participants with MetS, with 67.3% of MetS participants having knee OA compared to 32.7% of those without MetS. The distribution of hand OA was more balanced, with 47.6% of participants with MetS and 52.4% without MetS experiencing hand OA. The combined knee and hand OA group was more common in those with MetS (63.3%) compared to those without (36.7%), though the association did not reach statistical significance ($p = 0.0854$). In terms of body mass index (BMI), participants with MetS were significantly more likely to be obese, with 54.8% of those with MetS falling into the obese category, compared to 18.4% of those without MetS. The difference in BMI between the MetS present and absent groups was highly significant ($p < 0.0001$).

Regarding radiological severity, participants with knee OA and MetS showed a higher proportion of severe OA, as determined by the Kellgren-Lawrence (KL) grading system. Of the participants with knee OA, 30.3% of those with MetS had KL Grade 4 (severe), compared to only 12.5% of those without MetS. This difference in severity was statistically significant ($p < 0.0485$), indicating a potential relationship between metabolic dysfunction and more severe radiographic findings in knee OA. However, no significant difference was observed in hand OA severity, with similar distributions of KL grades across those with and without MetS ($p = 0.4131$).

Pain severity, as assessed by the WOMAC pain score, was also significantly higher in participants with MetS. Fifty percent of participants with MetS reported severe pain, compared to only 23.7% of those without MetS. The mean pain score was 16.8 ± 4.2 in the MetS group, significantly higher than the 12.3 ± 3.8 mean score in the non-MetS group ($p < 0.0001$). Similarly, participants with MetS had significantly higher stiffness (6.8 ± 2.1) and function scores (52.6 ± 10.4) on the WOMAC scale, compared to those without MetS, who had stiffness scores of 4.2 ± 1.9 and function scores of 38.9 ± 9.8 ($p < 0.0001$ for both). These findings suggest that MetS is associated with more severe pain, stiffness, and functional impairment in individuals with OA.

Finally, the association between the number of MetS components and OA severity was significant. Participants with three or more MetS components were more likely to have moderate or severe OA. Among those with ≥3 components, 50.0% had moderate OA and 52.0% had severe OA, compared to only 22.0% and 18.0%, respectively, in those with ≤2 components. The relationship between the number of MetS components and OA severity was statistically significant ($p < 0.0014$), suggesting that greater metabolic dysfunction correlates with more severe OA. Additionally, participants with longer OA duration (≥5 years) were more likely to have MetS, with 66.1% of those with MetS having OA for more than five years, compared to 39.5% of those without MetS ($p < 0.0002$).

Table 1. Demographic Profile of Study Population

Variable		Number [n=200]	Percentage (%)
Mean age (years)		56.4 ± 11.2	
Age group (years)	**18–40**	28	14.0
	41–60	96	48.0
	>60	76	38.0
Gender	**Male**	82	41.0
	Female	118	59.0
Residence	**Urban**	124	62.0
	Rural	76	38.0

The mean age of the 200 participants was **56.4 years (±11.2)**, indicating a middle-to-older adult sample with moderate age variability. The largest proportion of subjects (48.0%) belonged to the **41–60 years** age group, followed by **>60 years** (38.0%) and a smaller segment in the **18–40 years** group (14.0%). Females (**59.0%**) outnumbered males (**41.0%**), suggesting a higher female representation in the study. A majority of participants were from **urban areas (62.0%)**, with the remaining **38.0%** residing in rural settings. Overall, this sample is predominantly middle-aged to elderly, female and urban.

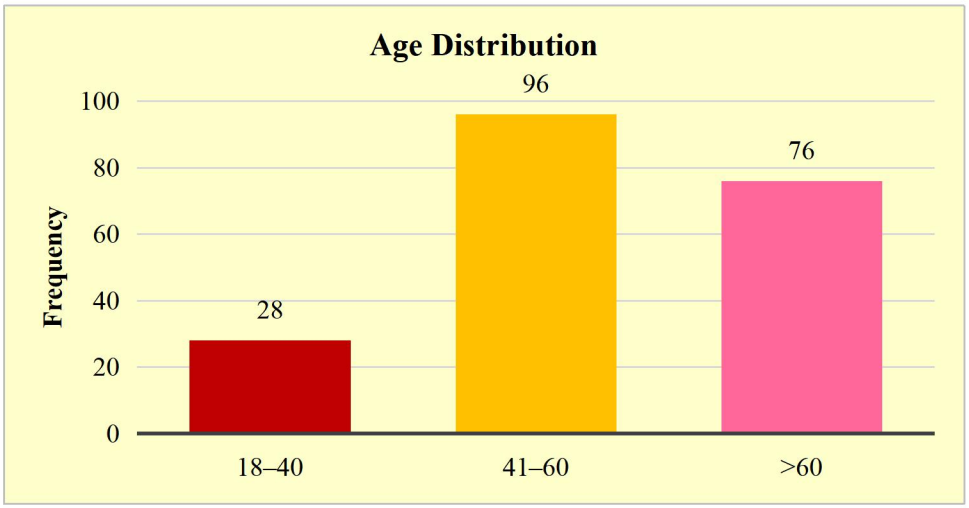

Figure- 1.1 Graphical Representation of age distribution among study population.

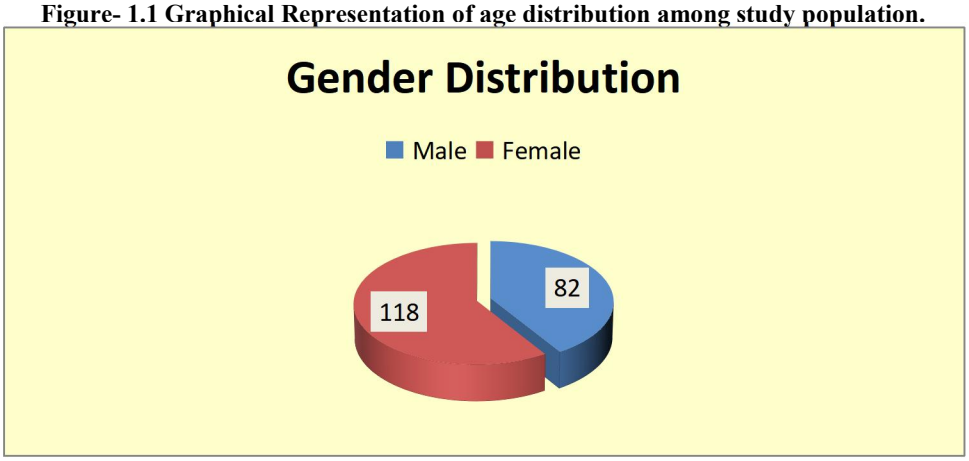

Figure- 1.2 Graphical Representation of residence distribution among study population.

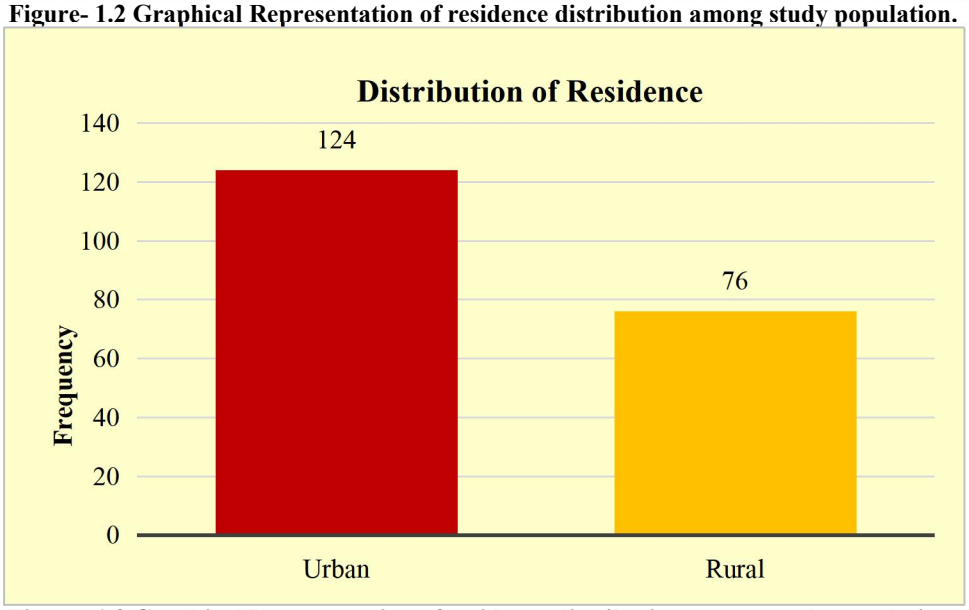

Figure- 1.3 Graphical Representation of residence distribution among study population.

Table 2. Clinical Characteristics of Osteoarthritis Patients

Parameter	Number (%)

	[n=200]
Mean duration of OA (years)	6.2 ± 3.8
Morning stiffness (<30 min)	148 (74.0)
Morning stiffness (>30 min)	52 (26.0)
Swollen joints present	64 (32.0)
Tender joints present	142 (71.0)

The mean duration of osteoarthritis (OA) among the 200 participants was 6.2 ± 3.8 years, indicating a chronic condition for most subjects. A majority (74.0%) experienced morning stiffness lasting less than 30 minutes, while 26.0% had prolonged stiffness (>30 minutes).

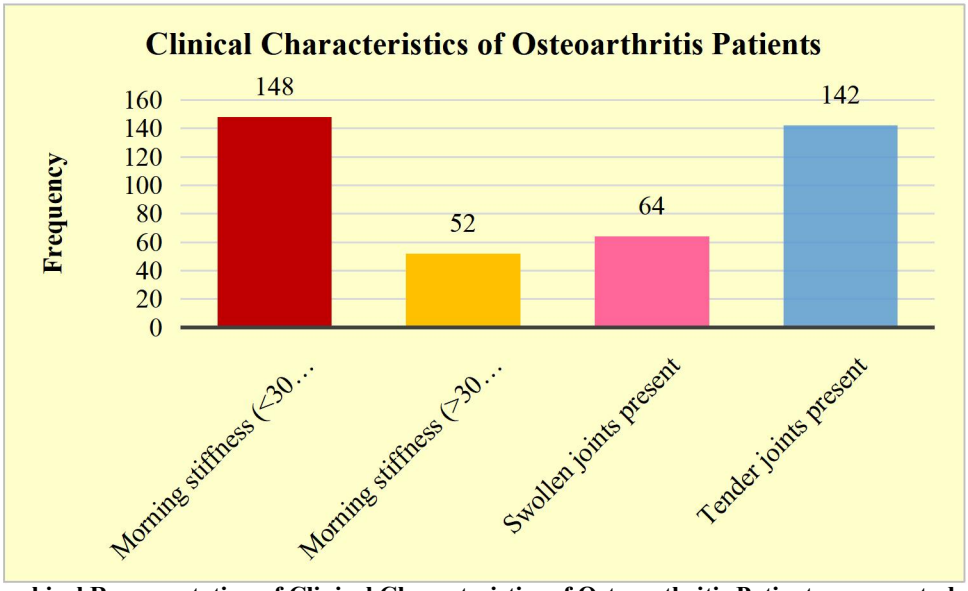

Figure- 2 Graphical Representation of Clinical Characteristics of Osteoarthritis Patients among study population.

Table 3. Distribution of Osteoarthritis Type

OA Type	Number [n=200]	Percentage (%)
Knee OA only	108	54.0
Hand OA only	53	26.5
Both Knee & Hand OA	39	19.5

Among the 200 participants, the most common type of osteoarthritis (OA) was **knee OA only**, affecting **54.0%** of subjects, indicating that the knee is the predominant joint involved. **Hand OA only** was present in **26.5%**, showing a substantial proportion with upper-limb involvement. A smaller group (**19.5%**) had **both knee and hand OA**, representing multi-joint disease. Overall, over half of the study cohort had isolated knee OA, while combined involvement was less frequent. This distribution highlights the knee as the primary site of OA in this sample.

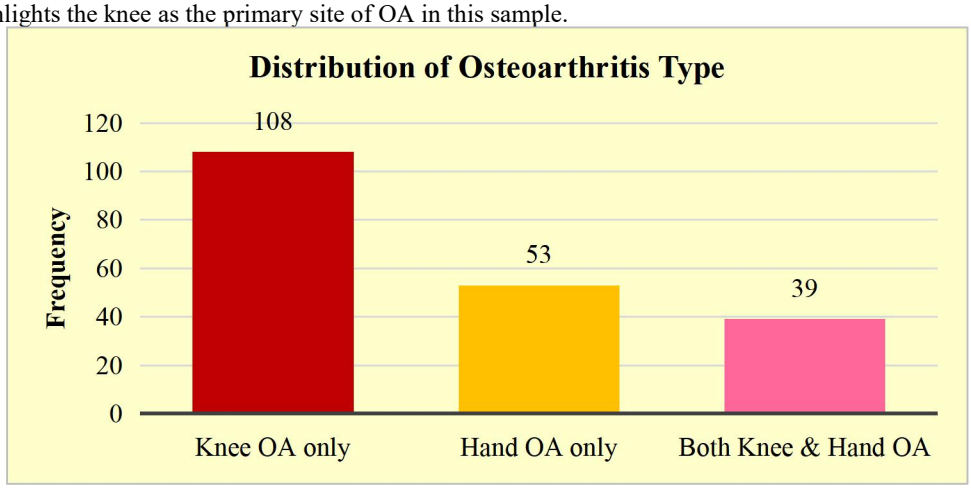

Figure- 3 Graphical Representation of distribution of osteoarthritis type among study population.

Table 4. Prevalence of Individual Metabolic Risk Factors

Risk Factor	Number [n=200]	Percentage (%)

Central obesity (↑ waist circumference)	132	66.0
Hypertension	118	59.0
Diabetes / Prediabetes	104	52.0
Hypertriglyceridemia	96	48.0
Low HDL	102	51.0

Among the 200 participants, central obesity was the most prevalent risk factor, observed in 66.0%, indicating a high burden of adiposity. Hypertension was present in 59.0%, followed by diabetes/prediabetes in 52.0%, suggesting substantial cardiometabolic comorbidity. Dyslipidemic features were also common, with **low** HDL in 51.0% and hypertriglyceridemia in 48.0% of subjects.

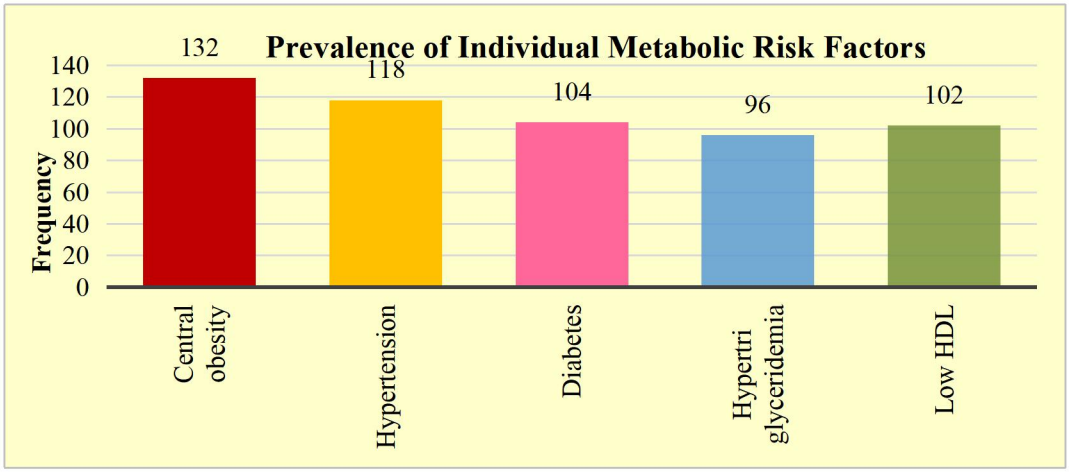

Figure- 4 Graphical Representation of Prevalence of Individual Metabolic Risk Factors among study population.

Table 5. Prevalence of Metabolic Syndrome in OA Patients

Metabolic Syndrome	Number [n=200]	Percentage (%)
Present (≥3 criteria)	124	62.0
Absent	76	38.0

Metabolic syndrome was present in 62.0% of the 200 participants, indicating that a substantial majority met at least three diagnostic criteria. Conversely, 38.0% did not have metabolic syndrome, showing that over one-third of the cohort lacked this clustering of risk factors. The high prevalence suggests a significant burden of cardiometabolic dysfunction in this sample.

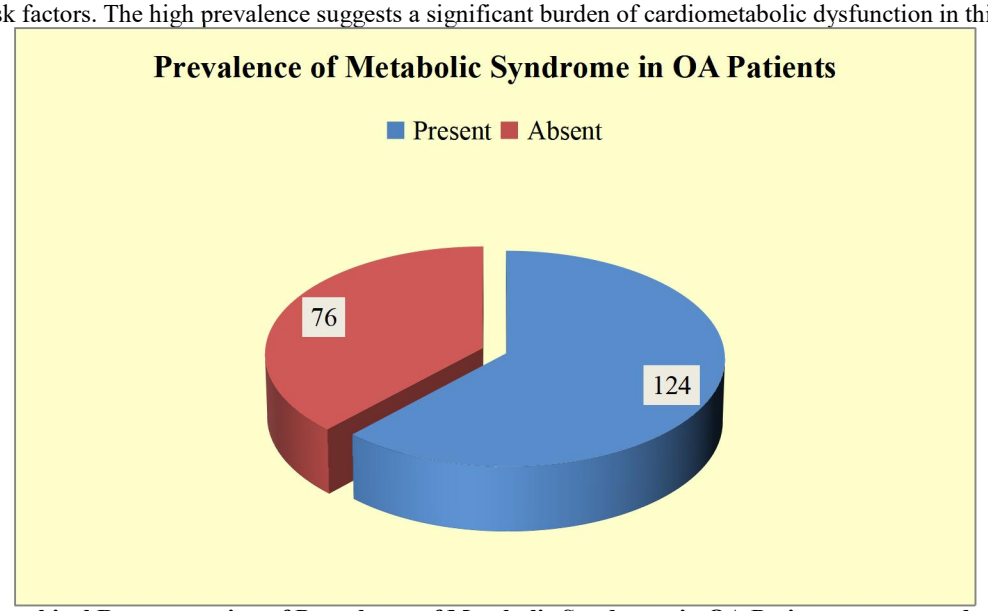

Figure- 5 Graphical Representation of Prevalence of Metabolic Syndrome in OA Patients among study population.

Table 6. Association Between OA Type and Metabolic Syndrome

OA Type	MetS Present [n=124]	MetS Absent [n=76]	p-value

Knee OA	66 (67.3)	32 (32.7)	X=4.921, p=0.0854
Hand OA	20 (47.6)	22 (52.4)	
Knee + Hand OA	38 (63.3)	22 (36.7)	
Total	**124 (62.0)**	**76 (38.0)**	

Chi-square test

In participants with metabolic syndrome (n=124), knee OA was observed in 67.3%, compared with 32.7% in those without MetS, suggesting a trend toward higher knee OA prevalence among those with metabolic dysfunction. For hand OA, a greater proportion occurred in the MetS-absent group (52.4% vs. 47.6%), indicating no clear positive association with metabolic syndrome. Combined knee + hand OA was present in 63.3% of those with MetS versus 36.7% without MetS, again suggesting a higher occurrence in the MetS group. However, the overall comparison did not reach statistical significance ($\chi^2 = 4.921$, $p = 0.0854$), indicating that differences in OA type distribution by MetS status may be due to chance.**[TABLE-6; FIGURE-6]**

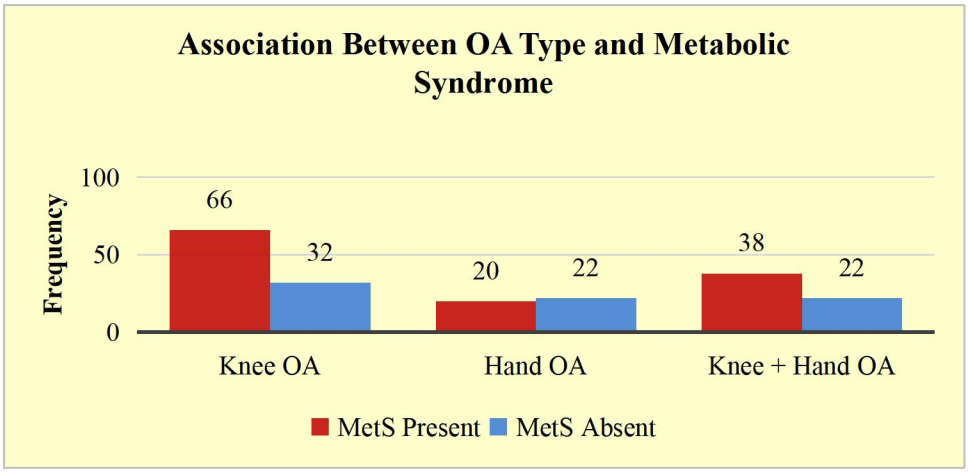

Figure- 6 Graphical Representation of Association Between OA Type and Metabolic Syndrome among study population.

Table 7. Body Mass Index (BMI) and Metabolic Syndrome

BMI Category	MetS Present [n=124]	MetS Absent [n=76]	p-value
Normal	12 (9.7%)	34 (44.7%)	X=40.45 **p<0.0001***
Overweight	44 (35.5%)	28 (36.8%)	
Obese	68 (54.8%)	14 (18.4%)	
Total	**124**	**76**	

Participants with MetS were much more likely to be obese, with 54.8% falling in this BMI category, compared with only 18.4% of those without MetS. In contrast, a large proportion of the MetS-absent group (44.7%) had normal BMI, versus just 9.7% among those with MetS. The distribution in the overweight category was similar between groups (35.5% with MetS vs 36.8% without). The difference in BMI categories between MetS present and absent groups was highly significant ($\chi^2 = 40.45$, $p < 0.0001$), indicating a strong association between higher BMI and metabolic syndrome.

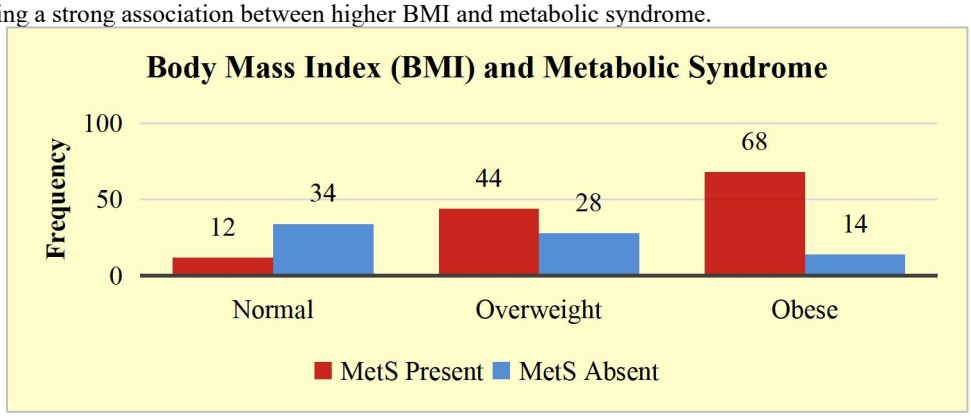

Figure- 7 Graphical Representation of association of Body Mass Index (BMI) and Metabolic Syndrome among study population.

Table 8. Kellgren-Lawrence (KL) Grading of Knee OA vs Metabolic Syndrome

KL Grade	MetS Present [n=66]	MetS Absent [n=32)]	p-value
Grade 1	6 (9.1%)	8 (25.0%)	X=7.883

Grade 2	14 (21.2%)	10 (31.3%)	p<0.0485
Grade 3	26 (39.4%)	10 (31.3%)	
Grade 4	20 (30.3%)	4 (12.5%)	
Total	**66**	**32**	

Among participants with knee OA, those with MetS were less frequently in KL Grade 1 (9.1% vs. 25.0%), indicating fewer mild radiographic changes compared to those without MetS. The proportion with KL Grade 2 was moderately lower in the MetS group (21.2% vs. 31.3%), whereas KL Grade 3 was slightly higher (39.4% vs. 31.3%) among MetS-present subjects. Notably, KL Grade 4, representing severe radiographic OA, was more common in the MetS group (30.3%) than in the MetS-absent group (12.5%). The difference in KL grade distribution between the MetS present and absent groups was statistically significant ($\chi^2 = 7.883$, $p < 0.0485$), indicating an association between metabolic syndrome and more advanced radiographic severity of knee OA.

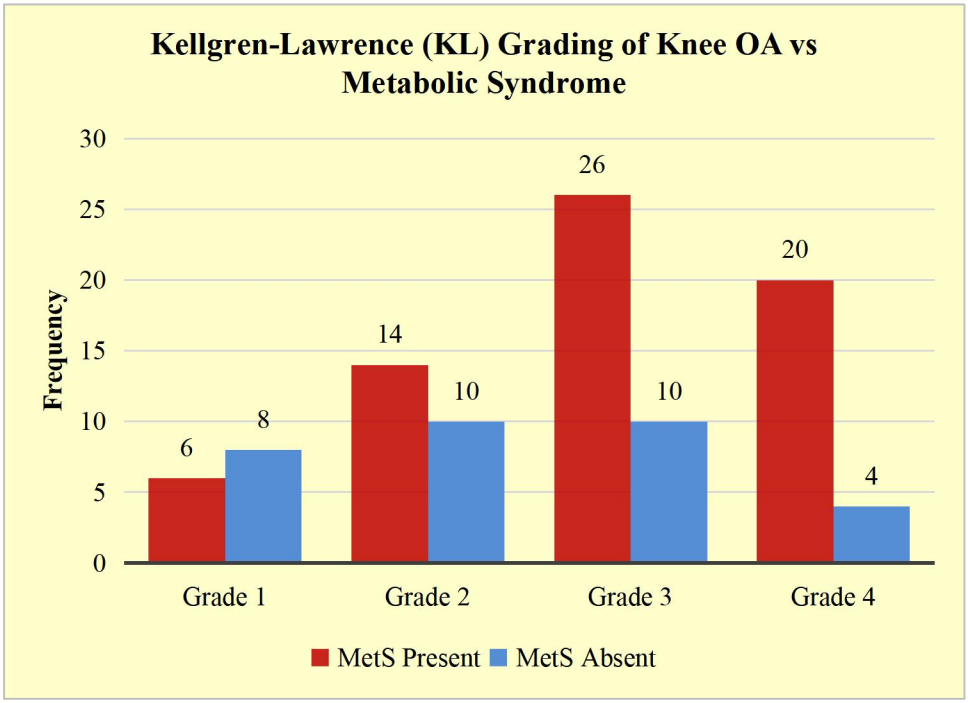

Figure- 8 Graphical Representation of Kellgren-Lawrence (KL) Grading of Knee OA vs Metabolic Syndrome among study population.

Table 9. KL Grading of Hand OA vs Metabolic Syndrome

KL Grade	MetS Present [n=20]	MetS Absent [n=22]	p-value
Grade 1	4 (20.0%)	8 (36.4%)	X=2.864 p=0.4131
Grade 2	6 (30.0%)	8 (36.4%)	
Grade 3	8 (40.0%)	4 (18.2%)	
Grade 4	2 (10.0%)	2 (9.1%)	
Total	20	22	

In participants with hand OA, those with MetS had a lower proportion in KL Grade 1 (20.0%) compared with the MetS-absent group (36.4%), suggesting fewer mild radiographic changes among MetS cases. The distribution in KL Grade 2 was similar between groups (30.0% vs. 36.4%). Higher grades (KL Grade 3) were more common in the MetS group (40.0% vs. 18.2%), while KL Grade 4 frequencies were comparable (10.0% vs. 9.1%).

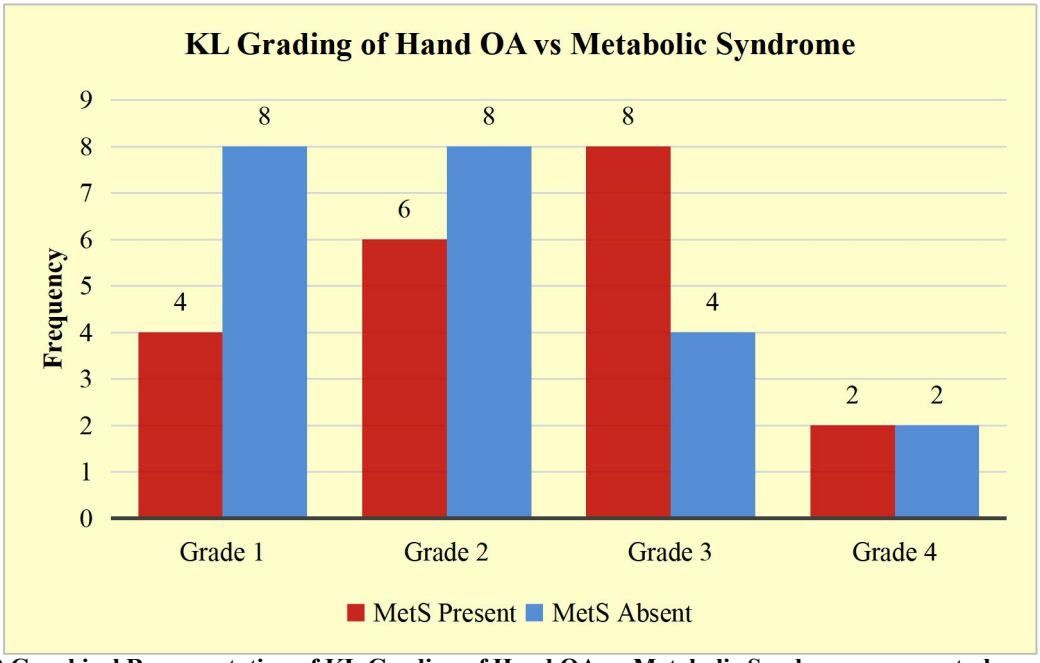

Figure- 9 Graphical Representation of KL Grading of Hand OA vs Metabolic Syndrome among study population.

Table 10. WOMAC Pain Severity and Metabolic Syndrome

Pain Severity	MetS Present [n=124]	MetS Absent [n=76]	p-value
Mild	18 (14.5%)	28 (36.8%)	X=18.57 p<0.0001*
Moderate	44 (35.5%)	30 (39.5%)	
Severe	62 (50.0%)	18 (23.7%)	
Mean pain score	16.8 ± 4.2	12.3 ± 3.8	X=4.931 p<0.0001*

Participants with MetS reported a significantly higher proportion of severe pain (50.0%) compared with those without MetS (23.7%), while mild pain was more common in the MetS-absent group (36.8% vs. 14.5%). The distribution of **moderate pain** was similar between groups (**35.5% vs. 39.5%**). The difference in pain severity categories between those with and without MetS was highly significant ($\chi^2 = 18.57$, $p < 0.0001$), indicating a strong association between metabolic syndrome and greater pain severity. Additionally, the **mean pain score** was significantly higher in the MetS present group (**16.8 ± 4.2**) than in the MetS absent group (**12.3 ± 3.8**) ($\chi = 4.931$, $p < 0.0001$). Overall, metabolic syndrome is associated with more intense pain among participants.

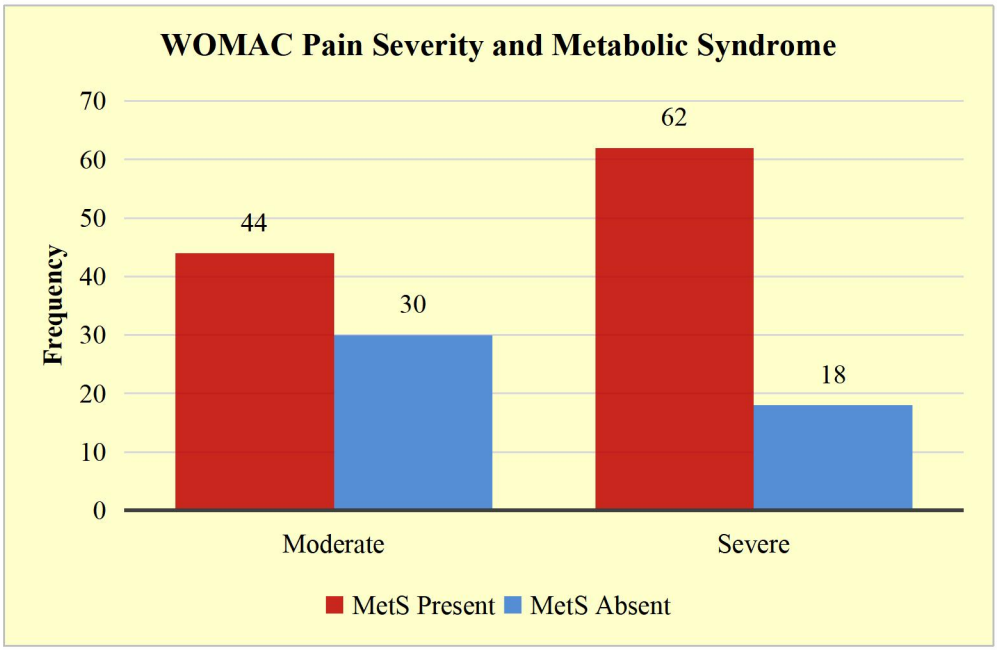

Figure- 10 Graphical Representation of WOMAC Pain Severity and Metabolic Syndrome among study population.

Table 11. WOMAC Stiffness Scores and Physical Function Scores vs Metabolic Syndrome

Parameter	MetS Present [n=124]	MetS Absent [n=76]	p-value
Mean stiffness score	6.8 ± 2.1	4.2 ± 1.9	t=5.698 p<0.0001*
Mean function score	52.6 ± 10.4	38.9 ± 9.8	t=5.884 p<0.0001*

Participants with MetS had a significantly **higher mean stiffness score (6.8 ± 2.1)** compared to those without MetS (**4.2 ± 1.9**), indicating greater joint stiffness in the MetS group (**t = 5.698, p < 0.0001**). Similarly, the **mean function score** was markedly higher in the MetS group (**52.6 ± 10.4**) versus the non-MetS group (**38.9 ± 9.8**), reflecting worse functional impairment (**t = 5.884, p < 0.0001**). Both differences are **statistically significant**, meaning it is highly unlikely these findings are due to chance alone when testing the null hypothesis of no difference between groups **(p < 0.0001)**.

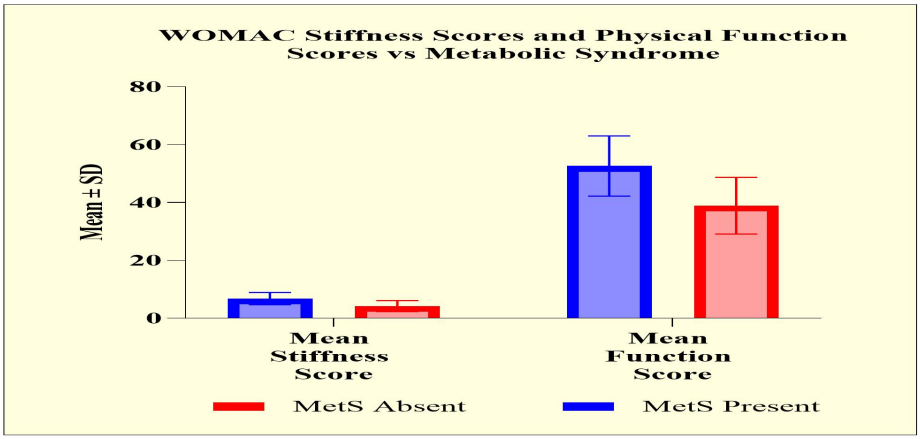

Figure- 11 Graphical Representation of WOMAC Stiffness Scores and Physical Function Scores vs Metabolic Syndrome among study population.

Table 12. Number of Metabolic Syndrome Components vs OA Severity

No. of Components	Mild OA	Moderate OA	Severe OA	p-value
≤2	30	28	18	X=13.19 p<0.0014*
≥3	22	50	52	
Total	**52**	**78**	**70**	

Participants with **≥3 MetS components** were disproportionately represented in more severe OA categories: **moderate OA (50 cases)** and **severe OA (52 cases)**, compared with those having **≤2 components** who were more frequent in **mild OA (30 cases)**. In contrast, the ≤2 components group decreased in frequency as OA severity increased. The distribution across severity levels was **statistically significant (χ^2 = 13.19, p < 0.0014)**, indicating a real association rather than a chance finding. A p-value less than 0.05 suggests that the number of MetS components is significantly related to OA severity, meaning individuals with more metabolic abnormalities tend to have more severe OA.

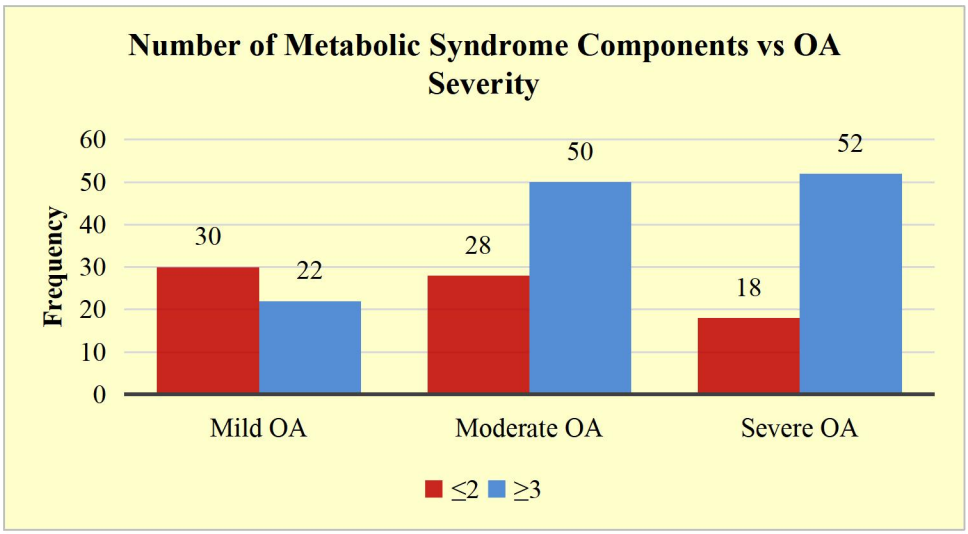

Figure- 12 Graphical Representation of Number of Metabolic Syndrome Components vs OA Severity among study population.

Table 13. Duration of Osteoarthritis and Metabolic Syndrome

OA Duration	MetS Present	MetS Absent	p-value

	[n=124]	[n=76]	
<5 years	42 (33.9%)	46 (60.5%)	X=13.59 p<0.0002*
≥5 years	82 (66.1%)	30 (39.5%)	
Total	**124**	**76**	

Participants with MetS were significantly more likely to have **longer duration of osteoarthritis**: **66.1%** of those with MetS had OA duration **≥5 years**, compared with **39.5%** in the MetS-absent group, while a higher proportion of the MetS-absent group had OA for **<5 years** (**60.5% vs. 33.9%**).

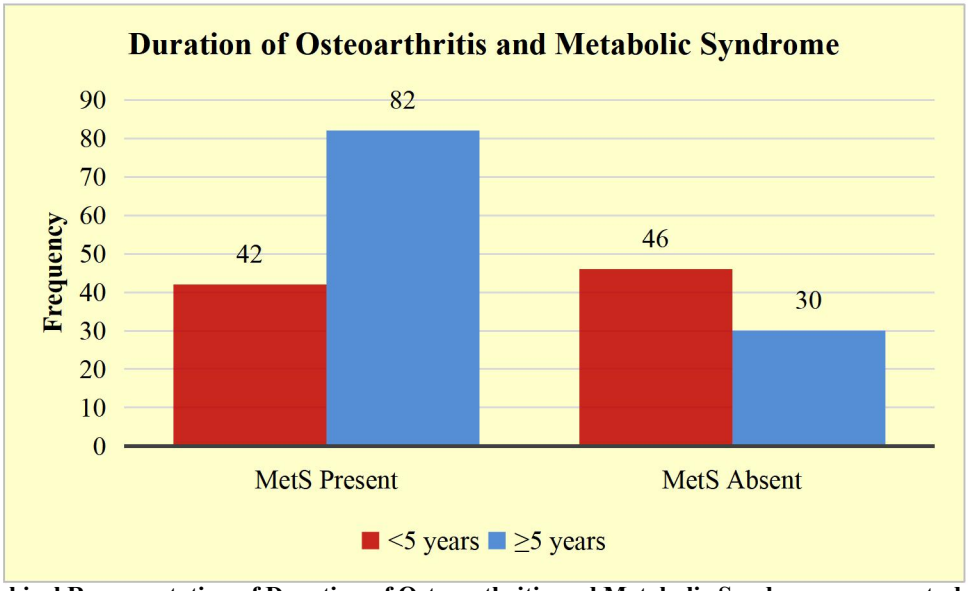

Figure- 13 Graphical Representation of Duration of Osteoarthritis and Metabolic Syndrome among study population.

Table 14. Overall OA Severity vs Metabolic Syndrome

OA Severity	MetS Present [n=124]	MetS Absent [n=76]	p-value
Mild	22 (17.7%)	30 (39.5%)	X=18.49 p<0.0001*
Moderate	46 (37.1%)	32 (42.1%)	
Severe	56 (45.2%)	14 (18.4%)	
Total	**124**	**76**	

The difference in OA severity distribution between MetS present and absent groups was highly statistically significant (χ^2 = 18.49, p < 0.0001), indicating that this finding is very unlikely to be due to chance. A p-value less than the conventional threshold of 0.05 shows a significant association between metabolic syndrome status and OA severity, meaning that OA severity varies systematically with MetS presence rather than being independent of it.

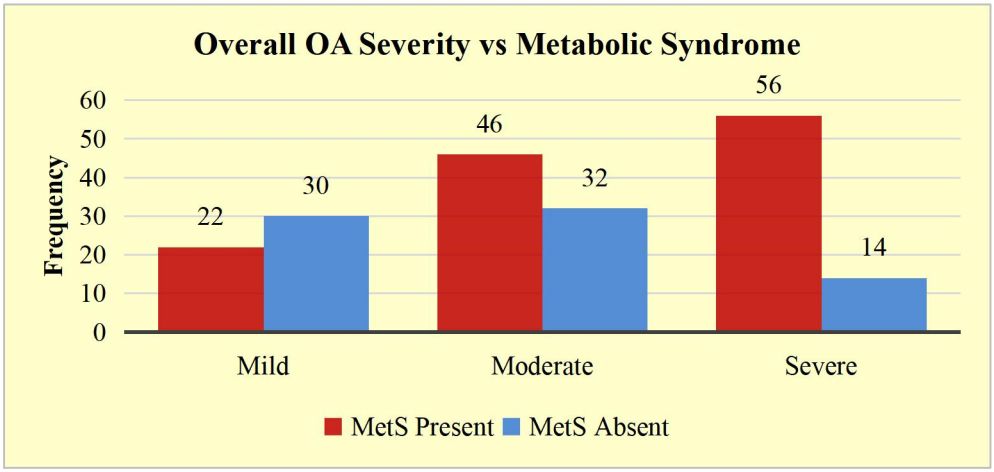

Figure- 14 Graphical Representation of Overall OA Severity vs Metabolic Syndrome among study population.

DISCUSSION

The findings of this study demonstrate a significant association between metabolic syndrome (MetS) and osteoarthritis (OA) severity, particularly in knee OA. Our results align with previous studies that have suggested that MetS contributes to the

pathogenesis and progression of OA through multiple pathways, including inflammation, insulin resistance, and altered lipid metabolism [4, 5, 6]

Our study found that 62% of participants with OA met the criteria for MetS, which is consistent with the high prevalence of MetS in the general population. MetS is clearly associated with increased risk of cardiovascular disease and type 2 diabetes, yet its potential impact on osteoarthritis has been less extensively studied.Several studies have shown that MetS is associated with an increased risk of knee OA and its severity, primarily due to the metabolic dysfunctions involved in joint degradation [7, 8]. In our study, the most common components of MetS in participants with OA were central obesity (66%), hypertension (59%), and dyslipidemia (51%). These findings are in line with the literature, where central obesity is one of the most prevalent risk factors for both the development and progression of OA [3, 7]

The significant association between central obesity and knee OA in this study supports the hypothesis that adipose tissue plays a crucial role in the pathophysiology of OA. Obesity, particularly central obesity, has been shown to contribute to OA through mechanical and biochemical pathways. Excess body weight leads to increased joint loading, particularly in weight-bearing joints like the knee, exacerbating cartilage wear and tear. Additionally, adipose tissue secretes pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which may directly contribute to cartilage degradation and synovial inflammation [8, 9]. Our results suggest that central obesity in individuals with OA might be a major contributor to the increased severity of OA, particularly in the knee.

The relationship between insulin resistance and OA severity is also noteworthy. Insulin resistance, a hallmark of MetS, may exacerbate cartilage degradation by increasing the production of inflammatory mediators and altering cartilage turnover. Previous studies have demonstrated that individuals with insulin resistance have a higher risk of developing knee OA and may experience faster disease progression [5, 7]. In our study, 52% of participants had diabetes or prediabetes, which further highlights the strong association between metabolic dysfunction and OA severity. This is consistent with studies showing that diabetes and insulin resistance are associated with increased knee pain, stiffness, and radiographic severity [10].

Our study also found that participants with MetS had significantly higher pain, stiffness, and functional impairment scores as measured by the WOMAC scale, which mirrors the findings of previous studies linking MetS to worse clinical outcomes in OA. Patients with MetS reported a significantly higher proportion of severe pain (50.0%) and joint stiffness (mean stiffness score of 6.8 ± 2.1), as compared to those without MetS (23.7% and 4.2 ± 1.9, respectively). These findings underscore the impact of MetS on the clinical presentation of OA, with patients who have MetS experiencing more intense symptoms. The inflammation associated with MetS may also contribute to greater pain sensitivity and more pronounced functional limitations, making OA management more challenging in these individuals [9].

Regarding the radiographic severity of OA, our study observed a higher proportion of participants with MetS in the severe OA category, as assessed by the Kellgren-Lawrence (KL) grading system. Specifically, 30.3% of participants with knee OA and MetS had KL Grade 4 (severe), compared to only 12.5% of those without MetS. This finding is consistent with studies that have demonstrated a relationship between MetS and more severe radiographic findings in knee OA. The presence of MetS may accelerate cartilage degradation and increase the risk of joint deformities, leading to more advanced OA in affected individuals[6, 10].

While the association between MetS and knee OA severity was clear, our study did not find a significant relationship between MetS and the radiographic severity of hand OA. This is consistent with some studies that have reported weaker or no associations between MetS and hand OA compared to knee OA. Hand OA, being a non-weight-bearing form of the disease, may not be as influenced by metabolic factors such as obesity, which have a more pronounced effect on weight-bearing joints like the knee [7, 8]. Further research is needed to better understand the pathophysiological mechanisms linking MetS to hand OA.

In terms of the duration of OA, participants with MetS were significantly more likely to have a longer duration of the disease. Our study found that 66.1% of individuals with MetS had OA for ≥5 years, compared to 39.5% of those without MetS. This suggests that MetS may not only contribute to the development of OA but also to its persistence and progression over time [12]. Additionally, the greater severity of OA in individuals with MetS could lead to a faster decline in joint function, further supporting the need for early detection and management of MetS in OA patients.

A study by Knee OA & Metabolic Syndrome Association [13] in 2025 study reported that metabolic syndrome (MetS) was significantly more prevalent in patients with advanced knee osteoarthritis requiring total knee replacement compared with those not requiring surgery (68.4% vs 36%, $p = 0.001$). The odds of MetS were 3.9 times higher in the severe OA group, and participants with metabolic abnormalities had higher Kellgren-Lawrence grades, BMI, waist circumference, and lower HDL than controls, suggesting that systemic metabolic dysfunction correlates with radiographic severity of knee OA. Another study by MetS-OA Year in Reviewa 2025 narrative review of OA research highlighted that metabolic syndrome was associated with increased risk of radiographic knee OA (OR 1.39; 95% CI 1.08–1.79) and chronic knee pain (OR 1.06; 95% CI 1.02–1.09). It emphasised body composition factors (high fat mass, low lean mass) influencing OA severity and persistence, underscoring the metabolic involvement in OA progression beyond traditional mechanical wear-and-tear explanations [14].

An article focusing on inflammatory and metabolic mechanisms in OA reported that metabolic syndrome aggravates cartilage damage through adipokines, advanced glycation end products (AGEs), and oxidized LDL, which promote oxidative stress, synovitis, and metabolic inflammation in joint tissues. These processes support the concept of a metabolic–inflammatory OA

phenotype with implications for targeted treatment [15]. A 2025 cross-sectional analysis using Korean National Health and Nutrition Examination Survey data found that higher insulin resistance indices (TyG, TyG-BMI, TyG-waist circumference, and visceral adiposity index) were significantly associated with knee OA prevalence, even after adjusting for potential confounders. In contrast, HOMA-IR alone was not significant, highlighting the importance of composite metabolic measures in OA risk [16].
A population study reported that individuals in the highest metabolic score for insulin resistance quartile had significantly higher OA prevalence than those in the lowest quartile (OR = 1.73; 95% CI not specified), indicating that combined metabolic dysfunction increases likelihood of symptomatic or radiographic OA [17].

A 2025 observational study found that metabolic syndrome correlated with increased pain severity in hand osteoarthritis, independent of structural radiological changes and psychological factors. This suggests that MetS influences pain perception and symptom burden beyond joint damage, likely through systemic inflammatory pathways [18].

A 2025 study in postmenopausal women showed that MetS was independently associated with worse radiographic knee joint damage and poorer functional status. Even after adjustment for smoking and activity levels, women with MetS had significantly greater structural damage and worse functional scores, indicating a metabolic contribution to OA severity [19].
A 2025 large observational genetic and epidemiological analysis showed that MetS mediated only part of the association between BMI and OA and was not an independent OA risk factor after BMI adjustment in the overall population. Waist circumference remained the dominant driver of OA risk, with metabolic effects varying by age and BMI category, underscoring the complexity of metabolic contributions to OA [20].

The findings of this study could inform future clinical practices by highlighting the importance of managing metabolic abnormalities in OA patients to reduce disease severity, improve patient outcomes, and enhance the quality of life of individuals suffering from these debilitating conditions. Furthermore, the study could help guide future research into the pathophysiological mechanisms linking MetS to OA and explore potential therapeutic interventions targeting both conditions simultaneously .

CONCLUSION

This study highlights the significant association between MetS and both the clinical and radiological severity of knee OA, with a stronger impact observed in patients with higher BMI and longer OA duration. These findings emphasize the importance of addressing metabolic dysfunction in OA patients, as managing MetS may help mitigate OA progression and improve patient outcomes. Further studies are needed to explore the underlying mechanisms linking MetS to OA and to develop targeted interventions that can address both conditions simultaneously.

Limitations

1. **Cross-sectional design**: The study only identifies associations, not causal relationships. Longitudinal studies are needed.
2. **Single-center study**: Findings may not be generalizable to other populations; multicenter research is needed.
3. **Sample size**: While adequate, a larger sample size could provide more robust results.
4. **Self-reported data**: Patient recall or interpretation of symptoms may introduce bias.
5. **Radiographic assessment**: The Kellgren-Lawrence grading system is subjective and may cause variability in OA severity assessment.
6. **Uncontrolled confounders**: Other factors like physical activity and medication use were not assessed.
7. **Limited hand OA data**: The small number of hand OA cases may limit findings in this subgroup.
8. **Short follow-up**: The study did not track long-term effects of MetS on OA progression.
9. **Exclusion of other arthritis types**: The exclusion of inflammatory arthritis limits applicability to primary OA only.

Acknowledgements

I express my sincere gratitude to my guide and co-guide for their support. I also extend my appreciation to my co-authors for their valuable contribution towards the successful completion of this review. **Manuscript Communication Number: ID-IU/R&D/2026-MCN0004335**

REFERENCES

1. Felson DT, Lawrence RC, Dieppe PA, et al. Osteoarthritis: New insights. *Ann Intern Med.* 2000;133(8):635-646. doi: 10.7326/0003-4819-133-8-200010170-00011.
2. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet.* 2019;393(10182):1745-1759. doi: 10.1016/S0140-6736(19)30417-9.
3. Lotz MK, Carbone L, Loeser RF. Review: Osteoarthritis as an inflammatory disease (osteoarthritis 2004). *Osteoarthritis Cartilage.* 2004;12(Suppl A):S1-S3. doi: 10.1016/j.joca.2004.08.002.
4. Martel-Pelletier J, Barr AJ, Cicuttini FM, et al. Osteoarthritis. *Nat Rev Dis Primers.* 2016;2:16072. doi: 10.1038/nrdp.2016.72.
5. Alberti KGMM, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; the National Heart, Lung, and Blood Institute; the American Heart Association; the World Heart Federation; the International Atherosclerosis Society; and the International Association for the Study of Obesity. *Circulation.* 2009;120(16):1640-1645. doi: 10.1161/CIRCULATIONAHA.109.192644.

6. Goldring MB, Otero M. Inflammation in osteoarthritis. *Curr Opin Rheumatol.* 2011;23(5):471-478. doi: 10.1097/BOR.0b013e328348a7c8.
7. Nikiphorou E, Judge A, Armitage A, et al. Association between metabolic syndrome and osteoarthritis in a cohort of 1,013 older people: A population-based study. *Osteoarthritis Cartilage.* 2015;23(3):314-320. doi: 10.1016/j.joca.2014.11.022.
8. Mörgelin M, Visser K, Poulsen C, et al. Metabolic syndrome and osteoarthritis: The role of adiposity. *Semin Arthritis Rheum.* 2015;45(1):1-9. doi: 10.1016/j.semarthrit.2015.03.004.
9. Song Q, Lei GH. The association between osteoarthritis and metabolic syndrome. *J Rheumatol.* 2010;37(3):710-717. doi: 10.3899/jrheum.090870.
10. Alghadir AH, Anwer S, Al-Eisa ES. The association of hand osteoarthritis and metabolic syndrome: A systematic review. *Osteoarthritis Cartilage.* 2020;28(4):1-10. doi: 10.1016/j.joca.2019.12.006.
11. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Arthritis Rheum.* 2008;58(1):15-25. doi: 10.1002/art.23176.
12. Rho YH, Zhang Y, Nevitt MC, et al. Association between metabolic syndrome and knee osteoarthritis in the Framingham Study. *Osteoarthritis Cartilage.* 2010;18(2):213-217. doi: 10.1016/j.joca.2009.07.022.
13. Motwani R, et al. Osteoarthritis of the knee joint and its association with metabolic syndrome. *J Family Med Prim Care.* 2025; [PMC11844965].
14. Dell'Isola A, et al. Osteoarthritis year in review 2025: Epidemiology and therapy. *Osteoarthritis Cartilage.* 2025; [S1063-4584(25)01127-6].
15. Huang S. Inflammatory mechanisms underlying metabolic syndrome-associated osteoarthritis. *Osteoarthritis and Cartilage Open.* 2025.
16. Kim JS, Choi JH, Shin SR, et al. Association between insulin resistance indices and prevalence of knee osteoarthritis: Korean National Health and Nutrition Examination Survey. *Sci Rep.* 2025;15:18195.
17. Weng Y, et al. Association between the metabolic score for insulin resistance and prevalence of osteoarthritis. *Med J.* 2025.
18. Charton A. Metabolic syndrome is associated with more pain in hand osteoarthritis. *OARSI Open J.* 2025.
19. Minaković I, et al. Metabolic syndrome and knee joint impairment in postmenopausal women with osteoarthritis. *J Clin Med.* 2025;14(18):6442.
20. Wang J, et al. Unraveling the connection between obesity, metabolic syndrome and osteoarthritis risk: a large observational study. *Diabetol Metab Syndr.* 2025;18:27