## METABOLIC SYNDROME INPATIENTS WITH

# **RHEUMATOID ARTHRITIS**

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#### ABSTRACT

**Objectives:**To determine the prevalence of metabolic syndrome (MetS) in patients with rheumatoid arthritis (RA) and to evaluate the relation between parameters of MetS and clinical aspects of RA.

Design: Cross-sectional study.

**Patients:**Patients with rheumatoid arthritis (RA) according to 2010 ACR/EULAR classification criteria for RA (n = 150).

**Methods:** Demographic data, arthritis history, medical and therapeutic history were evaluated. Height, weight, BMI, waist circumference (WC) and blood pressure (BP) were recorded. Disease activity was evaluated using DAS28 (ESR). Immunological investigations included RF, ESR, CRP, and anti-CCP. Fasting blood glucose and lipid profile were measured. The patient was diagnosed as having MetS according to 3 definitions; ATPIII (2004), IDF (2005), and JIS (2009).

**Results:**Prevalence of MetS in rheumatoid patients was 48% (ATPIII definition), 52 % (IDF definition), and 46 % (JIS definition with Egyptian cut-off of WC), respectively. The most prevalent component of MetS was central obesity (75.3-92 % according to the used definition).DAS28 was significantly higher in patients with MetS with higher number of tender joints and VAS (0-100) and most rheumatoid patients with MetS (68 %) had high disease activity.

**Conclusions:**The increased prevalence of MetS components in RA patients, suggests greater attention be given to modifiable risk factors, including improvement of dietary habits, physical activity and blood pressure control.

Key words: rheumatoid arthritis, metabolic syndrome, DAS28.

## **INTRODUCTION:**

immune complexes, and altered lipid particle that increase endothelial activation and potentially render atheromatous plaques unstable <sup>(4)</sup>.

Metabolic syndrome (MetS) is multiplex risk factor for type 2 diabetes and CVDs, including insulin resistance. abdominal obesity. atherogenic dyslipidemia, high blood pressure (BP), impaired fasting blood glucose (FBG), a pro-thrombotic state, and a pro-inflammatory state <sup>(5)</sup>.MetS is responsible for a three-fold increase in the risk of atherosclerotic CVDs and increased mortality from CVD, as well

Rheumatoid arthritis (RA) is one of prevalent chronic the most inflammatory diseases. It primarily involves the joints, but should be considered a syndrome that includes extra-articular manifestations, such as nodules. pulmonary rheumatoid vasculitis, involvement or and systemic comorbidities<sup>(1)</sup>. RA is the most common inflammatory arthritis <sup>(2)</sup>. RA is associated with increased rates of cardiovascular diseases (CVD) <sup>(3)</sup>. Circulating inflammatory pathways that are implicated in this risk include cytokines, acute phase reactants,

Demographic data (age, sex. residency, occupation and smoking) were obtained from all participants. Arthritis history including age at onset, disease course and duration, and morning stiffness was recorded. Medical history (DM, hypertension, CVDs, respiratory, renal and hepatic diseases) was documented for all patients. Therapeutic history (NSAIDs, DMARDs. glucocorticoid use. cardiovascular drugs, and hypoglycemic drugs) was discussed with all patients.

Height and weight were measured using standard equipments and methods. The body mass index (BMI) was calculated as  $(kg/m^2)$ . The WC was measured in the standing position using a non-stretchable tape, placed directly on skin, at end of expiration at midway between lower costal margin and upper border of iliac crest. Arterial BP measurement was done using a calibrated sphygmomanometer.

# II- Joint examination and disease activity:

Examination of 28 joints of the hands, wrists, elbows, shoulders, and knees was done with count of the swollen and tender joints to calculate DAS28. The disease activity was evaluated using DAS28 (ESR) according to the equation [DAS28]  $(ESR) = 0.56 \times \sqrt{(TJC \ 28)} + 0.28 \sqrt{}$  $(SJC 28) + 0.70 \times \ln (ESR) + 0.014 \times$ GH (range, 0-9)]. High disease activity was considered as DAS28 > 5.1, moderate as DAS28 >  $3.2 - \leq 5.1$ , and low disease activity in the range 2.6-3.2. DAS28 < 2.6 indicated disease remission<sup>(13)</sup>.

#### III- Laboratory investigations: III.A) Immunological tests:

<u>1-Rheumatoid factor (RF):</u>It was measured in patients' sera by rapid latex agglutination test using AVITEX RF kit (Omega diagnostics LTD, Scotland, United Kingdom).Positive as all-causes, compared to the general population <sup>(6)</sup>.

RA and MetS are considered to be diseases with common traits that can increase the risk of CVDs <sup>(7)</sup>, with previous research showing an association between the two <sup>(8)</sup>. RA is associated with various components of MetS, which increase CVD mortality <sup>(9)</sup>. The frequency of MetS in RA patients ranges from 14 to 56% <sup>(10)</sup>.

It was found that the risk of having a moderate-to-severe RA was higher in patients with MetS than in those without and that the disease activity correlated with the number of MetS parameters present <sup>(11)</sup>. This study was designed to determine the prevalence of MetS in patients with RA and to evaluate the relation between parameters of MetS and clinical aspects of RA.

## **PATIENTS AND METHODS:**

This study included 150patients patients; diagnosed as having RA according to the 2010 ACR/EULAR classification criteria forRA <sup>(12)</sup>; attending Rheumatology clinics at Sohag University Hospitals.The study was approved by Ethical and Research committees at Faculty of Medicine, Sohag University. All patients assigned an informed written consent.

## **Exclusion criteria:**

- **1.** Patients with other inflammatory diseases.
- 2. Patients with malignancies.
- **3.** Patients with chronic kidney disease.
- **4.** Patients with chronic liver disease.
- **5.** Patients with familial dyslipidemia or diseases known to cause dyslipidemia e.g. hypothyroidism, nephrotic syndrome.
- **6.** Female patients on oral contraceptive pills and pregnant patients.

**Methods:** Patients were evaluated as follow:

## **I-Initial evaluation:**

- Raised TG: ≥ 150 mg/dL, or specific treatment for this lipid abnormality.
- Reduced HDL-C: < 40 mg/dL in males, < 50 mg/dL in females.
- Raised BP: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised FBG: ≥ 100 mg/dL, or previously diagnosed T2D.
- <u>IV.2- IDF (2005)</u>: The presence of central obesity (WC  $\geq$ 94 cm for men, WC  $\geq$ 80 cm for women) with any two of the following <sup>(15)</sup>:
- Raised TG:  $\geq$  150 mg/dL, or specific treatment for this lipid abnormality.
- Reduced HDL-C: < 40 mg/dL in males, < 50 mg/dL in females, or specific treatment for this lipid abnormality.
- Raised BP: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised FBG: ≥ 100 mg/dL, or previously diagnosed T2D.
- *IV.3- JIS definition (2009):* The presence any three of the following <sup>(16)</sup>:
- Obesity: with the Egyptian cut-off values of WC (100.5 and 96.25 cm for men and women, respectively) (17).
- Raised TG:  $\geq$  150 mg/dL, or specific treatment for this lipid abnormality.
- Reduced HDL-C: < 40 mg/dL in males, < 50 mg/dL in females, or specific treatment for this lipid abnormality.
- Raised BP: systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised FBG: ≥ 100 mg/dL, or previously diagnosed T2D.

results were considered at RF serum concentration above 8 IU/ml.

2- Erythrocyte Sedimentation Rate (ESR): ESR was measured in the anticoagulated blood of the patients by Wintrobe's method. The reference range of first hour ESR was 3-5 mm/hr (for females) and 7-12 mm/hr (for males).

<u>3- C-reactive protein(CRP):</u> It was measured in patients' sera by rapid latex agglutination test using AVITEX CRP kit (Omega Diagnostics LTD, Scotland, United Kingdom).Positive results were considered at CRP serum concentration above 6 mg/Litre.

<u>4- Anti-cyclic citrullinated peptides</u> (<u>Anti-CCP</u>):was measured by a chemiluminescent microparticle immunoassay using ARCHITECT Anti-CCP Reagent Kit "1P65" (Axis-Shield Diagnostics LTD, Dundee, United Kingdom). Values more than 5 IU/ml were considered positive.

**III.B)** Fasting blood glucose (FBG):was measured in patients' sera using Glucose HK reagent on Cobas C311 analyzer (Roche Diagnostics GmbH, Germany). The reference range was 70-110 mg/dl.

**III.C)** Lipid profile:Serum total cholesterol (TC), high density lipoprotein (HDL-C) and triglycerides (TG) were assessed by enzymatic colorimetric methods using commercially available kits on Cobas C311 analyzer (Roche Diagnostics GmbH, Germany).TC between 50 and 200 mg/dl, TG between 40 and 150 mg/dl, HDL-C more than 35 mg/dl and LDL-C less than 110 mg/dl were considered normal values.

# IV- Diagnosis of metabolic syndrome (MetS):

The patient was diagnosed as having MetS according to 3 definitions:

- <u>**IV.1-**</u> <u>ATPIII</u> (2004): The presence any three of the following <sup>(14)</sup>:
- Central obesity: WC ≥ 102 cm for men, or WC ≥ 88 cm for women.

(SPSS, version 24).Qualitative variables were recorded as frequencies and percentages and were compared by chi-square test.Quantitative variables were presented as means  $\pm$  standard deviation (SD) for normally distributed data and median with interquartile non-normally range (IQR) for distributed dataand were compared by independent *t*-test.*P* value < 0.05 was considered statistically significant.

The 3 definitions were used to calculate only the prevalence. To compare demographic, clinical and laboratory findings between the group of patients with RA and MetS *versus* RA patients without MetS, we used the MetS rate calculated by JIS (2009). V- Statistical analysis:

Data were recorded in Excel data sheet and analyzed usingStatistical Package for Social Sciences soft ware program

## RESULTS

The mean age  $\pm$  SD of the patients was  $45.01\pm11.05$  years, with 126 (84%) of themwere females, and 102 (68%) were from rural areas. Only 17 (11.3%) of the patients were smokers. The mean  $\pm$  SD age at the disease onset of the study population was  $35.66 \pm 10.60$  years. The mean  $\pm$  SD duration of the disease was  $9.60\pm7.35$  years. The course of the disease was progressive in all patients. Morning stiffness was recorded in 77 (51.3%) of the study population.

History of hypertension was found in 28 (18.7%) of the study population and DM was documented in 19 (12.7%). History of CVDs was found in 4 (2.7%) of the study population; with history of ischemia in 3 patients and history of myocardial infarction in one patient. History of stroke was found in 1 patient (0.7%).

History of use of NSAIDs was found in 146 (97.3%) of the study population. Use of steroids (prednisone/ prednisolone) was demonstrated in 61 (40.7%). Regarding DMARDs; most patients (61.3%) were using two drugs. Hydroxychloroquinewas used by 112(74.7%), methotrexate by 106 (70.7%),leflunomideby 46(30.7%), and sulfasalazine by 31(20.7%)of the study population. The main findings in general examination are shown in table 1.

**Table 1:** Mean values of main parameters of general examination of the population study

(m = 150)
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Parameter	Mean ± SD
Systolic blood pressure (mm Hg)	128.83±19.37
Diastolic blood pressure (mm Hg)	82.13±15.53
Weight (kg)	79.93±14.25
Height (cm)	160.64±7.57
Waist circumference (cm)	109.78±17.56
Body mass index (kg/m <sup>2</sup> )	31.06±5.72

The mean values of DAS28 and its different components are shown in table 2. Categories of disease activity in the study population according to DAS28 are demonstrated in table 3.The CRP was positive in 136 (90.7%) of the study population, with median value of 12 mg/L (IQR: 8-25 mg/L). The RF was positive in 97 (64.7%) of the study population, with median value of 36 IU/ml (IQR: 8-128 IU/ml). The anti-CCP was positive in 99 (66%) of the study population.The mean  $\pm$  SD level of FBG was 86.53  $\pm$  28.75 mg/dl.The mean  $\pm$  SD level of TG was 124.64  $\pm$  39.55 mg/dl, TC was 193.02  $\pm$  42.42 mg/dl, and HDL-C was 46.7  $\pm$  8.81mg/dl.

**Table 2:** Mean values of DAS28 and its different components in the study population (n=

150).

Parameter	$Mean \pm SD$
Number of tender joints	$5.53 \pm 3.88$
Number of swollen joints	$2.23 \pm 2.58$
erythrocyte sedimentation rate	$50.89 \pm 27.03$
visual analogue scale (VAS 0-100)	$51.05 \pm 25.58$
DAS-28	$4.90 \pm 1.22$

Table 3: Categories of disease activity in the study population (n= 150) according to DAS28.

Parameter	Frequency (Percentage)
RA in remission (DAS <2.6)	4 (2.7%)
Low disease activity (DAS 2.6-3.2)	13 (8.7%)
Moderate disease activity (DAS 3.2-5.1)	55 (36.7%)
High disease activity (DAS >5.1)	78 (52%)

MetS diagnostic criteria in the study population were met in 72 (48%), 78 (52%), and 69 (46%) according to ATPIII (2004), IDF (2005), and JIS with Egyptian cut-off values of WC (2009), respectively. The prevalence of each parameter is shown in table 4.

Table 4: Prevalence of metabolic syndrome parameters in the study population (n=150).

Parameter	ATPIII (2004)	<b>IDF</b> (2005)	<b>JIS (2009)</b>	
Central obesity	126 (84 %)	138 (92 %)	113 (75.3 %)	
Raised BP or hypertension	81 (54 %)	81 (54 %)	81 (54 %)	
Raised TG	38 (25.3 %)	38 (25.3 %)	38 (25.3 %)	
Decreased HDL-C	85 (56.7 %)	85 (56.7 %)	85 (56.7 %)	
Raised FBG or T2D	36 (24 %)	36 (24 %)	36 (24 %)	
BP: blood pressure; TG: triglycerides; HDL-C: high density lipoprotein-cholesterol; FBG:				

fasting blood glucose; T2D: type 2 diabetes.

The study population was divided according to the presence of MetS (JIS definition with Egyptian cut-off values of WC) into two groups: RA patients with MetS (n= 69) and RA patients without MetS (n= 81). The demographic data of the study groups are shown in table 5. The arthritis history and therapeutic history of the study groups are shown in table 6.

Parameter	Rheumatoid patients without	Rheumatoid patients with	* P value
	<b>MetS</b> (n= 81)	<b>MetS</b> (n= 69)	
Age (Mean± SD)	$42.7 \pm 12.1$	$47.7 \pm 9.1$	0.004
Sex			
Male	19 (23.5 %)	5 (7.2 %)	0.007
Female	62 (76.5 %)	<b>64 (92.8 %)</b>	
Residence			
Urban	27 (33.3 %)	21 (30.4 %)	0.72
Rural	54 (66.7 %)	47 (69.6 %)	
Occupation			
Housewife	62 (76.5 %)	50 (61.7 %)	0.62
Farmer	7 (8.7 %)	5 (6.2 %)	
Worker	4 (4.9 %)	4 (5.8 %)	
Employee	8 (9.9 %)	10 (12.3 %)	
Smoking	13 (16.0 %)	4 (5.8 %)	0.07
* P value < 0.05 was s	ignificant.		

Table 5: Demographic data of the study groups according to presence of MetS (JIS, 2009).

	Metb (315, 2007).				
	Parameter	Rheumatoid patients without MetS (n= 81)	Rheumatoid patients with MetS (n= 69)	* P value	
Ag	ge at disease onset in years (Mean ± SD)	$33.40 \pm 10.69$	38.32 ± 9.93	0.004	
Dis	ease durationin years (Mean ± SD)	$\textbf{9.60} \pm \textbf{8.01}$	9.59 ± 6.96	0.96	
	No	46 (56.8 %)	27 (39.1 %)	0.17	
	5 minutes	1 (1.2 %)	4 (5.8 %)		
Mo	10 minutes	2 (2.5 %)	1 (1.4 %)		
In In	15 minutes	1 (1.2 %)	0		
ng	30 minutes	6 (7.4 %)	8 (11.6 %)		
	≥ 60 minutes	25 (30.9 %)	29 (42 %)		
l ii	Non-steroidal anti- nflammatory drugs	79 (97.5 %)	67 (97.1 %)	0.63	
	Steriods	30 (37 %)	31 (44.9 %)	0.51	
	Methotrexate	56 (69.14 %)	50 (72.46 %)	0.24	
H	ydroxychloroquine	<b>64 (79 %)</b>	48 (69.6 %)	0.19	
	Sulfasalazine	20 (24.7 %)	11 (15.9 %)	0.32	
	Leflunomide	24 (29.6 %)	22 (31.9 %)	0.86	

**Table 6:** Arthritis history and therapeutic history of the study groups according to presence of MetS (JIS, 2009).

\* P value < 0.05 was significant.

Comparison of the main findings in the general examination in the study groups are shown in table 7. The DAS28 parameters in the study groups are shown in table 8. Categories of disease activity in the study groups according to DAS28 are shown in table 9. Comparison of the immunological investigations in the study groups are shown in table 10.

**Table 7:** Comparison of main findings in the general examination in the study groups according to presence of MetS (JIS, 2009).

Parameter	Rheumatoid patients	Rheumatoid patients with	* P value
	without MetS (n= 81)	<b>MetS</b> (n= 69)	
	Mea	$n \pm SD$	
Systolic BP (mmHg)	$120.25\pm16.04$	$138.91 \pm 18.13$	<0.001
Diastolic BP (mmHg)	$76.17 \pm 14.28$	$89.13 \pm 14.01$	<0.001
Weight (kg)	$75.25 \pm 13.72$	$85.42 \pm 12.91$	<0.001
Height (m)	$1.61 \pm 0.79$	$1.60 \pm 0.71$	0.31
WC	$103.15 \pm 17.93$	$117.57 \pm 13.55$	<0.001
BMI (kg/m <sup>2</sup> )	$29.02 \pm 5.51$	$33.45 \pm 5.03$	<0.001

BP: blood pressure; WC: Waist circumference; BMI: body mass index.

\* P value < 0.05 was significant.

**Table 8:** Comparison of DAS28 parameters in the study groups according to presence of MetS.

Parameter	<b>Rheumatoid patients</b>	Rheumatoid patients	* P value
	without MetS (n= 81)	with MetS (n= 69)	
	Mean =	± SD	
Number of tender joints	$4.86 \pm 3.70$	$6.32 \pm 3.96$	0.02
Number of swollen joints	$1.98 \pm 2.55$	$\boldsymbol{2.54 \pm 2.60}$	0.16
ESR	$48.64 \pm 27.71$	$53.53 \pm 26.18$	0.27
VAS 0-100	$46.38 \pm 25.46$	$\textbf{56.52} \pm \textbf{24.78}$	0.02
DAS-28	$4.65 \pm 1.19$	$\textbf{5.18} \pm \textbf{1.19}$	0.008
ESR: erythrocyte sedimentation rate; VAS: visual analogue scale; DAS: disease activity score.			

\* P value < 0.05 was significant.

**Table 9:** Comparison of disease activity categories in the study groups according to presence of MetS (JIS, 2009).

Parameter	<b>Rheumatoid patients</b>	<b>Rheumatoid patients</b>	* P value
	without MetS (n= 81)	with MetS (n= 69)	
RA in remission (DAS <2.6)	3 (3.7 %)	1 (1.4 %)	< 0.001
Low disease activity (DAS 2.6-3.2)	6 (7.4 %)	7 (10.1 %)	
Moderate disease activity (DAS 3.2-	41 (50.6 %)	14 (20.3 %)	
5.1)			
High disease activity (DAS >5.1)	31 (38.3 %)	47 (68.1 %)	
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\* P value < 0.05 was significant.  $\setminus$ 

**Table 10:** Comparison of the immunological investigations in the study groups according to<br/>presence of MetS (JIS, 2009).

Parameter	Rheumatoid patients without MetS (n= 81)	Rheumatoid patients with MetS (n= 69)	* P value
C-reactive protein	74 (91.4 %)	62 (89.9 %)	0.78
Erythrocyte sedimentation rate	$48.64 \pm 27.71$	$53.53 \pm 26.18$	0.27
Rheumatoid factor	52 (64.2 %)	45 (65.2 %)	0.52
Anti-cyclic citrullinated peptides	52 (64.2 %)	47 (68.1 %)	0.37

\* P value < 0.05 was significant.

#### DISCUSSION

In the current study; most patients were females (84 %) with mean age  $45.01 \pm 11.05$  years and disease DAS28. This may be explained by the setting from which they were recruited (a tertiary-level referral hospital) and no use of biological theray in any of the patients.

In this study the prevalence of MetS in RA patients was 48% (ATPIII definition), 52 % (IDF definition), and 46 % (JIS definition with Egyptian cutoff), respectively. This was higher than that reported in a previous study on 3209 randomly selected Egyptian population; 42.5% (ATPIII definition), 44.3% (IDF definition), and 41.5% (JIS definition with Egyptian cut-off), respectively <sup>(17)</sup>. This indicates that of RA may increase presence possibility of presence of MetS.

This prevalence was near that previously reported in RA patients; 51.4 % (ATPIII) and 53.4 % (IDF definition) in 107 Brazilian rheumatoid patients <sup>(18)</sup>, and a recent Brazilian report of 50.3 % (ATPIII) <sup>(19)</sup>. However; this was lower than previous Italian study that reported 55.5% duration 9.60 $\pm$ 7.35 years. More than half of patients (52 %) had severe disease activity according to (25/45) (ATP III) <sup>(20)</sup>. The reported prevalence in the current study is one of the highest prevalences all over the world.

On the contrary; this prevalence was higher than that previously reported in RA patients; 40.1% (ATPIII) and 45.4 % (IDF) in 387 British rheumatoid patients (21), 25.5 % (ATPIII) of 98 rheumatoid patients in Portugal <sup>(22)</sup>, 32.4 % (ATPIII), 40.9 % (IDF), and 32.4 % (JIS) of 105 patients from Vietnam <sup>(23)</sup>, 10.6 % (53/499; IDF) in American patients  $^{(24)}$ , 42.6 % (23/54; IDF) in Turkey <sup>(25)</sup>, 36.4 % (59/162; ATPIII) in American patients <sup>(26)</sup>, 30 % (ATPIII), and 35 % (IDF) of 409 Argentinan patients <sup>(27)</sup>, and 38 % (ATPIII), 48.6 (IDF), and 32.3 % (JIS) in Morocco  $^{(28)}$ . The difference in prevalence may be related to ethnicity, geographic area, nutritional habits, and different inclusion criteria and disease characteristics.

In this study the most prevalent component of MetS was central

obesity (75.3-92 % according to the used definition) and was more common in females; while the lowest prevalence was high FBG (17.3-24 %). The highest prevalence of obesity was according to IDF definition (92 %: 94% in females, 75% in males), followed by ATPIII definition (84 %: 89.9% in females, 54.2% in males), and JIS definition with Egyptian cutoff (75.3 %: 79.6% in females, 54.2% in males). This may indicate the use of Egyptian WC cutoffs to avoid the overestimated prevalence of abdominal from obesity resulting European cutoffs<sup>(17)</sup>.

These results were also higher than that was previously reported in Greek patients rheumatoid with central obesity (ATPIII) in 74.8% (110/147) in female patients and 60.4% (32/53) in male patients <sup>(11)</sup>. Lower prevalence was also reported in Pakistan with central obesity (ATPIII) in 46.1 % of 384 rheumatoid patients <sup>(29)</sup>. This may be related to the socioeconomic, lifestyle, and nutritional changes which have been occurring in the Egyptian community; towards the unhealthy pattern.

In the current study; patients with Mets were significantly older than those without MetS. This was in accordance with previous reports <sup>(8, 19, 30-32)</sup>. This may be related to the fact that age is a variable known to increase the frequency of comorbidities, MetS among them. In this study; the age of disease onset was significantly higher in patients with MetS with no significant difference disease of duration. This was in accordance with previous reports <sup>(8, 10, 19, 27)</sup>. This enforces the value of age of patients over the disease duration in development of MetS.On the other side; other studies reported longer duration of RA in rheumatoid patients with MetS<sup>(11, 23, 30)</sup>. This may be related to different age groups.

duration of the disease, and the used drugs in these studies.

In the present study; there was no significant statistically difference between RA patients with and without MetS as regards used NSAIDs, steroids and DMARDs. This was in accordance with previous reports (8, 19, 32). On the contrary; a previous study showed a significant association between the absence of MetS and the use of MTX and suggested the possibility of a drugspecific protection mechanism for MTX <sup>(21)</sup>. This may be explained by that; in the current study; the use of NSAIDs and glucocorticoids may have compensated for the protective effect of MTX and hydroxychloroquine.

In the current study; DAS28 was significantly higher in patients with MetS with higher number of tender joints and VAS (0-100). This was in accordance with previous reports <sup>(8, 19,</sup> <sup>30)</sup>. On the opposite side; a previous study failed to confirm this finding  $^{(33)}$ . The authors explained their findings that the aggressive treatment with DMARDs and life style modifications may alter MetS prevalence. In the present study; most RA patients with MetS (68 %) had high disease activity. This was in accordance with previous studies <sup>(19, 34, 35)</sup>. This suggests that inflammation could play a role in the development of metabolic disturbance in RA patients.

In the present study; there was no significant statistically difference between rheumatoid patients with and MetS without as regards immunological investigations (CRP. RF, and anti-CCP). This was in accordance with previous reports <sup>(8, 11,</sup> <sup>19, 28)</sup>. On the contrary; higher ESR and CRP were found in RA patients with MetS <sup>(30)</sup>. This can be explained that the RA patients in the last study were treatment naïve.

In the current study; hypertension and use of antihypertensive drugs was

reported in 28 (18.7%) of the patients. However; elevated BP was found in higher proportion (54%). This was in accordance with previous reports of high prevalence of raised BP in RA <sup>(11, 36, 37)</sup>. Moreover; *Panoulas et al.* (2007) reported that hypertension is underdiagnosed, especially in young RA patients. This indicates the value of follow up of BP in rheumatoid patients to detect hypertension early and avoid development of CVDs.

None of the rheumatoid patients in this study was treated for dyslipidemia. However; raised TG was found in 38 (25.3 %) of patients and decreased HDL-C was detected in 85 (56.7 %) of the patients. The increased levels of dyslipidemia in RA patients were previously reported <sup>(11, 38, 39)</sup>. A recent study reported high prevalence of undiagnosed hypercholesterolemia in patients with RA<sup>(40)</sup>. These findings demonstrate the importance of searching for dyslipidemias in rheumatoid patients in order to decrease CVD events and all-cause mortality.

In the present study; only 19 (12.7%) of the patients had DM; while raised FBG was found in 36 (24%) of the patients. This was in accordance with previous reports<sup>(8, 31)</sup>. A recent study demonstrated that impaired FBG was a strong predictor of T2D after one year of follow up in rheumatoid patients <sup>(41)</sup>. This finding indicates the importance of studying impaired FBG in rheumatoid patients to avoid further development of T2D.

Despite interesting findings of this study, it was limited by its crosssectional design not allowing conducting any cause-effect inferences on relationship between RA characteristics MetS. Α and longitudinal study should be designed to establish the casualty of these findings. Another limitation is the risk of selection bias since our center is a tertiary referral center with recruitment of mostly active and severe disease patients, and potentially leading to an overestimation of the prevalence of MetS. Multicenter studies with larger number of rheumatoid patients are warranted in order to determine prevalence of MetS in Egyptian patients with RA.

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