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Prevalence and Complications of Metabolic Syndrome among Rheumatoid Arthritis Patients in Aswan

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Abstract

Rheumatoid Arthritis (RA) is the most common inflammatory rheumatic disease. Prevalence of metabolic syndrome (MetS) varies widely in the literature. We conducted this study to detect the prevalence and complications of metabolic syndrome among RA patients and its association to disease activity and chronicityThis Cross-sectional study was conducted between January 2023 and December 2023, included 200 patients who were diagnosed as RA. Data collected from the eligible patients included full medical history and investigations included complete blood count, lipid profile, fasting blood glucose (FBG), uric acid, urea, creatinine, Alanine Aminotransferase, Aspartate aminotransferase, alkaline phosphates, electrocardiography and echocardiography. Patients were allocated to four groups (50 for each group) based on RA disease activity and duration. Group 1: acute active RA patients, Group 2: acute inactive RA patients, Group 3: chronic active RA patients and Group 4: chronic inactive RA patients.The present study was conducted on 200 patients with RA; the majority of them were females (152). The patient's mean age was 47±11 years, the mean± SD of their waist circumference was 101.6± 13.96. MetS prevalence in RA patients was 52% (104 patients), with a higher occurrence in chronic RA cases (30%) compared to acute RA (22%). Our study demonstrates a significant difference in MetS prevalence among the four groups. MetS prevalence among RA patients is associated with disease activity and duration. Hyperuricemia, increased liver enzymes and renal chemistry are the most prevalent factors linked to MetS in RA.

Keywords: *Rheumatoid Arthritis, Metabolic Syndrome, Complications*

Introduction

Rheumatoid Arthritis (RA) represents the most prevalent inflammatory rheumatic disease, exhibiting a global prevalence ranging from 0.5% to 2%[1], it is a systemic autoimmune disease characterized by chronic inflammation that may cause damage to joints as well as extra-articular organs, which involves the nervous system, heart, lungs, kidneys, skin, digestive system and eyes[2]. The primary symptoms are stiffness and pain in the joints, particularly swelling and morning stiffness. Typically, symptoms onset is gradual and insidious; nevertheless, certain cases may exhibit an episodic pattern known as palindromic rheumatism[3]. The trigger of RA symptoms remains unclear; however, the immunological mechanisms within the synovial and synovium fluid have been documented[4].

RA patients exhibited 54% higher risk of mortality relative to the general population[5]. Nevertheless, Sokka et al. determined that the main factors of overall mortality are comparable to those in the general population, with an earlier incidence of cardiovascular disease [6]. RA patients exhibit 1.63-fold increase of myocardial ischemia, with an annual incidence of fatal myocardial infarction estimated at 13.3 per 1,000 RA patients[7].

Metabolic syndrome (MetS) comprises a group of traditional risk factors, including hypertension (HTN), abdominal obesity, insulin resistance and atherogenic dyslipidemia[8]. MetS presence serves as a significant indicator for cardiovascular diseases, strokes and type-2 diabetes mellitus (DM) [9]. MetS is highly prevalent among RA patients due to chronic inflammation as well as disease activity. Identifying high-risk patients is essential to mitigate cardiovascular mortality, as one-third of RA patients have MetS[10].

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MetS components and hyperuricemia entail a heightened risk of kidney disease in individuals with type 2 DM[11]. RA is closely associated with DM and it was reported that RA patients' serum insulin levels and fasting blood glucose were substantially elevated compared to healthy controls[12]. In Egyptian adults, elevated liver enzyme levels were linked to MetS and an association was observed with its components[13]

Patients and Methods

Study Design, Setting and Patients

The present cross-sectional study was performed at Aswan University Hospital (Rheumatology clinic and internal medicine department), conducted between January 2023 and December 2023. We included 200 adult RA patients' diagnosed based on 2010 ACR/ EULAR diagnostic criteria for RA.

Exclusion Criteria

- patients with other rheumatologic disorders
- glucocorticoid use for other diseases
- Pregnant women.

Data Collection

Data collected from the eligible patients included full medical history with a focus on sex, age, disease duration and history of diabetes, hypertension, drugs history (biologic and non-biologic Disease Modifying Anti Rheumatic Drugs (DMARDs), measurement of blood pressure and waist circumference (WC). Investigations included complete blood count, lipid profile (high-density lipoprotein (HDL) and triglyceride), fasting blood glucose (FBG), uric acid, urea, creatinine, Alanine Aminotransferase, Aspartate aminotransferase, alkaline phosphates, electrocardiography and echocardiography. Assessment of disease activity was done utilizing disease activity score 28 (DAS 28)

Patients were allocated to four groups (50 for each group) based on RA disease activity and duration. The disease is considered active if DAS28 ≥3.2, acute if the duration is less than 6 months and chronic if the duration is more than 6 months. Group 1: acute active RA patients, Group 2: acute inactive RA patients, Group 3: chronic active RA patients and Group 4: chronic inactive RA patients.

Study Outcomes

The study's primary outcome was the high MetS prevalence and it is complications among RA cases. The secondary outcome included the association between MetS and RA chronicity and activity.

Ethical Statement

The study complies with both national and international ethical guidelines. No possible risks exist for research participants in terms of economic, legal, physical, social, psychological or any other variables. The study's risks, objectives and advantages were detailed to participants. The participants in the study signed informed consent. The research complied with the Declaration of Helsinki regarding human subjects. Additionally, the Faculty of Medicine's ethics committee at Aswan University, Egypt, reviewed and approved the study (Asw.uni./523/3/21).

Statistical Analysis

The collected data underwent revision, coding and tabulation and was subsequently entered into a PC utilizing Microsoft Excel. Statistical analyses were conducted utilizing SPSS 25 and R (4.4.1). The qualitative

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data were expressed in the form of percentages and numbers; whereas numerical data were presented as mean (SD). We performed a chi-square test to compare categorical variables between two or more groups. To test the hypothesis of numerical variables between the two groups, we used an independent t-test. The prevalence was estimated using the prevalence package and the Wald method. The confidence interval was established at 95%, with an accepted margin of error of 5%. Consequently, a p-value of less than 0.05 was deemed statistically significant (*).

The sample size was determined using the "pwr" package in R version 4.0.4 to identify a significant difference in group proportions. The calculation was based on the following parameters: two-tailed test, effect size of 0.25, alpha error of 0.05, power of 0.80, and a 1:1 allocation ratio. The required sample size to detect the difference is 185. We included 200 subjects (50 for each group).

Results

The present study was conducted at Aswan University Hospital. Two hundred patients with RA were included; the majority of them were females (152). The patient's mean age was 47±11 years, the mean± SD of their waist circumference was 101.6± 13.96 and their weight was 97.67± 49.56. There were 36 (18%) diabetic patients, 28 (14.6%) hypertensive patients, and 7 (3.5%) patients with ischemic heart disease (IHD). There were 100 (50%) non active patients, 13 (6.5%) patients with low activity, 50 (25%) patients with moderate activity and 37 (18.5) patients with high activity. Regarding the patient's treatment, there were 131 (65%) patients on PlaquenilL, 56 (28 %) patients on methotrexate, 92 (46%) patients on Leflunamide and 90 (45 %) patients on Steroids.

MetS prevalence in RA patients was 52% (104 patients), with a higher occurrence in chronic RA cases (30%) compared to acute RA (22%) (P=0.02). Figure (1) demonstrates a significant differences in MetS prevalence among the four groups (P = 0.001). MetS prevalence in Groups 1, 2, 3 and 4 was 58%, 30%, 68% and 52%, respectively. Patients with MetS were older (P =0.04) and exhibited wider WC (P =0.00) than those without MetS.

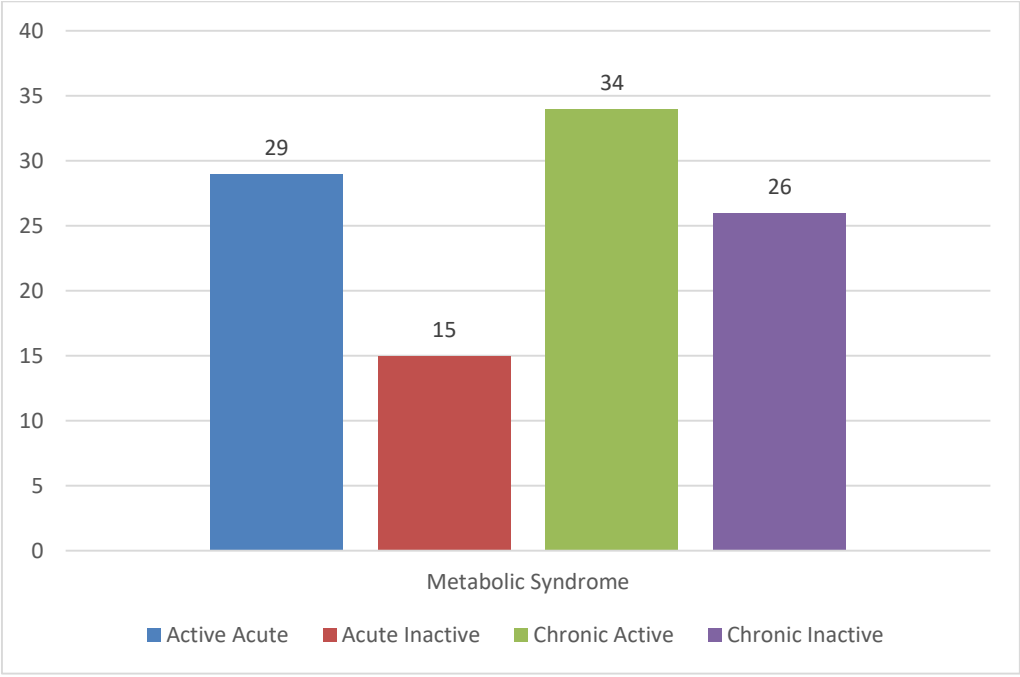

Figure 1. The Prevalence of Mets Among All Groups

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Table (1). Laboratory Investigations of the Studied Patients

		Mean (SD)
Blood picture	WBC	7.67 (2.45)
	HB	11.8 (1.27)
	Plt	266 (84)
Renal chemistry	Urea	28.8 (26.1)
	Creatinine	1.03 (0.43)
Liver function	ALT	35.2 (27.2)
	AST	26 (22)
Lipid profile	HDL	54 (15)
	TG	152 (51.7)
Uric Acid		5 (1.68)
Fasting Blood sugar		100 (34)

WBCs(white blood cells) , HB(hemoglobin) ,PLT(platelet) , ALT(Alanine Aminotransferase) ,AST(Aspartate Aminotransferase) , HDL(high density lipoprotein) , TG(triglyceride)

Table (1) shows the laboratory investigations of all studied groups. Our study revealed that the renal function, liver function, uric acid level and FBG were significantly elevated in the MetS group ($p < 0.01$). Moreover, HDL was significantly decreased in MetS than the non-MetS group ($p < 0.01$). Table (2)

Table 2. Laboratory Investigations According to Mets

		Patients with MetS n=104	Patients without MetS n= 96	P-value
CBC	WBC	7.65 (2.1)	7.68 (2.73)	0.94
	HB	11.63 (1.18)	11.97 (1.32)	0.06
	Plt	273 (81)	260 (86)	0.28
Renal chemistry Creatinine	Urea	45.89 (31.29)	32.63 (18.71)	0.001*
	Creatinine	1.18 (0.5)	0.91 (0.3)	0.001*
Liver function tests	ALT	46.5 (31.78)	25.39 (17.37)	0.001*
	AST	31.99 (29.31)	20.94 (9.97)	0.001*
Lipid profile	HDL	51.49 (15.04)	57.26 (14.45)	0.01*
	TG	157.76 (41.83)	148.25 (59.03)	0.20
Uric Acid		5.46 (1.89)	4.59 (1.27)	0.001*
Fasting Blood Glucose		111 (41)	91 (24)	0.001 *

Regarding the complications of MetS; hyperuricemia, elevated liver enzymes, and IHD were substantially elevated in the MetS group than those without MetS ($p < 0.01$), while there was no significant difference regarding increased renal function, as shown in Figure (2).

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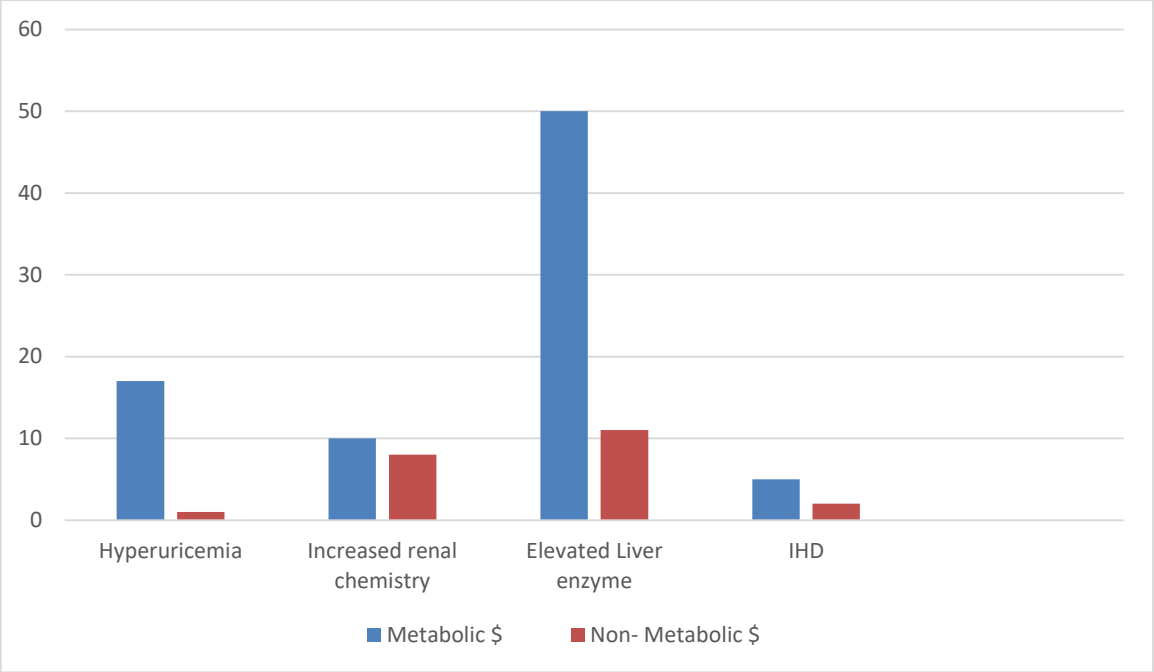

Figure 2. Complications of Mets

Discussion

MetS prevalence, as defined by the NCEP/ATP III, is substantially greater in RA patients compared to the general population, ranging from 12.1% to 45.3%, depending on the definition used[8].

This study was conducted on Two hundred RA patients. The study indicated a prevalence of MetS among RA patients at 52%. The prevalence of MetS among RA patients was statistically significant in relation to the disease chronicity and activity.

The prevalence rates exhibit significant variability, even among studies employing identical criteria. Dessein et al. [14] reported a MetS prevalence of 19% among 74 RA patients. In contrast, another study utilizing the same definition indicated a prevalence rate of 42% in individuals with long-standing RA and 30% in those recently diagnosed with RA. Furthermore, Crowson et al. [15] reported a prevalence of 33%. Against our results, MetS prevalence in RA cases (19%) was not substantially greater than that in healthy individuals; no notable differences in glucose, triglycerides or waist circumference were observed between both groups[16]. The high MetS prevalence in our study can be attributable to traditional risk factors like gender, hypertension, BMI and dyslipidemia, however, the role of chronic inflammation and endothelial cell activation should not be overlooked[17]. MetS variability reported in different studies can be explained by other factors associated with study population characteristics, such as demographic, clinical, genetic, cultural, ethnic and socioeconomic factors. Consequently, researches involving diverse populations are essential for identifying additional factors associated with MetS[18].

Our study indicated that FBG, uric acid, renal and liver function were markedly elevated in the MetS group. Moreover, HDL was substantially decreased in the MetS group compared to the non-MetS group. In line with our study, Gomes et al. [8] reported that the most common components of MetS in RA patients, assessed using NCEP/ATPIII criteria, included increased WC (64.4%), diminished HDL (51.1%) and hypertension (46.7%), followed by high levels of triglycerides (32.8%), glucose (26.4%) and type 2 DM (18%). Da Cunha et al. [19] reported that RA patients exhibited an increased waist circumference, blood pressure and fasting glucose than controls.

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The current study indicated that MetS has a strong association with RA activity and disease chronicity, which aligns with the findings reported in the literature. Gomes et al. [8] detected an association between MetS and disease activity, noting that high disease activity occurs more frequently in MetS patients. Furthermore, Lee et al. [16] found that prolonged disease duration as well as advanced age, were associated with a higher MetS frequency.

Conclusion

MetS prevalence among RA patients is associated with disease activity and duration. Therefore, we recommend routine monitoring for early MetS detection and management among RA patients. Hyperuricemia, increased liver enzymes and renal chemistry are the most prevalent factors linked to MetS in RA. Consequently, lifestyle modifications and renal protective measures should be considered.

The current study has some limitations; thus, additional longitudinal, multi-center studies with larger sample sizes are necessary to evaluate MetS prevalence in RA and its associated complications.

Abbreviations

DAS 28: disease activity score 28

DM: diabetes mellitus

DMARDs: Disease Modifying Anti Rheumatic Drugs

FBG: fasting blood glucose

HDL: high-density lipoprotein

HTN: hypertension

IHD: ischemic heart disease

MetS: metabolic syndrome

RA: Rheumatoid Arthritis

WC: waist circumference

Declarations

Availability of Data and Materials

The datasets used during the current study may be made available from the corresponding author upon reasonable request.

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Contributions

Aml Ahmed Sayed; wrote the main manuscript text & analysis and interpretation of data

Zein Elabdeen Ahmed Sayed; analysis and interpretation of data

Omar Abdelrahman Ahmed Abdallah; analysis and interpretation of data & collection of data

Marwa Ahmed Abdelhameid; analysis and interpretation of data

All authors reviewed the manuscript.

Corresponding author

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Conflict of Interest

All authors declare they have no conflicts of interest to this study.

Ethics Declarations

Ethical Approval and Consent to Participate

All procedures were performed in accordance with the Declaration of Helsinki and have been approved by the Ethics Committee of Faculty of Medicine, Aswan University, Egypt. An informed written consent was obtained from all participants before conducting the research

Consent for Publication

Not applicable

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