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

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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.[8]

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.[3] 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.[3,12]

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.[13] 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.[14]

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.[15] Also, participants' HRQOL was evaluated by the Health Assessment Questionnaire-Disability Index (HAQ-DI)[16] and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).[17] 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.[15,18,19]

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.[16,20]

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.[17,21]

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 $\geq$ 94 cm, females $\geq$ 80 cm), triglycerides $\geq$150 mg/dL, HDL (males $<$ 40 mg/dL, females $<$ 50 mg/dL) or history of taking lipid-lowering medication, hypertension ($\geq$130/85 mmHg or treatment for hypertension), fasting blood glucose $\geq$100 mg/dL, or previously diagnosed type 2 diabetes mellitus.[22]

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,[23] 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 $\times g$ 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 participants, 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.[25] 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.[26]

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.[27] 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 N = 58	OA N = 58	*P* VALUE
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/uL)	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/uL)	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 N = 58	OA N = 58	*P* VALUE
	Fasting insulin (μU/mL)	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	
HRQOL	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, palates; 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		WOMAC	
	CORRELATION COEFFICIENT	*P* VALUE	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.

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

		III	IV	*P* VALUE
		N = 17	N = 41	
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; HBA1 C, hemoglobin A1 C; 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.

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

circumference; these findings were in concordance with a study on 41 OA participants by Onkarappa et al,[30] 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[31] 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[10] 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,[32] 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.[32]

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.[29,32] Also, in a study by Shin,[33] 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[34] 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,[35] 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,[34] 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[29] found that positive CRP results were more significantly associated with OA individuals with MetS. Genser et al[36] 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.[29,32]

In line with our results, a study by Onkarappa et al[30] 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[37] suggested that higher levels of IL-6 may cause insulin resistance and MetS. It also can influence the secretion of adipokines from adipocytes.[38] 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[39] 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[40] 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.[40]

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.

Author Contributions

SFS conceptualization, methodology, writing original draft. SIT data collection, investigation, writing, reviewing, and editing.

Ethical Considerations

The study was conducted in line with the Declaration of Helsinki research regulations. We obtained the approval of the Ain Shams University Faculty of Medicine Research Ethics Committee, and all the included participants provided their written informed consent before the start.

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REFERENCES

1. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. *Curr Opin Rheumatol*. 2018;30:160-167. doi:10.1097/BOR.0000000000000479.

2. Kawano MM, Araújo IL, Castro MC, Matos MA. Assessment of quality of life in patients with knee osteoarthritis. *Acta Ortop Bras*. 2015;23:307-310. doi:10.1590/1413-785220152306150596.
3. Reyes-Llerena GA, Guibert-Toledano M, Penedo-Coello A, et al. Community-based study to estimate prevalence and burden of illness of rheumatic diseases in Cuba: a COPCORD study. *J Clin Rheumatol*. 2009;15:51-55. doi:10.1097/RHU.0b013e31819b61cb.
4. Heidari B. Knee osteoarthritis prevalence, risk factors, pathogenesis and features: part I. *Caspian J Intern Med*. 2011;2:205-212.
5. Neogi T. The epidemiology and impact of pain in osteoarthritis. *Osteoarthritis Cartilage*. 2013;21:1145-1153. doi:10.1016/j.joca.2013.03.018.
6. Wang XQ, Huang LY, Liu Y, et al. Effects of tai chi program on neuromuscular function for patients with knee osteoarthritis: study protocol for a randomized controlled trial. *Trials*. 2013;14:375. doi:10.1186/1745-6215-14-375.
7. Fu K, Robbins SR, McDougall JJ. Osteoarthritis: the genesis of pain. *Rheumatology (Oxford)*. 2018;57:iv43-iv50. doi:10.1093/rheumatology/kex419.
8. Louati K, Vidal C, Berenbaum F, Sellam J. Association between diabetes mellitus and osteoarthritis: systematic literature review and meta-analysis. *RMD Open*. 2015;1:e000077. doi:10.1136/rmdopen-2015-000077.
9. Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome—a new worldwide definition. *Lancet*. 2005;366:1059-1062. doi:10.1016/S0140-6736(05)67402-8.
10. 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.
11. Alenazi AM, Alothman S, Alshehri MM, et al. The prevalence of type 2 diabetes and associated risk factors with generalized osteoarthritis: a retrospective study using ICD codes for clinical data repository system. *Clin Rheumatol*. 2019;38:3539-3547. doi:10.1007/s10067-019-04712-0.
12. Richards MM, Maxwell JS, Weng L, Angelos MG, Golzarian J. Intra-articular treatment of knee osteoarthritis: from anti-inflammatories to products of regenerative medicine. *Phys Sportsmed*. 2016;44:101-108. doi:10.1080/00913847.2016.1168272.
13. Farr Ii J, Miller LE, Block JE. Quality of life in patients with knee osteoarthritis: a commentary on nonsurgical and surgical treatments. *Open Orthop J*. 2013;7:619-623. doi:10.2174/1874325001307010619.
14. Saboya PP, Bodanese LC, Zimmermann PR, Gustavo AD, Assumpção CM, Londero F. Metabolic syndrome and quality of life: a systematic review. *Rev Lat Am Enfermagem*. 2016;24:e2848. doi:10.1590/1518-8345.1573.2848.
15. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957;16:494-502. doi:10.1136/ard.16.4.494.
16. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: a review of its history, issues, progress, and documentation. *J Rheumatol*. 2003;30:167-178.
17. Theiler R, Spielberger J, Bischoff HA, Bellamy N, Huber J, Kroesen S. Clinical evaluation of the WOMAC 3.0 OA Index in numeric rating scale format using a computerized touch screen version. *Osteoarthritis Cartilage*. 2002;10:479-481. doi:10.1053/joca.2002.0807.
18. Kohn MD, Sassoon AA, Fernando ND. Classifications in brief: Kellgren-Lawrence classification of osteoarthritis. *Clin Orthop Relat Res*. 2016;474:1886-1893. doi:10.1007/s11999-016-4732-4.
19. Schiphof D, Boers M, Bierma-Zeinstra SM. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. *Ann Rheum Dis*. 2008;67:1034-1036. doi:10.1136/ard.2007.079020.
20. Hochberg MC, Chang RW, Dwosh I, Lindsey S, Pincus T, Wolfe F. The American College of Rheumatology 1991 revised criteria for the classification of global functional status in rheumatoid arthritis. *Arthritis Rheum*. 1992;35:498-502. doi:10.1002/art.1780350502.
21. McConnell S, Kolopack P, Davis AM. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC): a review of its utility and measurement properties. *Arthritis Rheum*. 2001;45:453-461. doi:10.1002/1529-0131(200110)45:5<453::aid-art365>3.0.co;2-w.
22. Alberti KG, 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; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009;120:1640-1645. doi:10.1161/CIRCULATIONAHA.109.192644.
23. Westergren A. The technique of the red cell sedimentation reaction. *Am Rev Tuberc*. 1926;14:94-101.
24. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. *Diabetes Care*. 2004;27:1487-1495. doi:10.2337/diacare.27.6.1487
25. Glyn-Jones S, Palmer AJ, Agricola R, et al. Osteoarthritis. *Lancet*. 2015;386:376-387. doi:10.1016/S0140-6736(14)60802-3.
26. Antony B, Jones G, Jin X, Ding C. Do early life factors affect the development of knee osteoarthritis in later life: a narrative review. *Arthritis Res Ther*. 2016;18:202. doi:10.1186/s13075-016-1104-0.
27. Dong N, Gao YH, Liu B, et al. Differential expression of adipokines in knee osteoarthritis patients with and without metabolic syndrome. *Int Orthop*. 2018;42:1283-1289. doi:10.1007/s00264-018-3761-x.
28. Pan F, Tian J, Mattap SM, Cicuttini F, Jones G. Association between metabolic syndrome and knee structural change on MRI. *Rheumatology (Oxford)*. 2020;59:185-193. doi:10.1093/rheumatology/kez266.
29. Al Hewala AE, Soliman SG, El Sharaqi DR, Fadel WA. The effect of metabolic syndrome on patients with knee osteoarthritis. *Menoufia Med J*. 2018;31:795-799. http://www.mmj.eg.net/text.asp?2018/31/3/795/248734. Accessed February 28, 2022.
30. Onkarappa RS, Chauhan DK, Saikia B, Karim A, Kanojia RK. Metabolic syndrome and its effects on cartilage degeneration vs regeneration: a pilot study using osteoarthritis biomarkers. *Indian J Orthop*. 2020;54:20-24. doi:10.1007/s43465-020-00145-z.
31. Morović-Vergles J, Salamon L, Marasović-Krstulović D, et al. Is the prevalence of arterial hypertension in rheumatoid arthritis and osteoarthritis associated with disease? *Rheumatol Int* 2013;33(5):1185-92. doi: 10.1007/s00296-012-2522-1.
32. Afifi AEA, Shaat RM, Gharbia OM, Boghdadi YE, Eshmawy MME, El-Emam OA. Osteoarthritis of knee joint in metabolic syndrome. *Clin Rheumatol*. 2018;37:2855-2861. doi:10.1007/s10067-018-4201-4.
33. Shin D. Association between metabolic syndrome, radiographic knee osteoarthritis, and intensity of knee pain: results of a national survey. *J Clin Endocrinol Metab*. 2014;99:3177-3183. doi:10.1210/jc.2014-1043.
34. Xie DX, Wei J, Zeng C, et al. Association between metabolic syndrome and knee osteoarthritis: a cross-sectional study. *BMC Musculoskelet Disord*. 2017;18:533. doi:10.1186/s12891-017-1890-9.
35. Yasuda E, Nakamura R, Matsugi R, et al. Association between the severity of symptomatic knee osteoarthritis and cumulative metabolic factors. *Aging Clin Exp Res*. 2018;30:481-488. doi:10.1007/s40520-017-0808-6.
36. Genser L, Casella Mariolo JR, Castagneto-Gissey L, Panagiotopoulos S, Rubino F. Obesity, type 2 diabetes, and the metabolic syndrome: pathophysiologic relationships and guidelines for surgical intervention. *Surg Clin North Am*. 2016;96:681-701. doi:10.1016/j.suc.2016.03.013.
37. Sarbijani HM, Khoshnia M, Marjani A. The association between Metabolic Syndrome and serum levels of lipid peroxidation and interleukin-6 in Gorgan. *Diabetes Metab Syndr*. 2016;10:S86-S89. doi:10.1016/j.dsx.2015.09.024.
38. Eder K, Baffy N, Falus A, Fulop AK. The major inflammatory mediator interleukin-6 and obesity. *Inflamm Res*. 2009;58:727-736. doi:10.1007/s00011-009-0060-4.
39. Livshits G, Zhai G, Hart DJ, et al. Interleukin-6 is a significant predictor of radiographic knee osteoarthritis: the Chingford study. *Arthritis Rheum*. 2009;60:2037-2045. doi:10.1002/art.24598.
40. Wiegertjes R, van de Loo FAJ, Blaney Davidson EN. A roadmap to target interleukin-6 in osteoarthritis. *Rheumatology (Oxford)*. 2020;59:2681-2694. doi:10.1093/rheumatology/keaa248.