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Original Article

The impact of metabolic syndrome on rheumatoid arthritis in a cohort of Egyptian patients

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ABSTRACT

Aim of the work: To assess the impact of metabolic syndrome (MetS) on the pattern and clinical presentation of rheumatoid arthritis (RA), and its relation to disease activity and functional status of the patients.
Patients and Methods: Sixty RA patients were equally grouped into those with MetS (group A) and those without (group B). The disease activity score (DAS-28) was assessed and functional status was measured using health assessment questionnaire (HAQ).
Results: The 30 patients with MetS had a mean age of 46.3 ± 9.9 years (27–66 years), disease duration of 5 (3–10) years and the 30 without were of matched age and sex. Joint deformities were detected in 8 patients (26.7%) in group A and in 10 patients (33.3%) in group B. While bone erosions were in 6 (20%) in group A, and 7 (23.3%) in group B. As regards the functional capacity; it was found to be more impaired in patients with MetS shown by the significantly higher HAQ in group A than group B ($p = 0.007$). While no significant differences were detected regarding the DAS28 and visual analogue scale (VAS)($p = 0.26$ and 0.13 respectively). In patients with MetS (group A), body weight and waist circumference were significantly increased in those with an increased frequency of joint deformities ($p = 0.047$ and $p = 0.018$ respectively). A significant correlation was found between fasting blood glucose and both joint deformities and erosions ($p = 0.016$ and $p = 0.004$ respectively).
Conclusion: MetS might have a negative impact on RA disease activity and functional status. Regular screening for MetS in RA patients is recommended.

1. Introduction

Rheumatoid arthritis (RA); an autoimmune inflammatory arthritis affecting nearly 1% of the world's adults; is characterized by symmetrical polyarticular inflammation of the synovium. It typically affects the small joints of the hands; the metacarpophalangeal (MCP) and the proximal interphalangeal (PIP) joints, wrists and feet. Inflammation not only causes pain and stiffness in the joints, but may also causes damage resulting in deformities and loss of function, in addition to the associated organ damage which also contributes to severe disability. Furthermore, secondary to chronic inflammation, RA patients experience an increased risk of cardiovascular disease (CVD) [1].

The metabolic syndrome (MetS) is a group of cardio-metabolic risk factors including central obesity, insulin resistance, hypertension, and dyslipidemia and is linked to increased risk of developing type-2 diabetes and CVD. Insulin resistance, an important component of the syndrome, comprises a major link between physical inactivity and MetS [2]. The impact of MetS has been infrequently studied in Egyptian patients with other rheumatic diseases as SLE [3,4], Behçets disease [5], gout [6] and seldom in RA [7,8].

In early RA, the prevalence of MetS has been recorded to range from 16-31% depending on the criteria used for assessment [9]. It has been shown that older age, presence of positive serology, or extra-articular manifestations increase the risk of developing MetS [10]. Many mechanisms had been suggested for the development of MetS in RA patients including; systemic inflammation and increased production of pro-inflammatory cytokines can contribute to the development of MetS and CVD in RA [11], medications used in treatment of RA as corticosteroids lead to impaired glucose metabolism and dyslipidemia while anti-tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) antagonist may also lead to dyslipidemia [12], vitamin D deficiency was reported to be associated with a decrease in the high density lipoprotein (HDL) [13]. Furthermore, immobilization as a result of joint inflammation and deformities results in being overweight [14]. Adipose

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tissue is regarded as an active endocrine organ that secretes adipocytokines like leptin, adiponetin, resistin, TNF-α, IL-1 and IL-6 [15]. Adipokine levels are elevated in RA patients [16], suggesting a role in the disease pathogenesis [17]. In another Egyptian study on RA patients, glucose-6-phosphate dehydrogenase (G6PD) deficiency was considered a potential risk factor for the development of MetS [8].

The aim of the present study is to evaluate of the impact of MetS on the pattern and clinical presentation of RA, and its relation to disease activity and functional status of the patients.

2. Patients and methods

Sixty Egyptian RA patients were enrolled in this cross sectional-observational study. All patients fulfilled the American College of Rheumatology (ACR) 1987 revised criteria for the classification of RA [18]. Patients were divided into two groups according to the presence of MetS. Group A: included 30 RA patients with MetS and group B: included 30 RA patients without MetS. The MetS was defined according to The International Diabetes Federation (IDF) proposed new definition [19]. All RA patients were recruited from the Rheumatology and Internal Medicine outpatient clinics in Ain Shams University Hospitals and Mattaria Teaching Hospital. All participants gave written informed consents to participate in the study, which was approved by our local Ethics Committee.

All patients were subjected to full medical history and thorough clinical examination with calculation of the body mass index (BMI), waist to hip ratio (WHR), assessment of RA disease activity using DAS-28 ESR score [20] and assessment of the functional status of the patients using health assessment questionnaire (HAQ) [21]. Laboratory investigations were done including: complete blood picture (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), kidney function tests, liver enzymes, fasting (FBS) and 2 h post-prandial blood sugar (2hPPBS), complete lipid profile and rheumatoid factor (RF) titre using Latex agglutination test. Plain X-ray hands, wrists and any other affected joint were considered.

Statistical analysis: Statistical Package for Social Science (SPSS) version 20 was used. Parametric quantitative data were presented as mean, standard deviations and ranges and non parametric data as median with interquartile range (IQR), while qualitative data were presented as number and percentage. Chi-square test was used to compare between groups with quantitative data and Fisher exact test was used when the expected count in any cell is < 5. Comparison between two parametric quantitative data was done using Independent t-test and for non parametric data by using Mann-Whitney test. The confidence interval was set to 95% and values were considered significant at $p < 0.05$.

3. Results

The present study included 60 RA patients; 30 with MetS (group A) with a mean age of 46.3 ± 9.9 years (27–66 years) and a male to female ratio 1:14 (2 males and 28 females), and 30 without MetS (group B) of matched age and sex. The disease duration, anthropometric measures, scores and laboratory investigations of both groups are displayed in Table 1. On radiological examination, joint deformities were detected in 8 patients (26.7%) in group A, and in 10 patients (33.3%) in group B. While bone erosions were detected in 6 patients (20%) in group A, and 7 patients (23.3%) in group B. Joint space reduction was found in 10 patients (33.3%) in group A and in 13 patients (43.3%) in group B. As regards the functional capacity; it was found to be more impaired in patients with MetS shown by the significantly higher HAQ in group A than group B ($p = 0.007$). While no significant differences were detected regarding the DAS28 and visual analogue scale (VAS) ($p = 0.26$ and 0.13 respectively) as shown in Table 2. In patients with MetS (group A), presence of joint deformities was inversely related to body weight and waist circumference ($p = 0.047$ and $p = 0.018$ respectively) (Table 3). Furthermore, no significant relations were detected between both joint deformities and bone erosions and anthropometry parameters in group B.

A significant direct relation was found between bone erosions and disease duration in both groups ($p = 0.015$ and $p = 0.002$ respectively). Group A Joint deformities in group A patients were significantly directly related to FBS ($p = 0.016$). Bone erosions showed a significant direct relation with ESR, FBS and 2 h PPBS ($p = 0.042$, $p = 0.004$, and $p = 0.031$ respectively) within the same group. However, in group B, there was only a significant direct relation between bone erosions and 2 h PPBS ($p = 0.02$).

Table 1
Clinical characteristics and laboratory investigations of the rheumatoid arthritis patients with (group A) and without (group B) metabolic syndrome.

Parameter Mean ± SD/Median (IQR)	Rheumatoid arthritis patients (n = 60)		
	Group A (n = 30)	Group B (n = 30)	p
Disease duration (years)	5 (3–10)	6 (3–15)	0.23
BMI	37.02 ± 6.73	26.03 ± 4.36	< **0.0001**
WHR	0.88 ± 0.05	0.82 ± 0.03	< **0.0001**
DAS-28 score	4.22 ± 1.12	3.91 ± 0.99	0.26
VAS	52 (23–70)	41 (10–56)	0.13
HAQ score	1.25 (0.5–2)	0.63 (0.38–1)	**0.007**
Hb (g/dL)	11.72 ± 1.35	11.85 ± 1.38	0.71
TLC (1000/cm^3)	7.12 ± 2.07	7.46 ± 2.63	0.58
Pl (1000/cm^3)	278.33 ± 63.32	292.50 ± 107.88	0.54
AST (U/L)	22.16 ± 6.12	21.07 ± 7.87	0.55
ALT (U/L)	19 (18–23)	18 (15–20)	0.07
sAlbumin (g/dL)	3.96 ± 0.30	3.90 ± 0.28	0.41
sUrea (mg/dL)	22.00 ± 4.86	19.73 ± 4.53	0.07
sCreatinine (mg/dL)	0.87 ± 0.15	0.79 ± 0.17	0.06
FBS (mg/dL)	126.33 ± 64.66	90.60 ± 6.91	**0.004**
2 h PPBS (mg/dL)	190.47 ± 99.16	118.90 ± 13.07	< **0.0001**
Rheumatoid factor	49.5 (9–81)	25 (11.4–65)	0.1
TG (mg/dL)	191.70 ± 44.86	166.27 ± 20.55	< **0.0001**
TC (mg/dL)	184.20 ± 73.31	106.03 ± 24.64	**0.007**
HDL (mg/dL)	112.88 ± 46.49	81.98 ± 21.91	< **0.0001**
LDL (mg/dL)	16 (5–40)	7.1 (3–28)	**0.002**
ESR (mm/hour)	40.84 ± 9.91	62.80 ± 7.60	0.49
CRP (mg/L)	46.20 ± 25.86	41.43 ± 27.15	0.3

BMI: body mass index, WHR: waist hip ratio, DAS 28: disease activity score, VAS: visual analogue scale, HAQ: health assessment questionnaire, Hb: hemoglobin, TLC: total leucocytic count, Pl: platelets, AST: aspartate aminotransferase, ALT: alanine aminotransferase, s: serum, FBS: fasting blood sugar, 2 h, PPBS: 2 h post prandial blood sugar, TG: triglycerides, TC: total cholesterol, HDL: high density lipoprotein, LDL: low density lipoprotein, ESR: erythrocyte sedimentation rate, CRP: C – reactive protein, IQR: interquartile range. Bold values are significant at $p < 0.05$.

Table 2
Comparison between rheumatoid arthritis patients with (group A) and without (group B) metabolic syndrome as regards disease activity and functional status scores.

Parameter Mean ± SD (range) or median (IQR)	Rheumatoid arthritis patients (n = 60)		
	Group A (n = 30)	Group B (n = 30)	p
DAS28 Sore	4.2 ± 1.12 (1.5–5.7)	3.9 ± 0.9 (2.3–6.1)	0.26
VAS	52 (23–70)	41 (10–56)	0.13
HAQ score	1.25 (0.5–2)	0.63 (0.38–1)	**0.007**

DAS-28: disease activity score, VAS: Visual analogue scale, HAQ: Health Assessment Questionnaire. Bold values are significant at $p < 0.05$.

4. Discussion

Rheumatoid arthritis is a mulifactorial chronic inflammatory autoimmune disease. It is characterized by the production of autoantibodies resulting in destruction of cartilage and joint malformation, in addition to systemic disorders as cardiovascular, pulmonary and psychological [22]. MetS is an increasingly rising global disease, owing to increased