Metabolic Syndrome In Egyptian Patients with Primary Knee Osteoarthritis

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Abstract: *Introduction*: Osteoarthritis (OA) is among the most common musculoskeletal disorders affecting millions of people throughout different races in different ages and sexes

Aim: The aim of the present study was to determine the prevalence of Metabolic Syndrome (MetS) in a group of Egyptian patients with primary knee Osteoarthritis (OA) and to detect its relation to the clinical, functional and radiographic findings.

Patients and methods: The present study included 380 patients (150 males, 230 females) diagnosed as having primary knee OA. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess disease specific self-reported disability. X-rays were classified according to the Kellgren–Lawrence (KL) radiographic rating scale. 400 (260females, 140 males) apparently healthy volunteers without knee OA were used as control group.

Results: MetS was prevalent in 53.7 % of the studied OA patients, in the control group was 37.3% of (P: <0.001). The prevalence of individual MetS components included 68.7 % for abdominal obesity, 66.8 % for hypertension, 36.1 % for hyperglycemia, 52.1 % for elevated triglycerides and 49.2 % for low high density lipoprotein (HDL). Patients with MetS had significantly higher body mass index (BMI) (P: 0.0013), longer disease duration (P: 0.021), more pain (P: 0.007), more stiffness (P: 0.043), worse functional impairment scores(P: 0.017) and advanced radiological progress (P:0.0001).

Conclusions: MetS is prevalent in patients with primary knee OA. It is associated with poor clinical performance and advanced radiological changes. The most common component of MetS in our study is abdominal obesity.

INTRODUCTION

Osteoarthritis (OA) is among the most common musculoskeletal disorders affecting millions of people throughout different races in different ages and sexes [1]. It is associated with cartilage destruction, subchondral bone remodeling and inflammation of the synovial membrane, although the etiology and pathogenesis underlying this debilitating disease are poorly understood [2].

Mechanical factors are one of others involved in causation. These comprise inflammatory and metabolic factors [3]. Risk factors contributing to development of OA include age, trauma and increased body weight [4]. However, OA commonly manifests in non-weight bearing joints [5].

Recent experimental data have shown that subchondral bone may have a substantial role in the OA process, as a mechanical damper, as well as a source of inflammatory mediators implicated in the OA pain process and in the degradation of the deep layer of cartilage [6].

Metabolic syndrome (MetS) is characterized by a combination of various cardiovascular risk factors (overweight, hypertension and dyslipidemia) that imply additional cardiovascular morbidity that is greater than the sum of the risks associated with each individual component. The frequency of MetS is higher in rheumatological diseases than in the control populations, suggesting that either the presence or the treatment of those diseases seems to influence the risk of developing metabolic syndrome [7-10].

Low-grade inflammation induced by the metabolic syndrome and innate immunity are some of the more recent arguments in favor of the inflammatory theory of OA [11].

AIM OF STUDY

The aim of the present study was to determine the prevalence of Metabolic Syndrome (MetS) in a group of Egyptian patients with primary knee Osteoarthritis (OA) and to detect its relation to the clinical, functional and radiographic findings.

PATIENTS AND METHODS

Evaluation of OA

The present study which was carried out at the outpatient clinic of Rheumatology and Rehabilitation

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Department at Mansoura University Hospital, Egypt. 380 patients with primary knee OA were recruited, they diagnosed as having primary knee OA according to the American College of Rheumatology (ACR) criteria [12].

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [13] was used to assess disease specific self-reported disability. Higher scores represent higher levels of pain, stiffness and functional impairment.

Most of our patients were on chondroprotective drugs and irregular courses of non steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy.

Exclusion criteria: patients with secondary knee OA, previous arthroscopy or knee surgery.

400 apparently healthy voluntaries not with knee OA among the hospital staff and some of their relatives who were age matched to the patients were chosen to serve as the control group.

Written consent was obtained from each eligible participant in this study after approval of this study from local Ethical Committee.

Clinical Assessment

The eligible participants completed preliminary questionnaires inquiring into demographic characteristics, medical history and history of receiving any medication and then underwent thorough clinical examination.

Diagnosis of MetS

For diagnosis of MetS, patients should had at least 3 of the following 5 criteria: (1) waist circumference ≥ 102 cm, ≥ 88 cm in women; (2) elevated triglycerides ≥150 mg/dl, or drug treatment for elevated triglycerides; (3) low HDL-cholesterol (<40 mg/dl in men, <50 mg/dl in women), or drug treatment for low HDL-cholesterol; (4) high blood pressure (systolic ≥130 mm Hg or diastolic ≥85 mm Hg) or drug treatment for hypertension; and (5) elevated fasting glucose ≥100 mg/dl or drug treatment for elevated fasting glucose. These criteria were mentioned and summarized in the paper of Grundy *et al*. [14].

We measured waist circumference, by locating top of right iliac crest, place a measuring tape in a horizontal plane around abdomen at level of iliac crest. Before reading tape measure, we ensure that tape is snug but does not compress the skin and is parallel to floor. Measurement is made at the end of a normal expiration.

Radiological Examination

Weight bearing anteroposterior knee X-rays were performed for all patients and all X-rays were classified according to the Kellgren–Lawrence (KL) radiographic rating scale [15] (1 = questionable osteophytes, 2 = definite osteophytes without joint space narrowing, 3 = definite osteophytes with moderate joint space narrowing and 4 = definite osteophytes with severe joint space narrowing). Stage 1–2 changes according to KL were grouped as 'early' and stage 3–4 as 'late' radiological OA. Radiological stage of the most affected knee was taken into account in the statistical evaluations.

Statistical Analysis

Continuous variables are presented as means ±standard deviations (SD). Categorical variables are reported as number and proportions. Data were checked for normality and equality of distribution, prior to any analysis being performed. Skewed continuous variables were logarithmically transformed to attain a normal distribution. To evaluate the association of the demographic, clinical and radiological data with MetS using the binary logistic regression test, the patients were dichotomized as patients with MetS versus patients without MetS. Comparisons between patients and controls as well as comparisons between patients with versus without MetS were made using independent t test for continuous normally distributed variables. For variables that did not attain a normal distribution by logarithmic transformation, nonparametric tests were used. Chi-square test was used for comparison between categorical variables. Adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) were estimated to ascertain association of individual clinical and laboratory data and MetS. All calculations were performed using SPSS 17.0 software for Windows. All analyses were 2-tailed.

RESULTS

Basic clinical and radiographic data are demonstrated in Table **1**. The study comprised 150 males (39.5 %) and 230 females (60.5 %). They had a mean age of 60.9 ± 9.2 years. The mean disease duration was 6.2 ± 3.6 years. Their mean WOMAC scores were 11.5 ± 3.8, 4.8 ± 1.9 and 42.4 ± 4.4 for

Table 1:   **Demographic, Clinical and Radiological Finding in the Studied Patients (n=380)**

		Patients		Controls		Student's t test	
		Range	Mean ±SD	Range	Mean ±SD	t	P
Age (years)		45 – 75	60.9 ± 9.2	45 – 75	59.7 ±9.5	1.7688	0.0773
BMI (kg/m^2)		21 – 56.6	32.0 ± 6.6	21 – 45	31.7 ±6.4	0.6361	0.5249
Disease duration (years)		1 – 12	6.2 ± 3.6				
WOMAC – Pain		5 – 20	11.5 ± 3.8				
WOMAC – Stiffness		2 – 8	4.8 ± 1.9				
WOMAC – functional		35 – 50	42.4 ± 4.4				
ESR		42 – 73	59.3 ±6.7	15 – 45	31.4 ±5.4	63.2024	<0.001
Total cholesterol (mg/dl)		187 – 118	145.4 ±19.8	111 – 178	143.9 ±17.3	2.5949	0.0096
LDL cholesterol		58 - 123	90.3 ±16.7	55 - 115	86.7 ±15.8	3.0525	0.0023
HDL cholesterol		38 – 65	51.4 ±6.5	34 – 71	57.5 ±7.9	11.6233	<0.001
Triglycerides		167 - 206	188.5 ±9.4	154 - 187	171.9 ±8.6	25.3988	<0.001
Bilateralism							
	Bilateral		239 (62.9 %)				
	Unilateral		141 (37.1 %)				
X ray							
	Early(Stage 1–2)		161 (42.4 %)				
	Late(Stage 3–4)		219 (57.6 %)				

BMI: body mass index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; ESR: erythrocyte sedimentation rate; SD: standard deviation, HDL: high density lipoprotein; LDL: low density lipoprotein.

pain, stiffness and functional impairment respectively. Bilateral OA was reported in 62.9 % of patients and 57.6 % of them had late radiological findings.

Table **2** illustrates the frequency of MetS and its components in the studied patients and control. MetS was highly significant in primary knee OA than control group (P: <0.001). MetS was prevalent in 53.7 % of the studied OA cohort. The prevalence of individual MetS components included for abdominal obesity 68.7 %, 66.8 % for hypertension obesity, 36.1 % for hyperglycemia, 52.1 % for elevated triglycerides and 49.2 % for low HDL. All components of MetS were significantly higher in patients than controls.

Tables **3** and **4** show the comparative and regression analyses. Patients with MetS were significant older in age, had significantly higher BMI, longer disease duration, worse functional impairment scores and advanced radiological progress.

DISCUSSION

In the present study, we found that the frequency of MetS and its components in the studied patients were

Table 2:   **Prevalence of MetS and its Components in the Studied Groups**

	Patients (380)	Control 400	P
	No (%)	No (%)	
MetS	204 (53.7)	149 (37.3%)	<0.001
Hypertension	254 (66.8)	231 (57.8%)	0.0097
Abdominal obesity	261(68.7)	244 (61%)	0.0296
Hyperglycemia	137 (36.1)	109 (27.3%)	0.0088
Elevated triglycerides	201 (52.1)	169 (42.3%)	0.0033
Low HDL	187 (49.2)	166 (41.5%)	0.0312

MetS: Metabolic syndrome; HDL: high density lipoprotein.

Table 3:   Comparison between Patients with MetS and Patients without MetS Regarding Demographic, Clinical and Radiological Data

			MetS +ve (n=205)	MetS –ve (n=175)	P value
Age			63.4 ± 7.7	58.3 ± 10.1	< 0.001
Gender		Male	77 (37.6 %)	73 (41.7 %)	0.41
		Female	128 (62.4 %)	102 (58.3)	
BMI			37.3 ± 4.9	28.2 ± 5.4	0.0013*
Disease duration			8.7 ± 2.9	4.9 ± 3.1	0.021*
WOMAC – Pain			14.6 ± 2.4	9.5 ± 5.3	0.007*
WOMAC – Stiffness			5.7 ± 1.3	3.2 ± 2.4	0.043*
WOMAC – functional			46.1 ± 3.3	38.7 ± 1.5	0.017*
Bilateralism		Bilateral	125 (61.0 %)	114 (65.1 %)	0.4
		Unilateral	80 (39.0 %)	61 (34.9 %)	
X ray		Early (Stage 1–2)	58 (28.3 %)	103 (58.9 %)	0.0001*
		Late (Stage 3–4)	147 (71.7 %)	72 (41.1 %)	

MetS: Metabolic syndrome; BMI: body mass index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Table 4:   Regression Analysis for Demographic, Clinical and Radiological Variables Related to MetS

	OR	CI	P
Age	0.93	0.7 – 1.2	0.56
Gender	0.67	0.5 – 2.4	0.72
BMI	2.3	1.3 – 4.5	0.0054*
Disease duration	1.7	1.4 – 3.2	0.001*
WOMAC – Pain	1.1	1.1 – 2.4	0.037*
WOMAC – Stiffness	1.4	1.5 – 2.4	0.029*
WOMAC – functional	1.3	1.3 – 2.2	0.041*
Bilateralism	0.7	0.4 – 1.7	0.48
Radiology	2.8	1.8 – 5.2	0.00087*

MetS: Metabolic syndrome; BMI: body mass index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

significantly higher in primary knee OA than control group. MetS was prevalent in 53.7 % of the studied OA patients based on the definition ACR and 37.3% in the controls.

This figure is lower than that reported by National Health and Nutrition Examination Survey III (NHANES III). In their study, MetS was diagnosed in 59% of the OA population and 23% of the population without OA [16]. Notably, their study used the same criteria as our study for diagnosis of MetS.

In another study from Japan, the authors concluded that accumulation of MetS components is significantly related to the occurrence and of knee OA, and MetS prevention may be useful to reduce cardiovascular disease and knee OA risk. [17].

However, the study of Engström *et al.* [18] noted that in spite of the significant association between MetS and knee OA, this relationship was attenuated and non-significant after adjustment for body mass index. This argument may find support in the study of Dahaghin *et al.* [19] who found that no intermediate effect of metabolic factors on the association of overweight with hand OA (HOA) was found. Nevertheless, they noted an increase in the prevalence of HOA, however, this seems to be present when overweight occurs together with hypertension and diabetes especially at a relatively young age.

In our study, the prevalence of individual MetS components was 68.7 % for abdominal obesity, 66.8 % for hypertension, 36.1 % for hyperglycemia, 52.1 % for elevated triglycerides and 49.2 % for low HDL. These findings show variable agreement with the conclusions of Puenpatom and Victor [13] which reported that hypertension (75%), abdominal obesity (63 %), hyperglycemia (30%), elevated triglycerides (47%), and low HDL cholesterol (44 %) were present in their studied patients.

In our study, comparison between OA patients with MetS and without revealed noteworthy relations. Patients with MetS had significantly higher BMI, longer disease duration, worse functional impairment scores and advanced radiological progress. These data meets the results of Yoshimura *et al.* [14] who documented the significant linkage between MetS, components and knee OA severity and progression. They concluded that progression of KOA significantly increased according to the number of MetS components present.

In addition to the clinical evidence, the experimental study performed by Griffin *et al.* [20] to test the hypotheses that obesity due to a very high-fat diet induces knee OA and that short-term wheel-running exercise protects against obesity-induced knee OA by reducing systemic inflammation and metabolic dysregulation. In Griffin *et al.* [20] study, obesity induced by a very high-fat diet in mice causes OA and systemic inflammation in proportion to body fat. Increased joint loading is not sufficient to explain the increased incidence of knee OA with obesity, as wheel running is protective rather than damaging. Exercise improves glucose tolerance and disrupts the coexpression of proinflammatory cytokines, suggesting that increased aerobic exercise may act independently of weight loss in promoting joint health.

In fact, MetS components can contribute to the development and progression of knee OA by many mechanisms. Hypertension associates with OA through subchondral ischaemia, which can compromise nutrient exchange into articular cartilage and trigger bone remodelling. Ectopic lipid deposition in chondrocytes induced by dyslipidemia might initiate OA development, exacerbated by deregulated cellular lipid metabolism in joint tissues. Hyperglycaemia and OA interact at both local and systemic levels; local effects of oxidative stress and advanced glycation end-products are implicated in cartilage damage, whereas low-grade systemic inflammation results from glucose accumulation and contributes to a toxic internal environment that can exacerbate OA [11].

CONCLUSIONS

MetS is prevalent in patients with knee OA. It is associated with poor clinical performance and advanced radiological changes. The most common component of MetS in our study is abdominal obesity followed by hypertension.

RECOMMENDATION

Weight reduction by diet regimen, aerobic exercise will help in decreasing the incidence of MetS, help joint health, protects against obesity-induced knee OA and prevent progression of knee OA. Moreover, weight reduction will help in controlling and prevention of metabolic dysregulation.

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DISCLOSURE

None.

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