Study of metabolic syndrome frequency in elderly patients with knee osteoarthritis and its impact on the physical activity

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Background
Obesity is associated with an increased risk of osteoarthritis (OA). Metabolic syndrome (Met S) has been associated with a state of chronic low-grade inflammation and increased macrophages in the fat tissue. Hypertension and hyperglycaemia seem to be important BMI-independent factors of changes in osteoarthritic joints. Moreover, type 2 diabetes mellitus (DM) has been found to be an independent risk predictor for arthroplasty.
Aim of the work
To determine frequency and association of metabolic syndrome with knee osteoarthritis in elderly patients and its impact on the physical activity in elderly patients with knee osteoarthritis.
Patients
The study included patients aged above 65 years complaining of primary knee OA. The study included two groups: Gp A: Sixty patients >65 years with primary OA. Gp B: Forty apparently healthy elderly persons without knee OA as a control group. Exclusion Criteria: Patients with secondary knee OA.
Methods
All Patients were subjected to the following: Complete history taking, self-rated was measured by (SF-36), BMI, complete clinical musculoskeletal examination. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) 1st hr,fasting glucose level, 2 hr-post-prandial glucose level, triglycerides (TG), cholesterol, uric acid, high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and radiographic imaging of affected knee joints.
Results
According to (k/L) score of severity; grade 3 and grade 4 OA were significantly higher in patients with Met S than patients without Met S. The mean WOMAC pain subscale score was significantly higher in patients with OA and Met S than in patients with OA and without Met S with *P* value (<0.001). There was a significant positive correlation between the both joint pain, stiffness and fasting blood glucose level (r=–0.463 P=<0.001; r=0.324, P=0.012 respectively); systolic, diastolic blood pressure and waist circumference in OA patients (group I) with Met S.
Conclusion
Elevated systemic markers of inflammation are linked with components of Met S, with an increased prevalence of radiographic OA and joint symptoms.

Keywords:
hyperglycaemia, knee osteoarthritis, metabolic syndrome

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Introduction

Osteoarthritis (OA) is the most prevalent chronic joint disease and a major cause of pain and disability worldwide [1]. Although the pathophysiologic mechanisms of OA are inconclusive, growing evidence has supported that metabolic factors may contribute to the initiation and progression of OA process [2]. Epidemiological studies have demonstrated a positive association between OA and several metabolic risk factors, such as dyslipidemia, hyperglycaemia, and hypertension [3–5]. Metabolic syndrome (MetS) is a common metabolic disorder that results from the increasing prevalence of obesity and is associated with an increased risk of cardiovascular disease [2,6]. Recently, metabolic OA has been nominated as the fifth component of Met S [2], therefore; OA was classified into three phenotypes including metabolic OA, age-related OA and injure-related OA [7]. In view of the shared mechanisms, it can be concluded that MetS is closely related to OA, and OA is even a part of the generalized metabolic

disorder [2,7–9]. OA is characterized by the pathologic features of joint space narrowing and osteophyte formation. Because accumulating evidences have shown that these two abnormalities have distinct etiologic mechanism [7–9], it would be helpful to elucidate the pathogenesis of MetS or OA by gaining more in-depth understanding of the associations of MetS with joint space narrowing and osteophyte formation.

OA has a multifactorial etiology [10] and is an illness affecting not only the quality of all of the synovial joint structures but also function and quality of surrounding tissues and the nociceptive signaling pathway. OA has many risk factors, including age, sex, family history, obesity, metabolic factors, occupation, injury, and joint morphology. Some of these are common in patients with MetS, including increased age and BMI [11–13]. OA development has been linked to several components of the MetS, such as dyslipidemia [7,8], type 2 diabetes [9–11], and central obesity [3,14]. This may explain the increased overall and cardiovascular mortality seen in both MetS and symptomatic knee OA [15].

The relationship between OA and components of MetS has the potential to identify complications, individuals at risk, and prevent secondary complications.

Systemic inflammatory adipokine concentrations have also been associated with obesity and visceral fat accumulation [16]. Furthermore, leptin has been associated with reduced cartilage thickness, symptomatic radiographic knee OA, and MRI-defined knee cartilage defects, bone marrow lesions, osteophytes, synovitis, and joint effusion. Inflammatory adipokine levels are associated with subclinical inflammation [17]. This reduces OA changes and improves the inflammatory profile. Some inflammatory adipokines have been shown to enhance production of the enzymes responsible for cartilage degradation and promote neutrophil mobilization, cytotoxic lymphocyte, and macrophage activation.

Aim

The aim was to determine frequency and association of MetS with knee osteoarthritis in elderly patients and its effect on the physical activity in elderly patients with knee osteoarthritis, study of epidemiological characteristics and frequency assessment of the studied patients, and assessment of cardiovascular risk factors in patients presenting with osteoarthritis.

Patients

The study included patients aged 65 years and above attending the Geriatric outpatient clinic at Alexandria Main University Hospital complaining of primary knee osteoarthritis.

The study included two groups:

Group I: Sixty patients more than 65 years with primary knee osteoarthritis diagnosed according to American College Of Rheumatology clinical criteria [18].

Table 1 Comparison between the two studied groups according to demographic data

	Osteoarthritis (n=60) [n (%)]	Control (n=40) [n (%)]	Test of Significance	P
Sex				
Male	12 (20.0)	14 (35.0)	χ^2=2.807	0.094
Female	48 (80.0)	26 (65.0)		
Age (years)				
Young (65–74)	30 (50.0)	25 (62.5)	χ^2=3.892	0.139
Old (75–84)	25 (41.7)	15 (37.5)		
Very old (≥85)	5 (8.3)	0		
Minimum–maximum	65.0–88.0	65.0–83.0	t=1.758	0.082
Mean±SD	73.87±7.37	71.63±5.37		
Median	74.0	69.50		
Smoking				
Yes	20 (33.3)	11 (27.5)	χ^2=0.382	0.537
No	40 (66.7)	29 (72.5)		
Marital statutes				
Single	7 (11.7)	1 (2.5)	χ^2=9.410*	^{MC}P=0.020*
Married	34 (56.7)	24 (60.0)		
Widow	10 (16.7)	14 (35.0)		
Divorced	9 (15.0)	1 (2.5)		

χ^2-Test for comparing between the two groups ^{MC}P; P value for Monte Carlo for χ^2-test for comparing between the two groups. t, P, t and P values for Student t-test for comparing between the two groups. *P≤0.05, statistically significant.

Table 2 Comparison between the two studied groups according to comorbidities

	Osteoarthritis (*n*=60) [*n* (%)]	Control (*n*=40) [*n* (%)]	Test of Significance	*P*
Diabetes				
No	27 (45.0)	31 (77.5)	χ^2=10.406*	0.001*
Yes	33 (55.0)	9 (22.5)		
Hypertension				
No	27 (45.0)	22 (55.0)	χ^2=0.960	0.327
Yes	33 (55.0)	18 (45.0)		
Heart disease (IHD or HF)				
No	49 (81.7)	38 (95.0)	χ^2=3.772	0.052
Yes	11 (18.3)	2 (5.0)		

HF, heart failure; IHD, ischemic heart disease. χ^2, *P*: χ^2 and *P* values for χ^2-test for comparing between the two groups. *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups.

Table 3 Comparison between the two studied groups according to weight, height, and waist circumference

Measures	Osteoarthritis (*n*=60)	Control (*n*=40)	Test of significance	*P*
Weight (kg)				
Minimum–maximum	60.01–40.0	60.0–137.0	*U*=1041.0	0.261
Mean±SD	92.37±17.95	88.75±16.58		
Median	92.0	85.0		
Height(cm)				
Minimum–maximum	115.0–178.0	153.0–175.0	*U*=1145.5	0.701
Mean±SD	160.4±8.32	161.60±6.23		
Median	160.0	162.0		
BMI (kg/m^2)				
Minimum–maximum	24.22–54.68	24.65–51.25	*U*=933.0	0.060
Mean±SD	35.75±7.03	33.65±6.24		
Median	34.50	31.30		
Waist circumference (cm)				
Minimum–maximum	65.0–145.0	79.0–134.0	*t*=2.083*	0.040*
Mean±SD	112.5±19.92	105.5±13.68		
Median	112.0	102.0		

χ^2, χ^2-test for comparing between the two groups ^{MC}P: *P* value for Monte Carlo for χ^2-test for comparing between the two groups *U*, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups. *$P \leq 0.05$, statistically significant.

Group II: Forty apparently healthy elderly persons without knee osteoarthritis as a control group. Exclusion Criteria: Patients with secondary knee osteoarthritis, previous arthroscopy, or knee surgery were excluded.

Methods

All patients were subjected to the following: complete history taking, BMI, complete clinical examination of affected joint (s), detection of pain and stiffness, acute phase reactants, C-reactive protein (CRP) [19], erythrocyte sedimentation rate (ESR) first hour [20], fasting glucose level, 2 h postprandial glucose level [21], triglycerides (TG), cholesterol [22], uric acid [23], high density lipoprotein cholesterol (HDL-c), and low density lipoprotein cholesterol (LDL-c) [7].

Radiological examination

Weight-bearing anteroposterior knee radiograph was performed for patients complaining of OA (group I), and all radiographic findings were classified according to Kellgren and Lawrence, 1957 (K/L) radiological score of severity into the following: stage 1: incipient osteoarthritis and beginning of osteophyte formation on eminences; stage 2: definite osteophyte and possible narrowing of joint space; stage 3: multiple osteophytes, definite narrowing of joint space, and some sclerosis and possible deformity of bone ends; and stage 4: osteophytes, marked narrowing of joint space, subchondral bone sclerosis, and definite deformity of bone ends. Stage 1–2 changes according to K/L were grouped as 'early' and stage 3–4 as 'late' radiological OA.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [24] was used to assess disease-specific self-reported disability [25].

Patients with MetS should have at least three of the following five criteria [26]:

(1) Waist circumference at least 102 cm in men and at least 88 cm in women .

Table 4 Comparison between the two studied groups according to classes of obesity

Measures	Osteoarthritis (*n*=60) [*n* (%)]	Control (*n*=40) [*n* (%)]	Test of significance	*P*
Obesity				
Normal	4 (6.7)	0	χ^2=2.778	^{FE}P=0.148
Over weight	6 (10.0)	5 (12.5)	χ^2=0.153	^{FE}P=0.751
I	23 (38.3)	26 (65.0)	χ^2=6.82*	0.009*
II	11 (18.3)	4 (10.0)	χ^2=1.307	0.253
III	16 (26.7)	5 (12.5)	χ^2=2.903	0.088

χ^2, χ^2-test for comparing between the two groups. ^{MC}P: *P* value for Monte Carlo for χ^2-test for comparing between the two groups. *U*, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two groups *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups. *$P\leq0.05$, statistically significant.

Table 5 Comparison between the two studied groups according to laboratory investigations

	Osteoarthritis (*n*=60)	Control (*n*=40)	Test of significance	*P*
FBS				
Minimum–maximum	70.0–476.0	85.0–215.0	*U*=756.0*	0.002*
Mean±SD	155.88±76.11	119.17±39.71		
Median	136.50	100.50		
PPBG				
Minimum–maximum	100.0–582.0	115.0–300.0	*U*=1114.50	0.546
Mean±SD	209.63±101.62	180.40±52.98		
Median	197.0	190.0		
Uric acid				
Minimum–maximum	2.50–8.50	3.0–7.0	*U*=932.50	0.056
Mean±SD	4.04±1.18	4.37±0.96		
Median	4.0	4.0		
ESR				
Minimum–maximum	5.0–75.0	2.0–25.0	*U*=334.0*	<0.001*
Mean±SD	25.95±17.02	8.13±7.85		
Median	20.0	4.0		
CRP				
Minimum–maximum	1.0–55.0	1.0–10.0	*U*=854.50*	0.013*
Mean±SD	6.60±11.60	2.50±1.76		
Median	4.50	2.0		

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PPBG, post prandial blood glucose. χ^2, *P*: χ^2 and *P* values for χ^2-test for comparing between the two groups *U*, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two groups. *$P\leq0.05$, statistically significant.

Table 6 Comparison between the two studied groups according to lipid profile

Lipid profile	Osteoarthritis (*n*=60)	Control (*n*=40)	Test of significance	*P*
Total cholesterol				
Minimum–maximum	100.0–308.0	85.0–286.0	*t*=2.123*	0.036*
Mean±SD	215.10±46.47	194.20±50.79		
Median	205.50	199.50		
HDL				
Minimum–maximum	30.0–98.0	21.0–90.0	*U*=993.0	0.144
Mean±SD	52.68±13.77	55.45±17.15		
Median	50.0	54.50		
LDL				
Minimum–maximum	60.0–221.0	40.0–200.0	*t*=3.661*	<0.001*
Mean±SD	134.95±38.89	104.93±42.06		
Median	130.0	110.0		
TG				
Minimum–maximum	73.0–295.0	89.0–160.0	*U*=730.0*	0.001*
Mean±SD	145.12±44.38	119.58±24.60		
Median	141.0	109.0		

TG, triglycerides. *U*, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two groups *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups. *$P\leq0.05$, statistically significant.

(2) Elevated triglycerides at least 150 mg/dl, or drug treatment for elevated triglycerides.
(3) Low HDL–cholesterol less than 40 mg/dl in men, less than 50 mg/dl in women, or drug treatment for LDL-cholesterol.
(4) High blood pressure (systolic blood pressure at least 130 mmHg or diastolic ≥85 mmHg) or drug treatment for hypertension.
(5) Elevated blood glucose at least 100 mg/dl or drug treatment for elevated fasting glucose.

Results

Table 1 shows the clinical data of the studied groups. There was a statistically significant difference between the two studied groups regarding the number of diabetic patients, which was higher in group I than group II, with a *P* value of 0.001. Table 2 shows the anthropometric measures of the studied group, such as weight, height, waist circumference, and calculated BMI. Table 3 shows the assessment of classes of obesity in the studied groups according to BMI. Table 4 shows fasting blood sugar, 2-h post-prandial blood glucose level, uric acid, ESR, and CRP of the studied cases. The mean FBS level was significantly higher in group I (155.88±76.1) than group II (119.17±39.71), with a *P* value of 0.002. The mean ESR level was significantly higher in group I (25.95 ±17.02) than group II (8.13±7.85) with a *P* value of less than 0.001. The mean CRP level was significantly higher in group I (6.60±11.60) than group II (2.50±1.76), with a *P* value of 0.01. Table 5 shows lipid profile of the studied groups; the mean serum total cholesterol level was significantly higher in group I (215.10±46.47) than in group II (194.20±50.79), with a *P* value of 0.036. The mean triglyceride level was significantly higher in group I (145.12±44.38) than in group II (119.58±24.60), with a *P* value of 0.001. The mean low-density lipoprotein level was significantly higher in group I (134.95±38.89) than group II (104.93±42.06), with a *P* value of less than 0.001. Table 6 shows the severity of OA according to knee radiographic findings regarding K/L score for severity. Table 7 shows the WOMAC score regarding pain subscale, stiffness, and physical subscale. Table 8 shows MetS and its components among studied groups. MetS was significantly higher in group I than group II, with a *P* value of 0.049. Table 9 shows comparison between the two studied groups according to MetS. Table 10 shows the components of the MetS in studied groups: waist circumference, systolic blood pressure, diastolic blood pressure, fasting blood glucose level, and triglyceride. Patients whose fasting blood glucose level was at least 100 mg/dl were significantly higher in group I (81.7%, *n*=49) than group II (62.5%, *n*=25), with a *P* value of 0.039. Patients whose triglyceride level was at least 150 mg/dl were significantly higher in group I (45%, *n*=27) than group II (15%, *n*=6), with a *P* value of 0.002. Table 11 shows the relation between the presence of MetS in patients with knee osteoarthritis and the severity of osteoarthritis in radiographs. Grade 2 OA was significantly higher in patients without MetS than in patients with MetS, with a *P* value of less than 0.001. Grade 3 and grade 4 OA were significantly higher in patients with MetS than patients without MetS. Table 12 describes the relation between WOMAC subscale scores and the presence of MetS. The mean WOMAC pain subscale score was significantly higher in

Table 7 Distribution of the studied cases according to radiograph in osteoarthritis group (*n*=60)

Radiograph	*N* (%)
Early	23 (38.4)
Grade 1	1 (1.7)
Grade 2	22 (36.7)
Severe	37 (61.7)
Grade 3	21 (35.0)
Grade 4	16 (26.7)

Table 8 Descriptive analysis of the studied cases according to Western Ontario and McMaster Universities Osteoarthritis Index grading of severity in osteoarthritis group (*n*=60)

Western Ontario and McMaster Universities Osteoarthritis Index	Minimum–maximum	Mean ±SD	Median
Pain	3.0–20.0	9.08 ±5.49	6.0
Joint stiffness	0.0–8.0	3.68 ±2.30	3.0
Physical	20.0–65.0	42.72 ±9.71	40.0

Table 9 Comparison between the two studied groups according to presence of metabolic syndrome

	Osteoarthritis (*n*=60) [*n* (%)]	Control (*n*=40) [*n* (%)]	χ^2	*P*
Metabolic syndrome				
No	27 (45.0)	26 (65.0)	3.854*	0.049*
Yes	33 (55.0)	14 (35.0)		
Male	5 (15.2)	8 (57.1)		
Female	28 (84.8)	6 (42.9)		

χ^2, *P*: χ^2 and *P* values for χ^2-test for comparison between the two groups *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups.

Table 10 Comparison between the two studied groups according to metabolic syndrome components

	Osteoarthritis (*n*=60) [*n* (%)]	Control (*n*=40) [*n* (%)]	χ^2	*P*
DM				
No	27 (45.0)	33 (77.5)	10.406*	0.001*
Yes	33 (55.0)	9 (22.5)		
HTN				
No	27 (45.0)	22 (55.0)	0.960	0.327
Yes	33 (55.0)	18 (45.0)		
Systolic≥130	38 (63.3)	26 (65.0)	0.029	0.865
Diastolic≥85	38 (63.3)	21 (52.5)	1.164	0.281
Waist circumference				
Males (≥102)	3 (5.0)	11 (27.5)	FE	
Females (≥88)	45 (75.0)	24 (60.0)		
Hyperglycemia				
FBS (≥100)	49 (81.7)	25 (62.5)	4.582*	0.039*
Elevated TG (>150)	27 (45.0)	6 (15.0)	9.769*	0.002*
Low HDL				
Males (<40)	2 (10.0)	0	FE	
Females (<50)	18 (90.0)	6 (100.0)		

DM, diabetes mellitus; HTN, hypertension; TG, triglycerides. χ^2, χ^2-test for comparison between the two groups. ^{FE}P: *P* value for Fisher exact for χ^2-test for comparing between the two groups. *t*, *P*: *t* and *P* values for Student *t*-test for comparing between the two groups.

Table 11 Relation between metabolic syndrome and severity of osteoarthritis in radiograph for group I (*n*=60)

	Metabolic syndrome (no) (*n*=27) [*n* (%)]	Radiograph (yes) (*n*=33) [*n* (%)]	χ^2	*P*
Early	19 (70.4)	0 (12.1)	21.315*	<0.001*
Grade 1	1 (3.7)	4 (0.0)	1.243	^{FE}P=0.450
Grade 2	18 (66.7)	4 (12.1)	19.026*	<0.001*
Severe	8 (29.6)	29 (87.9)	21.315*	<0.001*
Grade 3	5 (18.5)	16 (48.5)	5.862*	0.015*
Grade 4	3 (11.1)	13 (39.4)	6.074	0.014*

χ^2, *P*: χ^2 and *P* values for χ^2-test for comparing between the two groups. *$P\leq0.05$, statistically significant.

patients with osteoarthritis and MetS (11.67±5.58) than in patients with osteoarthritis and without MetS (5.9 ±3.35), with a *P* value of less than 0.001. Table 13 shows the correlation coefficient (*r*) between fasting blood glucose level and WOMAC subscale scores (pain, stiffness, and physical function) in group I. There was a significant positive correlation between the fasting blood glucose level and both pain and stiffness (*r*=-0.463, $P\leq0.001$, and *r*=0.324, *P*=0.012, respectively), Furthermore, there was a significant positive correlation between the fasting blood glucose level and physical function(*r*=-0.450, $P\leq0.001$). Table 14 shows the correlation coefficient (*r*) between systolic pressure and WOMAC subscales scores (pain, stiffness, and physical function) in group I. There was a significant positive correlation between systolic blood pressure and pain subscale score (*r*=0.297, *P*=0.021). Table 15 shows the correlation coefficient (*r*) between diastolic pressure and WOMAC subscale scores (pain, stiffness, and physical function) in group I. Furthermore, there was a significant positive correlation between diastolic blood pressure and physical function (*r*=0.294, *P*=0.023). Table 16 shows the correlation coefficient (*r*) between waist circumference (cm) and WOMAC subscales scores (pain, stiffness, and physical function) in group I .There was a significant positive correlation between waist circumferences (cm) with both stiffness and physical function scores (*r*=0.261, *P*=0.044, and *r*=0.320, *P*=0.013, respectively).

Statistical analysis

Data shown are the mean±SEM. All statistical analyses for data were performed using SPSS software. Data were analyzed between two groups using Student *t*-test, whereas among more than two groups, data were analyzed by the one-way analysis of variance method. Differences of *P* value less than 0.05 were considered significant.

Discussion

Obesity is regarded as a chronic inflammatory state, and it is associated with an increased risk of OA and MetS. Obesity is associated with a high-risk of developing symptomatic knee [27] and hand OA [9,28,29]. The association with hip OA is more variable, with studies demonstrating either no association or positive weak associations [28,30]. The relationship of obesity with hand OA suggests that it is not simply owing to the effect of weight on weight-bearing joints, and there may be a metabolic component of the association. Additionally, even after

Table 12 Relation between metabolic syndrome and Western Ontario and McMaster Universities Osteoarthritis Index subscales scores for group I (*n*=60)

	Western Ontario and McMaster Universities Osteoarthritis Index subscales (no) (*n*=27)	Metabolic syndrome in group I (*N*=60) (yes) (*n*=33)	*U*	*P*
Pain				
Minimum–maximum	3.0–17.0	5.0–20.0	146.0*	<0.001*
Mean±SD	5.9±3.35	11.67±5.58		
Median	5.0	11.0		
Stiffness				
Minimum–maximum	0.0–7.0	1.0–8.0	193.0*	<0.001*
Mean±SD	2.56±1.93	4.61±2.19		
Median	2.0	4.0		
Physical				
Minimum–maximum	20.0–55.0	35.0–65.0	116.0*	<0.001*
Mean±SD	36.37±7.73	47.9±7.97		
Median	35.0	47.0		

U, *P*: *U* and *P* values for Mann–Whitney test for comparing between the two groups. *$P \leq 0.05$, statistically significant.

Table 13 Correlation between FBS and Western Ontario and McMaster Universities Osteoarthritis Index for group I (*n*=60)

FBS	r_s	*P*
Pain	0.463*	<0.001*
Joint stiffness	0.324*	0.012*
Physical	0.450*	<0.001*

r_s: Spearman coefficient. *$P \leq 0.05$, statistically significant.

Table 14 Correlation between systolic and Western Ontario and McMaster Universities Osteoarthritis Index subscale score for group I (*n*=60)

Systolic	r_s	*P*
Pain	0.297*	0.021*
Joint stiffness	0.125	0.342
Physical	0.169	0.196

r_s: Pearson coefficient. *$P \leq 0.05$, statistically significant.

Table 15 Correlation between diastolic blood pressure and Western Ontario and McMaster Universities Osteoarthritis Index for group I (*n*=60)

Diastolic	r_s	*P*
Pain	0.305*	0.018*
Joint stiffness	0.406*	0.001*
Physical	0.294*	0.023*

r: Spearman coefficient. *$P \leq 0.05$, statistically significant.

Table 16 Correlation between waist circumference (cm) and Western Ontario and McMaster Universities Osteoarthritis Index for groups I (*n*=60)

Waist circumference (cm)	*r*	*P*
Pain score	0.246	0.058
Stiffness score	0.261*	0.044*
Physical score	0.320*	0.013*

r: Spearman coefficient. *$P \leq 0.05$, statistically significant.

adjustment for age, sex, and BMI, hand OA has been shown to be an independent predictor for the future development of hip and knee OA [31]. This suggests either genetic predisposition to OA development or a systemically driven process. The present study demonstrated that according to K/L radiographic score of severity, grade 3 and grade 4 OA were significantly higher in patients with MetS than patients without MetS. The mean WOMAC pain subscale score was significantly higher in patients with osteoarthritis and MetS than in patients with osteoarthritis and without MetS, with a *P* value of less than 0.001. There was a significant positive correlation between joint pain , stiffness and fasting blood glucose level (r=–0.463, $P \leq 0.001$; r=0.324, P=0.012 respectively), also; a significant positive correlation is present between systolic, diastolic BP and waist circumference in OA patients (group I) with Met S.

A recent study by Monira Hussain *et al.* [30] reported positive relationship with severe knee OA requiring total joint replacement and MetS even in model adjusted for relative weight. This is in line with observation by Shin [31] who reported higher intensity of knee pain in individuals with an accumulation of MetS component.

Previous studies found that MetS and its components (e.g. overweight, hypertension, and dyslipidemia) were associated with the prevalence of radiographic knee OA in a Chinese population with adjustment of a number of confounding factors. With the accumulation of MetS components, the prevalence of knee OA increased. The positive association remained significant after adding CRP into the multivariable model. In addition, MetS as a whole was only associated with knee osteophytes but not joint space narrowing.

Yoshimura *et al.* [32] illustrated that the number of MetS components (e.g. overweight, hypertension,

dyslipidemia, and impaired glucose tolerance) were positively related to knee osteophytes but not joint space narrowing. This may be explained by some mediators like adipocytokines, which are involved in many metabolic processes in the body. Mooney *et al.* [33] and Lwata *et al.* [34] have demonstrated that high-fat diet increased the osteophyte diameter or volume in OA or type 2 diabetic mouse models. Similarly, Munter *et al.* [35] showed that the accumulation of low-density lipoprotein within synovial lining cells led to increased activation of synovium and osteophyte formation. This interesting finding of the present study may give evidence to a better understanding of the pathogenesis of osteoarthritis .

A study conducted by Gandhi *et al.* [36] showed that the prevalence of MetS in the Asian population was even higher than that in the White and Black population.

Some studies suggest that chronic low-grade inflammation may not be a very important mediator between MetS and OA. The relationship between obesity and OA has traditionally been explained as increased cartilage degeneration owing to abnormal mechanical loading of the joints. While this explanation is plausible for the knee and hip, it is unlikely to be the main factor in determining the association between obesity and hand OA. There is increasing interest in a metabolic and inflammatory mechanism as a potential explanation for the association.

Adipose tissue is an organ that, in excess, is associated with increased levels of systemic inflammation, which is postulated to be the mechanism mediating the association between cardiovascular diseases, diabetes, and the MetS [37,38]. White adipose tissue (WAT) produces adipokines such as leptin, resistin and chemerin, and also inflammatory cytokines such as tumour necrosis factor (TNF), interleukin-1 (IL-1) and IL-6 which produced by adipose tissue contributes to around a third of circulating IL-6 and is strongly associated with increasing obesity [40]. Both adipokines and cytokines have been linked with development of both components of MetS and osteoarthritis [39,40].

MetS is a cluster of physiological, biochemical, and clinical factors considered to be a manifestation of metabolic abnormalities associated with obesity and increased systemic low-grade inflammation [41]. Dysregulated glucose, insulin homeostasis, and visceral obesity are cornerstones of this process. Components of the MetS, including increased waist circumference, fasting glucose, and triglyceride concentrations, have been independently associated with concentrations of proinflammatory adipokine leptin in population-based study [42,43]. It has been postulated that three main adipokines, leptin, adiponectin, and resistin, act through overlapping pathways and have been closely linked to glucose sensitivity, glucose intolerance, and development of type 2 diabetes [44–46].

Statins have been shown to reduce systemic inflammation in a dose-dependent manner [47] and decrease cardiovascular complications in high-risk individuals. OA is associated with an increased risk of cardiovascular disease [48]. Some studies have found that statin use reduces progression and incidence of knee but not hip osteoarthritis [49–51].

Conclusion

The current epidemiological evidence supports a need for a joint-specific approach while describing association between the components of MetS and OA. Evidence of an association of a common pathological process with obesity and chronic inflammation. A direct detrimental effect of hyperglycemia, dyslipidemia, and chronic low-grade inflammation on cartilage metabolism was noted. Elevated systemic markers of inflammation are linked with components of MetS, with an increased prevalence of radiographic osteoarthritis and joint symptoms.

Recommendations

The systemic role of MetS in osteoarthritis pathophysiology is now better understood, but new further research studies are needed for better determining the MetS-associated osteoarthritis phenotype .

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Conflicts of interest

There are no conflicts of interest.

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