Prevalence and Clinical Significance of Metabolic Syndrome in Fibromyalgia Patients

Prävalenz und klinische Bedeutung des metabolischen Syndroms bei Fibromyalgie-Patienten

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ABSTRACT

Background and Objective Fibromyalgia syndrome (FMS) is a distressing clinical condition. Metabolic syndrome (MetS) is a biochemical and clinical condition characterised by visceral obesity, dyslipidaemia, hyperglycaemia and hypertension. The relation between the two conditions is rarely discussed. This study aimed to determine the prevalence of MetS in FMS patients and to uncover its association with the clinical severity of FMS.

Patients and Methods This cross-sectional study included 200 patients with newly diagnosed FMS. The diagnosis of FMS was established on the basis of the American College of Rheumatology (ACR) 2016 revised criteria. Patients were assessed using the validated Arabic version of Fibromyalgia Impact Questionnaire (FIQ). FMS severity was categorised according to FIQ scores into mild (≤ 45), moderate (> 46 and ≤ 65), and severe (> 65).

Results The study included 200 FMS patients. They comprised 180 females (90.0 %) and 20 males (10.0 %). Among the studied patients, there were 96 patients (48.0 %) who fulfilled the criteria of MetS diagnosis. A comparison between FMS patients with MetS and patients without MetS revealed a significantly higher Widespread Pain Index (WPI) [median (IQR): 12.0 (10.0–17.0) vs. 9.0 (6.0–11.0), $p < 0.001$], a higher Symptoms Severity Scale (SSS) (10.5 ± 1.04 vs. 8.1 ± 1.8, $p < 0.001$) and a higher FIQ (58.8 ± 20.7 vs. 45.4 ± 16.6) in patients with MetS. Patients with MetS had a significantly higher frequency of severe FMS (31.2 vs. 10.6 %, $p < 0.001$). Using binary logistic regression analysis, significant predictors of severe FMS included WPI, SSS and MetS in a univariate analysis. However, in a multivariate analysis, only WPI and SSS remained significant.

Conclusions This study found that MetS is prevalent in FMS patients and it may be associated with more severe forms of the disease.

ZUSAMMENFASSUNG

Hintergrund und Ziel Das Fibromyalgie-Syndrom (FMS) ist eine belastende klinische Erkrankung. Das metabolische Syndrom (MetS) ist eine biochemische und klinische Erkrankung, die durch viszerale Adipositas, Dyslipidämie, Hyperglykämie und Hypertonie gekennzeichnet ist. Die Beziehung zwischen den beiden Erkrankungen wird selten diskutiert. Ziel dieser Studie war es, die Prävalenz des MetS bei FMS-Patienten und den Zusammenhang mit dem klinischen Schweregrad des FMS zu ermitteln.

Patienten und Methoden Die vorliegende Querschnittsstudie umfasste 200 Patienten mit neu diagnostiziertem FMS. Die Diagnose FMS wurde auf der Grundlage der überarbeiteten Kriterien des American College of Rheumatology (ACR) 2016 gestellt. Die Patienten wurden anhand einer validierten arabischen Version des Fibromyalgie-Impact-Fragebogens (FIQ) bewertet. Der Schweregrad der Fibromyalgie wurde anhand

der FIQ-Werte als leicht (≤ 45), mittel (> 46 und ≤ 65) und schwer (> 65) eingestuft.

Ergebnisse Die vorliegende Studie umfasste 200 FMS-Patienten, 180 Frauen (90,0 %) und 20 Männer (10,0 %). Von den untersuchten Patienten erfüllten 96 (48,0 %) die Kriterien der Diagnose MetS. Ein Vergleich zwischen Patienten mit und Patienten ohne MetS ergab für Patienten mit MetS einen signifikant höheren WPI [Median (IQR): 12,0 (10,0–17,0) gegenüber 9,0 (6,0–11,0), p <0,001], einen höheren SSS (10,5 ± 1,04 gegenüber 8,1 ± 1,8, p < 0,001) und höhere FIQ-Werte (58,8 ± 20,7 gegenüber 45,4 ± 16,6). Die Häufigkeit eines schweren FMS (31,2 % gegenüber 10,6 %, p < 0,001) war bei Patienten mit MetS signifikant höher. Unter Verwendung der binären logistischen Regressionsanalyse waren WPI, SSS und MetS signifikante Prädiktoren für ein schweres FMS. In der multivariaten Analyse verblieben nur WPI und SSS als signifikante Prädiktoren für ein FMS.

Schlussfolgerungen Die vorliegende Studie ergab, dass MetS bei FMS-Patienten weit verbreitet ist und mit schwereren Formen der Krankheit assoziiert sein kann.

Introduction

Fibromyalgia syndrome (FMS) is characterized by widespread pain and tenderness, disturbed sleep, fatigue, cognitive impairment and emotional stress. The condition affects 2–4 % of the general population all over the world [1]. The pathogenesis of FMS is not fully understood. However, reduced conditioned pain modulation and neural over-sensitization are suggested mechanisms [2].The association between FMS and other medical and psychiatric comorbidities is a common encounter [3–4].

Metabolic syndrome (MetS) is a biochemical and clinical condition characterized by visceral adiposity, dyslipidemia, hyperglycemia and hypertension. The features of MetS are related to low grade inflammation induced by the excessive release of proinflammatory adipokines from the adipose tissue [5].

MetS was linked to many musculoskeletal conditions. It is frequent in osteoarthritis (OA) patients and its presence is associated with more severe symptoms [6]. Mechanisms implicated in the MetS associated OA include altered gut microbiota. impaired circadian rhythm regulation, adipokine-mediated inflammation and the mechanical effects of obesity [7]. In addition, patients with rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, antiphospholipid syndrome and vasculitis exhibit notably increased prevalence of MetS [8, 9].

Interestingly, chronic fatigue syndrome (CFS) patients also showed higher prevalence of MetS in comparison to healthy counterparts [10]. It is known that CFS and FMS share many pathogenic mechanisms and clinical features [11]. However, studies assessing the relation between FMS and MetS are scarce. The present study

▶ **Table 1** Clinical characteristics in FMS patients with and without MetS.

	All patients N = 200	FMS + MetS n = 96	FMS only n = 104	P value
Age (years) mean ± SD	28.2 ± 6.6	28.1 ± 7.1	28.3 ± 6.2	0.83
Female/male n	180/20	85/11	95/9	0.51
Married n (%)	48 (24.0)	23 (24.0)	25 (24.0)	0.99
Residence n (%)				
Urban	145 (72.5)	68 (70.8)	77 (74.0)	0.61
Rural	55 (27.5)	28 (29.2)	27 (26.0)	
Education n (%)				
Elementary	18 (9.0)	8 (8.3)	10 (9.6)	0.82
Secondary	101 (50.5)	47 (49.0)	54 (51.9)	
University	81 (40.5)	41 (42.7)	40 (38.5)	
WPI median (IQR)	10.0 (9.0–13.0)	12.0 (10.0–17.0)	9.0 (6.0–11.0)	< 0.001
SSS mean ± SD	9.2 ± 1.9	10.5 ± 1.04	8.1 ± 1.8	< 0.001
FIQ mean ± SD	51.9 ± 19.8	58.8 ± 20.7	45.4 ± 16.6	< 0.001
FMS severity n (%)				
Mild	88 (44.0)	28 (29.2)	60 (57.7)	< 0.001
Moderate	71 (35.5)	38 (39.6)	33 (31.7)	
Severe	41 (20.5)	30 (31.2)	11 (10.6)	

Data presented as mean ± SD, median (IQR) or number and percent. FIQ: Fibromyalgia impact questionnaire, FMS: Fibromyalgia syndrome, MetS: Metabolic syndrome, SSS: Symptoms severity scale, WPI: Widespread pain index.

aimed to determine the prevalence of MetS in FMS patients and to uncover its association with FMS clinical severity.

Patients and Methods

The present cross-sectional study was conducted at Al-Azhar University Hospitals. The study protocol was approved by the Institutional Review Board and all patients gave informed consent to participate in the study.

The study included 200 patients with newly diagnosed FMS. Diagnosis of FMS was established on the basis of the American College of Rheumatology (ACR) 2016 revised criteria. To fulfill the 2016 revised criteria, patients should meet all the following: generalized pain, defined as pain in at least four of five regions; symptoms have been present at a similar level for at least 3 months; and widespread pain index (WPI) ≥ 7 and symptoms severity scale (SSS) ≥ 5 OR WPI of 4–6 and SSS ≥ 9.

For the WPI, patients indicated the number of painful bodily regions experienced during the previous 7 days (range 0–19): neck, upper back, lower back, abdomen, and the following left/right: jaw, shoulder, upper arm, lower arm, hip/buttocks, upper leg, and lower leg.

The SSS is based on the sum of severity of fatigue, unrefreshed sleep and cognitive impairment (memory and concentration) (scores 0: no problem to 3: severe problem) in the past 7 days, plus the sum (0–3) of the number of the following symptoms the patient has been bothered by that occurred during the previous 6 months: headaches (0–1), pain or cramps in lower abdomen (0–1), and depression (0–1). The final symptoms severity score is between 0 and 12. [12].

Exclusion criteria were associated musculoskeletal condition, liver or kidney disease or malignancy.

In addition, patients were assessed using the a validated Arabic version of Fibromyalgia Impact Questionnaire (FIQ) [13]. The FIQ is an assessment tool developed to measure patient status, progress, and outcomes in FM. The FIQ is composed of ten items related to physical functioning, the number of days they felt well, and the number of days they were unable to work (including housework) because of FMS symptoms, how the patient rates work difficulty, pain, fatigue, morning tiredness, stiffness, anxiety, and depression. The total maximum score is 100. [14]. Fibromyalgia severity was categorized according to FIQ scores as mild (≤ 45), moderate (> 46 and ≤ 65), and severe (> 65) [15].

Diagnosis of MetS was based on the Harmonized Joint Scientific Statement (HJSS) on metabolic syndrome recommendations. MetS criteria included elevated waist circumference (≥ 80 cm), elevated triglycerides levels (≥ 150 mg/dL), reduced HDL-C (< 50 mg/dL), elevated blood pressure (systolic ≥ 130 and/or diastolic ≥ 85 mm Hg) and elevated fasting glucose (≥ 100 mg/dL). MetS was diagnosed in the presence of any three criteria [16].

Data obtained from the present study were reported as mean and standard deviation (SD) or number and percent. Comparison between the studied variables were achieved using t test, one way ANOVA with post-hoc analysis, Fisher exact test or chi-square test as appropriate. Logistic regression analysis was used to identify predictors of severe FMS. SPSS 25 was used to compute the statistical procedures with p value less than 0.05 considered statistically significant.

Results

The present study included 200 FMS patients. They comprised 180 females (90.0 %) and 20 males (10.0 %). Among the studied patients, there were 96 patients (48.0 %) who fulfilled the criteria of MetS diagnosis. Comparison between FMS patients with MetS and patients without revealed significantly higher WPI [median (IQR): 12.0 (10.0–17.0) vs. 9.0 (6.0–11.0), p < 0.001], higher SSS (10.5 ± 1.04 vs. 8.1 ± 1.8, p < 0.001) and higher FIQ (58.8 ± 20.7 vs. 45.4 ± 16.6) in patients with MetS. Patients with MetS had significantly higher frequency of severe FMS (31.2 vs. 10.6 %, p < 0.001) (▶ **Table 1**).

Comparison between patients with different grades of FMS severity regarding various MetS components showed significant association between increased FMS severity and MetS components apart from FBS which showed no significant differences between patients with various grades of FMS severity (▶ **Table 2**).

Using binary logistic regression analysis, significant predictors of severe FMS included WPI, SSS and MetS in univariate analysis. However, in multivariate analysis, only WPI and SSS remained as significant predictors of severe FMS (▶ **Table 3**).

▶ **Table 2** Comparison between FMS severity grades regarding MetS components.

	Mild n = 88	Moderate n = 71	Severe n = 41	p value
BMI (Kg/m^2) mean ± SD	28.7 ± 4.0 *	30.8 ± 3.4	30.3 ± 3.8	0.003
Waist circumference (cm) mean ± SD	71.9 ± 8.7 * #	76.9 ± 7.6	78.4 ± 4.9	< 0.001
Triglycerides (mg/dl) mean ± SD	138.5 ± 54.0 * #	170.4 ± 52.4	176.8 ± 50.3	< 0.001
HDL (mg/dl) mean ± SD	53.4 ± 12.6 * #	42.3 ± 10.9	40.8 ± 8.9	< 0.001
SBP (mmHg) mean ± SD	122.7 ± 9.4 #	126.4 ± 12.6	129.0 ± 12.8	< 0.001
DBP (mmHg) mean ± SD	78.4 ± 7.0 * #	82.4 ± 8.7	82.7 ± 9.1	< 0.001
FBG (mg/dl) mean ± SD	95.3 ± 12.0	93.9 ± 16.0	96.7 ± 15.7	0.57

Data presented as mean ± SD, *significant differences vs. moderate FMS, # significant differences vs. severe FMS. BMI: Body mass index, DBP: Diastolic blood pressure, FBG: Fasting blood glucose, HDL: High-density lipoprotein, SBP: Systolic blood pressure.

▶ **Table 3** Predictors of severe FMS in the studied patients.

	Univariate analysis			Multivariate analysis		
	OR	95 % CI	P	OR	95 % CI	P
Age	1.04	0.99–1.1	0.12	–	–	–
Sex	0.18	0.02–1.41	0.1	–	–	–
BMI	1.04	0.95–1.1	0.36	–	–	–
WPI	1.34	1.21–1.5	0.001	1.32	1.17–1.5	0.001
SSS	1.64	1.29–2.08	0.001	1.5	1.11–1.03	0.008
MetS	3.84	1.8–8.21	0.001	0.41	0.12–1.38	0.15

BMI: Body mass index, FMS: Fibromyalgia syndrome, MetS: Metabolic syndrome, SSS: symptoms severity index, WPI: widespread pain index.

Discussion

In spite of the fact that the literature is replete with studies assessing the relation between MetS and a wide range of systemic and musculoskeletal conditions, documenting the effect of coexisting MetS on FMS patients is manifestly lacking. To the best of our knowledge, the only report that investigated this issue was the study of Ursini et al. [17] using older criteria for diagnosis of FMS. In the present study, MetS was prevalent in 96 (48.0 %) FMS patients. In comparison, Ursini et al. [17] report identified MetS in 39.77 % of FMS patients.

It's interesting to learn that almost every individual component of MetS were previously related to FMS by a way or another. Obesity and overweight were linked to increase of pro-inflammatory markers, increased pain sensitivity, easy fatiguability and disturbed sleep in FMS patients [18–21].

It was also reported that obese FMS patients had worse depression scores, lower upper body strength, worse disability scores and more use of FMS medications than non-obese counterparts [18, 22]. In addition, obese FMS patients were more likely to experience self-reported memory impairment, anxiety, shortness of breath, urinary frequency and higher tender point counts [23].

In the contrary, the Korean study of Kang et al. [24] found no relation between FMS severity and obesity contradicting most Western studies. Mechanisms suggested to explain the relation between FMS and obesity include impaired endogenous opioid system, altered growth hormone/Insulin-like growth factor-1 axis and thyroid dysfunction [25].

Increased blood pressure was also reported in FMS patients [26]. Moreover, FMS patients were reported to have significantly higher serum total cholesterol and LDL cholesterol [27]. In addition, the study of Cordero et al. [28] suggested a significant relation between altered lipid profile and FMS symptoms.

In conclusion, the present study found that MetS is prevalent in FMS patients and it may be associated with more severe forms of the disease. The present study is not without limitations. The cross-sectional design of the study didn't allow follow up of patients to assess the impact of MetS on their clinical performance on the long-term. Also, the prevalence of MetS in FMS patients wasn't compared to a healthy control group. Moreover, the study allowed us to point to an association only between the 2 syndromes regardless any other underlying conditions.

Future longitudinal and case control studies are strongly recommended to elucidate the various aspects of the relation between FMS and MetS.

Conflict of Interest

The authors declare that they have no conflict of interest.

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