The Impact of Metabolic Syndrome on Quality of Life Among Individuals With Knee Osteoarthritis Living in Egypt

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ABSTRACT

BACKGROUND: Several studies have linked metabolic syndrome (MetS) to osteoarthritis (OA), but they have not looked into how MetS can affect the health-related quality of life (HRQOL) of OA individuals.

OBJECTIVES: We aimed to assess the association of MetS and its components, including obesity, hypertension, hyperglycemia, and dyslipidemia, with HRQOL among Egyptians with knee OA.

METHODS: This cross-sectional study comprised 116 adult Egyptian participants with knee OA. They were divided into 2 groups based on whether or not they had the MetS. All participants were subjected to a thorough medical history taking and a detailed medical examination. The Kellgren and Lawrence (K/L) scale evaluated OA in all individuals using anteroposterior knee radiographs. The Health Assessment Questionnaire-Disability Index (HAQ-DI) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used to assess participants’ HRQOL; their higher scores indicate more disability. Spearman rank and Pearson’s correlation analyses were used to assess the association between variables.

RESULTS: Diabetes, hypertension, dyslipidemia, and obesity were significantly associated with the OA + MetS group with a prevalence of 77.6%, 82.8%, 77.6%, and 50.0%, respectively. According to the K/L scale, 70.7% of the OA + MetS group had grade IV knee affection. The HAQ-DI and WOMAC scores were significantly (P< .001) higher among the OA + MetS individuals compared with the OA individuals. Interleukin (IL)-6 serum levels were also significantly higher in the OA + MetS group (P=.036) and increased significantly with the more serious radiological damage and functional disability. We found significant positive correlations between HAQ-DI and WOMAC with waist circumference (P=.004, .001), as well as triglycerides (P=.006, .008), cholesterol (P=.041, .048), fasting blood sugar (P< .001, <.001) and significant negative correlations with high-density lipoprotein levels (P=.628, .002).

CONCLUSIONS: Individuals with knee OA with MetS showed more significant radiological damage, severe functional disability, and poor HRQOL. They also had higher levels of IL-6, which correlated significantly with the degree of disability, promoting it as a significant therapeutic target.

KEYWORDS: HAQ-DI, interleukin-6, knee, metabolic syndrome, osteoarthritis, quality of life, WOMAC

Introduction

Osteoarthritis (OA) is the most common rheumatic disease in adults. According to the American College of Rheumatology, this condition is characterized by diverse symptoms and causes structural abnormalities in the subchondral bone and joint borders.¹-³ OA affects roughly 30% of people over 60, increasing functional impairment and causing mechanical discomfort and stiffness.⁴,⁵ Hip and knee OA individuals die at a rate roughly 20% higher than age-matched normal controls.⁶ They usually seek medical advice because of reduced joint function and osteoarticular discomfort.⁷

OA is a heterogeneous disorder with 3 phenotypes (age-related, metabolic, and post-traumatic). Because metabolic syndrome (MetS) and OA are epidemiologically associated, metabolic OA is broader than obesity-related OA. The relationship between each component of the MetS and OA has to be investigated further.⁸

Components of MetS, including abdominal obesity, high blood pressure, high blood sugar, high serum triglycerides, and low serum high-density lipoprotein (HDL), may have a role in OA pathogenesis, either together or separately.⁹-¹¹

Furthermore, the harmful effect of glucose excess in the formation of advanced glycation end products, oxidative stress, and the stimulation of low-grade systemic inflammation may alter the subchondral bone microvasculature or cause neuromuscular impairment supporting the relationship between the two disorders.⁹

The World Health Organization defines the health-related quality of life (HRQOL) as an individual’s subjective assessment of their quality of life. It includes both the individual’s...
values in relation to their goals, expectations, and interests. Physical, psychological, social, cognitive, and general well-being are the 5 primary components of HRQOL. This idea is vital since individuals' reactions to similar stresses, like pain, differ widely. Unlike isolated disease-specific outcomes, HRQOL measurements are highly predictive of death and health care resource consumption as they reflect therapy effectiveness and illness progression.

Compared with age-matched normal controls, individuals with musculoskeletal disorders had the lowest HRQOL of all chronic conditions. Also, HRQOL declines in knee OA individuals with disease progression. Despite advances in MetS research and treatment, it remains a major public health concern. Moreover, the influence of MetS on HRQOL has received little attention in the medical literature and hence remains controversial and unclear.

To learn more about the link between OA and MetS and their combined impact on HRQOL, we conducted this study on a sample of Egyptian individuals with symptomatic primary knee OA.

**Methodology**

**Study design and participants**

This cross-sectional study included 116 adult Egyptian participants with knee OA stratified into two equal groups according to the existence of the MetS. All participants were recruited from the outpatient clinics or the inpatient wards of the Rheumatology Department of Ain Shams University Internal Medicine Hospital. All participants were subjected to detailed medical history taking and complete clinical evaluation.

In all participants, OA was assessed radiologically using the Kellgren and Lawrence (K/L) scale. Also, participants' HRQOL was evaluated by the Health Assessment Questionnaire–Disability Index (HAQ-DI) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Individuals with traumatic or inflammatory arthritis, a history of knee surgery, and those who had received arthrocentesis and/or an intra-articular steroid injection were excluded from the study.

**The Kellgren and Lawrence (K/L) scale**

The K/L classification is used to measure the severity of knee OA using anteroposterior knee radiographs (x-rays). Each radiograph is given a rating ranging from 0 to 4, with 0 indicating no OA and 4 indicating severe OA. Grade 0 (none): lack of osteoarthritis x-ray alterations; grade I (uncertain): potential osteophytic lipping and doubtful joint space narrowing; grade II (minimal): obvious osteophytes and possible joint space narrowing; grade III (moderate): moderate numerous osteophytes, clear narrowing of joint space, some sclerosis, and likely deformation of bone ends; grade IV (severe): large osteophytes, significant restriction of joint space, severe sclerosis, and evident deformity of bone ends.

**The Health Assessment Questionnaire–Disability Index (HAQ-DI)**

The HAQ-DI evaluates a participant's normal functional ability to use their normal equipment over the course of a week. Each item has a 4-level difficulty scale that ranges from 0 to 3, with 0 being normal (no difficulty), 1 representing some difficulty, 2 representing great difficulty, and 3 representing inability to do. Dressing, rising, eating, walking, hygiene, reach, grip, and normal activities are among the 20 questions divided into 8 functional groups. The high dependence on equipment or physical assistance raises a lower score to level 2 to better reflect the underlying disability.

**The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)**

With 5, 2, and 17 questions, the WOMAC assesses 3 different aspects: pain, stiffness, and physical function, respectively. It is scored on an ordinal scale of 0 to 4. Each subscale is scored out of a possible total of 20, 8, or 68 points, respectively. Lower scores indicate less symptoms or physical disability. A global score, known as an index score, is derived by adding the results from the 3 subscales. It takes 5 to 10 minutes to complete this self-administered assessment.

**Diagnosis of MetS**

According to the International Diabetes Federation (IDF2009), MetS is diagnosed depending on the presence of any 3 components of the following: waist circumference (males ≥ 94 cm, females ≥ 80 cm), triglycerides ≥ 150 mg/dL, HDL (males < 40 mg/dL, females < 50 mg/dL) or history of taking lipid-lowering medication, hypertension (≥ 130/85 mmHg or treatment for hypertension), fasting blood glucose ≥ 100 mg/dL, or previously diagnosed type 2 diabetes mellitus.

**Laboratory investigations**

All investigations were performed at the Central Laboratories of Ain Shams University Hospitals according to the standard methods; including complete blood count (CBC) using Sysmex XT-1800i auto-analyzer (Sysmex, Japan), erythrocyte sedimentation rate (ESR) first hour using Westergren method, C-reactive protein (CRP) and hemoglobin A1C (HBA1C) using COBAS e411 and C311 auto-analyzers (Roche Diagnostics GmbH, Mannheim, Germany), and fasting and 2-hour postprandial blood glucose (FBS&2HPP), serum uric acid and lipid profile using AU680 Beckman Coulter auto-analyzer (Beckman Coulter, Inc., Brea, CA). Three milliliters of blood was taken via venipuncture under stringent aseptic circumstances into a plain tube with no additives from each participant, and serum was separated by centrifugation at 3500 × g for 15 minutes. The sera were kept at −80°C until they were tested by enzyme-linked immunosorbent assay (ELISA) kits.
for fasting insulin (E-EL-H2665, Elabscience, USA) and interleukin-6 (IL-6) (CUSABIO Technology LLC, USA; Cat. N.: CSB-E04638H) according to manufacturers’ guidelines.

We calculated the Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) using the following formula: (fasting insulin in μU/mL × fasting glucose in mg/dL)/405.24

Statistical analysis

We used the IBM SPSS Statistics for Windows 23.0 (IBM, Armonk, NY) for data analysis. The chi-square test was used to compare qualitative data. The independent t test was used to compare quantitative parametric data, while the Mann–Whitney test was used for quantitative nonparametric data. Spearman rank correlation was used to test the degree of association between nonparametric data, while parametric data association was tested by Pearson’s correlation. The P value was significant at < .05.

Results

This study comprised 116 Egyptian individuals with knee OA divided into two equal groups: 58 participants with knee OA only and 58 participants with knee OA and MetS. We found no significant difference between both groups as regards age (P = .169) and a significant difference in the male to female ratio (P = .023); in the OA group, 70.7% were males, and 29.3% were females, while in the OA + MetS group 50.0% were males and 50.0% were females. The mean (±SD) waist circumference was significantly higher among the OA + MetS group (123.17 ± 17.84 cm vs 95.93 ± 15.60 cm; P < .001). Diabetes, hypertension, dyslipidemia, and obesity were significantly associated with the OA + MetS group with a prevalence of 77.6%, 82.8%, 77.6%, and 50.0%, respectively (Table 1). There were significant differences regarding x-ray grading (K/L scale) and severity of knee OA between the study groups; grade II was found in 25.9% of the OA participants but was not found among participants in the OA + MetS group. Grades III and IV were found in 29.3% and 70.7% of the OA + MetS group and 29.3% and 44.8% of the OA group, respectively (Table 1).

According to OA participants’ HRQOL, compared with the OA group, the median (IQR) HAQ-DI (30 [20–42] vs 10 [6–20]; P < .001) and the mean (±SD) WOMAC (71.76 ± 11.23 vs 60.14 ± 13.58; P < .001) were significantly higher among the OA + MetS participants. In addition, HOMA-IR was significantly higher among the OA + MetS participants (4.5 [2.4–7.9] vs 2.9 [1.6–4.4]; P < .001) (Table 1). IL-6 serum levels were significantly higher in the OA + MetS group compared with the OA group (mean ± SD): 7.69 ± 3.06 pg/mL vs 2.28 ± 0.85 pg/mL; P = .036) (Table 1).

Spearman rank and Pearson’s correlation analyses showed significant positive correlations between waist circumference (P = .004), as well as triglycerides (P = .006), cholesterol (P = .041), FBS (P < .001), HBA1C (P = .002), and IL-6 (P = .017) levels with the HAQ-DI scores but HDL levels (P = .628) showed a significant negative correlation. Likewise, the WOMAC scores were significantly positively correlated to waist circumference (P = .001), as well as triglycerides (P = .008), cholesterol (P = .048), FBS (P < .001), and IL-6 (P = .044) levels and significantly negatively correlated to HDL levels (P = .002) (Table 2).

When participants within the OA + MetS group were compared according to their x-ray grading (K/L scale), grade IV participants were significantly older than participants of grade III (60.07 ± 7.66 years vs 54.71 ± 9.68 years; P = .029), they also showed significant higher values of waist circumference (128.90 ± 15.81 cm vs 109.35 ± 14.89 cm; P < .001), CRP (5 mg/L [3–16] vs 1.2 mg/L [1–4.8]; P < .001) triglycerides (213.95 ± 57.05 mg/dL vs 170.06 ± 71.12 mg/dL; P < .016), FBS (150 [140–166] mg/dL vs 100 [95–110] mg/dL; P < .001), 2HPP (286.59 ± 128.41 mg/dL vs 212.20 ± 47.66 mg/dL; P = .002), and IL-6 levels (4.88 ± 1.23 pg/mL vs 7.69 ± 2.06 pg/mL; P = .002) (Table 3).

Discussion

The current study examined the relationship between MetS and its components, including abdominal obesity, hypertension, diabetes, high serum triglycerides and low HDL, and HRQOL in Egyptians with knee OA. We included 116 adult Egyptians with knee OA and split them into 2 groups based on MetS status. All participants had a full medical history assessment. Anteroposterior knee radiographs were utilized to assess OA using the K/L scale. The HAQ-DI and WOMAC were also utilized to assess individuals’ HRQOL. According to the findings of the current study, individuals with knee OA with MetS had more serious radiological damage, severe degrees of functional disability and poorer HRQOL than those with knee OA without MetS.

OA is the oldest known rheumatic disease that can affect any joint, with the knees and hips being the most commonly affected. It is a destructive joint disease characterized by articular cartilage degradation, synovial membrane inflammation, and subchondral bone remodeling; it is thus regarded as a whole joint disease. There are currently no established therapies that can stop or slow OA progression. As a result, early identification of risk factors that affect knee OA individuals’ HRQOL could be critical for disease prevention.

Previously, it was thought that people with MetS were predisposed to knee OA simply due to a mechanical reason connected to obesity. The inclusion of non-weight-bearing joints, on the other hand, raised concerns about the need to look into explanations other than mechanical factors. MetS has been shown in several studies to have a multifaceted effect on OA of the knee joint, including greater articular cartilage deterioration, higher pain scores, and early onset of disease. The
Table 1. Characteristics of the knee OA individuals compared according to the existence of MetS.

| PARAMETER STUDIED                    | OA + METS | OA   | P VALUE |
|--------------------------------------|-----------|------|---------|
|                                      | N=58      | N=58 |         |
| Age (years)                          | Mean ± SD | 58.50 ± 8.58 | 55.78 ± 12.28 | .169 |
|                                      | Range     | 40-70 | 34-70   |         |
| Sex, n (%)                           | Female    | 29 (50.0%) | 17 (29.3%) | .023  |
|                                      | Male      | 29 (50.0%) | 41 (70.7%) |         |
| Waist circumference (cm)             | Mean ± SD | 123.17 ± 17.84 | 95.93 ± 15.60 | <.001 |
|                                      | Range     | 95-155 | 78-150  |         |
| Smoking, n (%)                       | No        | 45 (77.6%) | 35 (60.3%) | .045  |
|                                      | Yes       | 13 (22.4%) | 23 (39.7%) |         |
| Comorbid conditions                  | DM, n (%) | No    | 13 (22.4%) | 54 (93.1%) | <.001 |
|                                      |           | Yes   | 45 (77.6%) | 4 (6.9%)  |         |
|                                      | HTN, n (%)| No    | 10 (17.2%) | 48 (82.8%) | <.001 |
|                                      |           | Yes   | 48 (82.8%) | 10 (17.2%) |         |
|                                      | Dyslipidemia, n (%)| No | 13(22.4%) | 48 (82.8%) | <.001 |
|                                      |           | Yes   | 45(77.6%) | 10 (17.2%) |         |
|                                      | Obesity, n (%)| No | 29 (50.0%) | 56 (96.6%) | <.001 |
|                                      |           | Yes   | 29 (50.0%) | 2 (3.4%)  |         |
| X-ray grade, n (%)                   | II        | 0 (0.0%) | 15 (25.9%) | <.001 |
|                                      | III       | 17 (29.3%) | 17 (29.3%) |         |
|                                      | IV        | 41 (70.7%) | 26 (44.8%) |         |
| Laboratory investigations            | TLC (10^3/μl) | Mean ± SD | 7.75 ± 2.74 | 6.68 ± 2.17 | .021 |
|                                      |           | Range   | 4-13     | 3.5-11   |         |
|                                      | Hemoglobin (gm/dL) | Mean ± SD | 10.49 ± 1.85 | 10.23 ± 2.13 | .490 |
|                                      |           | Range   | 7-14     | 6-14     |         |
|                                      | PLT (10^3/μl) | Median (IQR) | 290 (181-360) | 238.5 (156-324) | .112 |
|                                      |           | Range   | 88-496   | 43-409   |         |
|                                      | ESR (mm/h) | Median (IQR) | 15 (10-26) | 13.5 (6-30) | .463 |
|                                      |           | Range   | 4-60     | 2-110    |         |
|                                      | CRP (mg/L) | Median (IQR) | 4.9 (2-8) | 5 (2-11) | .550 |
|                                      |           | Range   | 0.5-48   | 0.5-40   |         |
|                                      | Uric acid (mg/dL) | Median (IQR) | 5 (4-7) | 5 (4-6) | .914 |
|                                      |           | Range   | 2.7-12   | 3-12     |         |
|                                      | FBG (mg/dL) | Median (IQR) | 140 (115-160) | 90 (86-94) | <.001 |
|                                      |           | Range   | 84-456   | 79-140   |         |
|                                      | 2HPP (mg/dL) | Mean ± SD | 234.00 ± 85.96 | 120.72 ± 15.97 | <.001 |
|                                      |           | Range   | 140-528  | 100-170  |         |
|                                      | HBA1C %   | Mean ± SD | 7.27 ± 2.47 | 4.85 ± 0.64 | <.001 |
|                                      |           | Range   | 4-13     | 4-6.5    |         |

(Continued)
Table 1. (Continued)

| PARAMETER STUDIED | OA + METS | OA | P VALUE |
|-------------------|-----------|----|---------|
|                   | N=58      | N=58 |         |
| Fasting insulin  | Median (IQR) | 12 (7-20) | 13 (7.6-17) | .774 |
|                   | Range | 2-84 | 3-47 |
| TG (mg/dL)        | Mean ± SD | 201.09 ± 64.11 | 112.02 ± 20.77 | <.001 |
|                   | Range | 78-343 | 55-146 |
| Cholesterol (mg/dL) | Mean ± SD | 199.79 ± 59.69 | 123.98 ± 29.06 | <.001 |
|                   | Range | 88-348 | 26-170 |
| HDL (mg/dL)       | Mean ± SD | 31.62 ± 11.74 | 39.26 ± 10.07 | <.001 |
|                   | Range | 15-58 | 20-60 |
| LDL (mg/dL)       | Mean ± SD | 156.29 ± 58.64 | 86.83 ± 29.12 | <.001 |
|                   | Range | 38-265 | 42-178 |
| Interleukin-6 (pg/mL) | Mean ± SD | 7.69 ± 3.06 | 2.28 ± 0.85 | .036 |
|                   | Range | 3.2-11.4 | 0.5-4.1 |
| HAQ-DI            | Median (IQR) | 30 (20-42) | 10 (6-20) | <.001 |
|                   | Range | 5-60 | 4-36 |
| WOMAC             | Mean ± SD | 71.76 ± 11.23 | 60.14 ± 13.58 | <.001 |
|                   | Range | 52-92 | 40-88 |
| Insulin resistance | HOMA-IR | Median (IQR) | 4.5 (2.4-7.9) | 2.9 (1.6-4.4) | <.001 |
|                   | Range | 0.4-29 | 0.6-9.9 |

Abbreviations: 2HPP, 2-hour post prandial; CRP, C-reactive protein; DM, diabetes mellitus; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; HAQ-DI, Health Assessment Questionnaire-Disability Index; HBA1C, hemoglobin A1C; HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model Assessment-Insulin Resistance; HRQOL, health-related quality of life; HTN, hypertension; IQR, interquartile range; LDL, low-density lipoprotein; MetS, metabolic syndrome; OA, osteoarthritis; PLT, platelets; SD, standard deviation; TG, triglyceride; TLC, total leucocyte count; WOMAC, Western Ontario and McMaster Universities Arthritis index. Significance was set at <.05. Bold P values are significant.

Table 2. Correlation of HAQ-DI and WOMAC with components of metabolic syndrome.

| HAQ-DI | CORRELATION COEFFICIENT | P VALUE | WOMAC | CORRELATION COEFFICIENT | P VALUE |
|--------|--------------------------|---------|--------|--------------------------|---------|
| HOMA-IR | .130 | .331 | .100 | .454 |
| Waist circumference (cm) | .370 | .004 | .431 | .001 |
| TG (mg/dL) | .354 | .006 | .344 | .008 |
| Cholesterol (mg/dL) | .269 | .041 | .260 | .048 |
| HDL (mg/dL) | -.065 | .628 | -.391 | .002 |
| LDL (mg/dL) | .065 | .626 | .153 | .250 |
| FBG (mg/dL) | .586 | <.001 | .634 | <.001 |
| 2HPP (mg/dL) | .208 | .117 | .079 | .554 |
| HBA1C (%) | .392 | .002 | .221 | .096 |
| Interleukin-6 (pg/mL) | .308 | .017 | .379 | .044 |

Abbreviations: 2HPP, 2-hours post prandial; FBG, fasting blood glucose; HAQ-DI, Health Assessment Questionnaire-Disability Index; HBA1C, hemoglobin A1C; HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model Assessment-Insulin Resistance; LDL, low-density lipoprotein; TG, triglyceride; WOMAC, Western Ontario and McMaster Universities Arthritis index. Significance was set at <.05. Bold P values are significant.
proinflammatory state and oxidative stress generated by MetS have been proposed to be significant triggers for OA.28

In our study, participants’ age ranged between 18 and 70 years, 39.7% of all participants were females, and 60.3% were males. In concordance with Al Hewala et al,29 our results showed no significant difference between participants in terms of age.

Also, 69.0% of our included participants were smokers, 42.2% were diabetics, 50% were hypertensive, 47.4% were dyslipidemic, 26.7% were obese, and 86% had elevated waist

### Table 3. Comparison of characteristics according to x-ray grading (K/L scale) among the OA + MetS group.

|                         | III  | IV  | P VALUE |
|-------------------------|------|-----|---------|
| Age (years)             | Mean ± SD | 54.71 ± 9.68 | 60.07 ± 7.66 | .029 |
|                        | Range | 40-65 | 47-70 |
| Waist circumference (cm)| Mean ± SD | 109.35 ± 14.89 | 128.90 ± 15.81 | <.001 |
|                        | Range | 95-150 | 100-155 |
| ESR (mm/h)              | Median (IQR) | 12 (8-32) | 17 (10-25) | .355 |
|                        | Range | 4-60 | 5-40 |
| CRP (mg/L)              | Median (IQR) | 1.2 (1-4.8) | 5 (3-16) | <.001 |
|                        | Range | 0.5-8 | 2-48 |
| Interleukin-6 (pg/mL)   | Mean ± SD | 4.88 ± 1.23 | 7.69 ± 2.06 | .002 |
|                        | Range | 3.0-8.2 | 6.2-11.4 |
| Uric acid (mg/dL)       | Median (IQR) | 5 (3-7) | 5 (4-8.6) | .232 |
|                        | Range | 2.7-9 | 2.8-12 |
| TG (mg/dL)              | Mean ± SD | 170.06 ± 71.12 | 213.95 ± 57.05 | .016 |
|                        | Range | 78-290 | 130-343 |
| Cholesterol (mg/dL)     | Mean ± SD | 198.00 ± 73.53 | 200.54 ± 53.96 | .884 |
|                        | Range | 88-348 | 88-348 |
| HDL (mg/dL)             | Mean ± SD | 31.76 ± 15.49 | 31.56 ± 10.02 | .953 |
|                        | Range | 16-58 | 15-52 |
| LDL (mg/dL)             | Mean ± SD | 177.53 ± 39.39 | 147.49 ± 63.30 | .075 |
|                        | Range | 115-224 | 38-265 |
| FBG (mg/dL)             | Median (IQR) | 100 (95-110) | 150 (140-166) | <.001 |
|                        | Range | 84-139 | 100-456 |
| 2HPP (mg/dL)            | Mean ± SD | 212.20 ± 47.66 | 286.59 ± 128.41 | .002 |
|                        | Range | 140-289 | 140-528 |
| HBA1C (%)               | Mean ± SD | 7.66 ± 2.41 | 7.11 ± 2.51 | .451 |
|                        | Range | 4.9-12 | 4-13 |
| HOMA-IR                 | Median (IQR) | 2.6 (1.7-15) | 5.6 (2.4-7.4) | .925 |
|                        | Range | 1.3-29 | 0.4-20 |

Abbreviations: 2HPP, 2-hour post prandial; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FBG, fasting blood glucose; HAQ-DI, Health Assessment Questionnaire-Disability Index; HBA1C, hemoglobin A1C; HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model Assessment-Insulin Resistance; IQR, interquartile range; K/L, Kellgren and Lawrence; LDL, low-density lipoprotein; MetS, metabolic syndrome; OA, osteoarthritis; SD, standard deviation; TG, triglyceride; WC, waist circumference; WOMAC, Western Ontario and McMaster Universities Arthritis index.

Significance was set at <.05. Bold P values are significant.
circumference; these findings were in concordance with a study on 41 OA participants by Onkarappa et al., in which 90.24% of the study population had abnormal waist circumference, 43.9% were diabetic, and 41.46% had hypertension. Similarly, a cross-sectional study by Morović-Vergles et al. found that among the 352 OA individuals included, 60% had hypertension after adjusting for age and body mass index (BMI). In addition, Puenpatom and Victor stated that cardiovascular risk factors involved in MetS were more prevalent in OA individuals than those without OA.

In our study, the prevalence of smoking, diabetes, hypertension, dyslipidemia, obesity and increased waist circumference was significantly higher among OA + MetS participants than OA participants, a finding that was in concordance with Afifi et al., who stated that knee OA was common in MetS individuals, and it was associated with worse pain, functional disability, and radiological abnormalities. In their study, Obesity, hypertension, and diabetes were the most common MetS components in knee OA individuals..

Our results revealed that radiologically OA + MetS individuals showed significantly worse signs and higher grades of affection (mainly grade IV) by the K/L grading system than OA individuals. Several other studies revealed similar results. Also, in a study by Shin, which was performed on 2363 individuals with knee OA, they found a highly significant association between MetS and the radiographic knee OA K/L score. They reported that OA + MetS people experience more intense arthritic knee pain independently of body weight, a finding that drove them to conclude that proper treatment of MetS might be essential as a management approach for arthritic knee pain. Furthermore, a recent cross-sectional Chinese study by Xie et al. demonstrated that individuals with MetS were associated with a higher number of knee osteophytes which usually exist next to OA joints.

On the other hand, our radiologic findings contradict Yasuda et al., who found no significant link between radiographic knee OA findings and individual or cumulative MetS variables. They did, however, discover an association between the severity of knee OA symptoms and hypertension, dyslipidemia, hyperglycemia, and the total MetS variables. Furthermore, both radiographic and symptomatic clinical findings of knee OA were positively linked with cumulative MetS variables and hypertension in the study of Xie et al., but not with dyslipidemia. They also discovered a link between hyperglycemia and OA in terms of radiology but not in terms of clinical symptoms.

Our study showed a significant association between CRP levels and K/L radiological grades of knee OA. Also, the values of HOMA-IR and HAQ-DI and WOMAC scores were significantly higher in the OA + MetS group than the OA group. Similarly, Al Hewala et al. found that positive CRP results were more significantly associated with OA individuals with MetS. Genser et al. also stated that insulin resistance plays a central role in promoting the development of MetS. Several studies reported significant differences in the WOMAC score between the OA + MetS than OA individuals.

In line with our results, a study by Onkarappa et al. found that the clinical severity of knee OA was significantly higher in individuals with MetS compared with non-MetS individuals. They also stated that WOMAC scores at presentation and after 6 months were significantly higher in the MetS group.

Sarbijani et al. suggested that higher levels of IL-6 may cause insulin resistance and MetS. It also can influence the secretion of adipokines from adipocytes. Furthermore, our study revealed that serum levels of IL-6 were significantly higher among the OA + MetS group than the OA group and were associated with a higher degree of radiological affection and functional disability.

Similarly, Livshits et al. reported that individuals with a greater BMI and higher circulating levels of IL-6 were more likely to have radiographic knee OA. These findings should prompt greater research into IL-6 as a possible therapeutic target. On the other hand, Wiegertjes et al. reported that IL-6 is a proinflammatory cytokine that could be linked to the development of cartilage pathology, including the stimulation of matrix-degrading enzymes. However, IL-6 promotes anti-catabolic gene expression, indicating a protective effect. They stated that this dual role of IL-6 is yet unknown and may be driven by differences in IL-6 classic and trans-signaling effects.

Finally, our study was not free of limitations; one major limitation was the relatively small sample size and the single-center nature. Further multi-center studies on a broader scale are recommended. In conclusion, individuals with knee OA and MetS have more radiological damage and severe grades of functional disability with poor HRQOL compared with individuals with OA without MetS. They also had greater levels of IL-6, which linked with disability, suggesting it as a therapeutic target.
