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Prevalence of metabolic syndrome in female patients with rheumatoid arthritis in Erbil city

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Abstract

Background: Rheumatoid arthritis and metabolic syndrome are closely linked, which considerably raises the risk of cardiovascular complications, and consequently, morbidity and mortality. Treatment of the metabolic syndrome reduces mortality and morbidity of cardiovascular disease.
Objective: To assess the prevalence of metabolic syndrome in a population of female patients with Rheumatoid arthritis, and association with comorbidities and Disease-modifying anti-rheumatic drugs (DMARDs).
Patients and Methods: This cross-sectional analytic study was conducted in Erbil City. A total of 110 female patients with the diagnosis of rheumatoid arthritis were included during the period of July 2021-March 2022. Anthropometric indices, blood pressure, fasting blood sugar, lipid profile, and proteinuria were investigated. The metabolic syndrome defining criteria from the international diabetes federation (IDF-2005) were applied.
Results: Out of 110 patients with rheumatoid arthritis, 63 (57.3%) were found to have metabolic syndrome, in whom the majority of them 52 (71.2%) were obese class 1. A significant association of metabolic syndrome was found with comorbidities (hypertension, diabetes, and hypothyroidism), p-value 0.019, and TNF-alpha inhibitor drugs were shown to be associated with a reduced risk for metabolic syndrome.
Conclusion: Metabolic syndrome is common in rheumatoid arthritis patients, and it increases the risk of other comorbidities (hypertension, diabetes, and hypothyroidism) as well as cardiovascular diseases. Patients on biologic disease modifying anti-rheumatic drugs are at a lower risk of metabolic syndrome.
Keywords: Metabolic syndrome, rheumatoid arthritis, obesity, hypothyroidism

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Introduction

Rheumatoid arthritis (RA) is a type of inflammatory disease that affects women in their 4th to 6th decades of life. Synovitis, which is the main characteristic feature, leads to irreversible joint destruction and damage. It can also be accompanied by multiple organ disorders [1]. In the last 20 years, patients with rheumatoid arthritis (RA) have been demonstrated to have three to ten year shorter life expectancy than the general population

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[2]. Systemic inflammation in RA is thought to be responsible for accelerated atherogenesis, which accounts for a significant proportion of arthritis related mortality. Apart from these alterations in vascular pathology, RA is also related to several components of metabolic syndrome, which enhance cardiovascular disease(CVD) mortality[3]. Metabolic syndrome (MetS) is characterized by a group of interrelated variables that raise the risk of coronary heart disease (CHD), various kinds of cardiovascular atherosclerosis and type2 diabetes (DMT2). Dyslipidemia (elevated triglycerides and low high-density lipoproteins (HDL)) with high blood pressure and impaired fasting glucose are the key components of MetS, although abdominal obesity and/or insulin resistance (IR) have attracted growing attention as the syndrome's fundamental features [4]. MetS affects around a quarter of the world's adult population[5], and those who have it are twice as likely to die from it, and three times more likely to suffer a myocardial infarction or stroke, than those who do not[6]. People with MetS are five times more likely to acquire type 2 diabetes [7]. The MetS has five different definitions, however, it has been demonstrated that the relative utility of the various metabolic syndrome criteria in terms of prognosis and therapy is similar. These five classifications had comparable relationships with cardiovascular risk factors in women, and it was clear that they performed better in females than in males [8]. The presence of MetS may influence the formation of accelerated atherosclerosis and an elevated risk of CV disease in people with Rheumatoid arthritis [9], There is also evidence of a link between RA and MetS inflammatory activity, Patients with RA have also been observed to have a high incidence of MetS [10]. Toms *et al*. found that treating RA patient with methotrexate medication have independently lower incidence of MetS than other disease-modifying antirheumatic drugs (DMARDs) or glucocorticoids, implying a drug-specific mechanism and making methotrexate a good first-line DMARD in RA patients at high risk of MetS[11].A study which is conducted in Erbil city by Ismail et al, showed that MetS is prevalent in females by three times than males [12]. According to ministry of health-Iraq (MOH) statistics, the prevalence of MetS risk factors in our region is rising, particularly obesity, diabetes, and cardiovascular consequences from untreated MetS [13] . There are many studies on the prevalence of MetS in RA, were conducted across the world. The frequency identified in the different populations ranges from 14 to 63 percent [14]. This variation in frequency can be explained by using different MetS definitions, ethnicity, socioeconomic status, sample size, genetic, and the presence of comorbidities. The aim of this studyis to demonstrate the prevalence of MetS in female patients with RA, and association with comorbidities and Disease-modifying anti-rheumatic drugs (DMARDs).

Patients and Methods

This is a cross sectional study, conducted in outpatient clinic rheumatology department of Hawler teaching Hospital and Rizgary teaching Hospital in Erbil city, Iraq. Cases were collected from July 2021 to March 2022, a total of 110 female patients with RA were enrolled in the study.

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Inclusion criteria include female patient with rheumatoid arthritis diagnosed according to ACR/EULAR 2010 criteria, with an age, 18 years and older.

Exclusion criteria are chronic kidney disease (CKD), ischemic heart disease, malignancy, abdominal hernia that affects the contour of abdomen, other rheumatological diseases, and pregnancy.

Data collection

Participants were interviewed in outpatient clinic of rheumatology department and a comprehensive history with focusing on other medical comorbidities, drug history and history of smoking. Thorough general physical examination including blood pressure measurement, measurement of weight, height, waist circumference and calculating body mass index (BMI). All patients were categorized into six categories, according to BMI; underweight (BMI<18.5), normal (18.5-24.9), overweight (25-29.9), obese class1 (30-34.9), obese class 2 (34.9-39.9), and obese class 3 (≥40)(15). We measure the mid waist circumference (WC mid) in the morning at the end of normal expiration by tape measure in the horizontal plane, halfway between the lowest rib and the iliac crest with the patient standing balanced on both feet[16]. After an overnight fasting for at least 8 hours, venous blood was collected in the morning for checking fasting blood sugar, serum triglyceride, HDL, total cholesterol, creatinine, and erythrocyte sedimentation rate (ESR). Proteinuria was measured by using a urine dipstick with reference values of trace (15mg/dl), 1+ (30mg/dl), 2+ (100mg/dl), 3+ (300mg/dl) and 4+ (1000mg/dl or more).

Regarding the definition for metabolic syndrome, international diabetes federation (IDF) criteria (2005) was used[17]:- Central obesity (defined as waist circumference but can be assumed if BMI > 30 kg/m2) with ethnicity-specific values, plus two of the following features: triglycerides 150 mg/dl or greater, HDL-cholesterol < 40 mg/dl in men and < 50 mg/dl in women, BP 130/85 mmHg or greater, fasting glucose 100 mg/dl or greater. To meet the criteria, waist circumference must be: for Europeans, > 94 cm in men and > 80 cm in women; and for South Asians, Chinese, and Japanese, > 90 cm in men and > 80 cm in women. For ethnic South and Central Americans, South Asian data are used, and for sub-Saharan Africans and Eastern Mediterranean and Middle East (Arab) populations, European data were used.

Statistical Analysis

The information was recorded on a prepared questionnaire in the patients' native language. A Microsoft excel worksheet (Excel 2010) was used for data entry, Statistical Package for Social Sciences (SPSS) version 25 was used. We compared the results in patients with different variables, and a statistical significance level of ≤ 0.05. The results presented as rates, ratio, frequencies, percentages in tables and figures, and analyzed using t-test and Chi square tests.

Results

Table (1) shows that the majority of participants (68.2%) are in the age group of (40–60) years, while only one quarter is above the age of 60 (27.3%). One third (33.6%) of participants are free of comorbidities, while 29.1% of subject has hypertension and 22.7% of respondents has

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more than one disease. About 17.3% of respondents were smokers. More than half (51.8%) of the participants taking methotrexate. Patients without proteinuria constitute about 89.1%. More than half (57.3%) of participants have metabolic syndrome, 66.4% of them had obesity class 1, while only (2.7%) had normal BMI.

Table (1): General characteristics of participants

Variables	Categories	Frequency	Percent
Age	< 40 years	3	4.7
	40 to 60 years	75	68.2
	> 60 years	30	27.3
Marital status	Married	106	96.4
	Single	4	3.6
Residence	Urban	88	80
	Rural	22	20
Comorbidities	None	37	33.6
	Diabetes mellitus	9	8.2
	Hypertension	32	29.1
	Hypothyroidism	7	6.4
	More than one	25	22.7
Smoking	Ex-smoker	8	7.3
	Current smoker	19	17.3
	No	83	75.5
Methotrexate	No	53	48.2
	Yes	57	51.8
Hydroxyl chloroquine	No	71	64.5
	Yes	39	35.5
Leflonamide	No	89	80.9
	Yes	21	19.1
bDMARDs	No	70	63.6
	Yes	40	36.4
NSAIDS	No	66	60.0
	Yes	44	40.0
Proteinuria	None	98	89.1
	+	9	8.2
	++	3	2.7
Metabolic syndrome	Yes	63	57.3
	No	47	42.7
BMI	Normal	3	2.7
	Over-weight	30	27.3
	Obesity class 1	73	66.4
	Obesity class 2	4	3.6
	Total	110	100

In this study 110 participants enrolled, 57.27% of respondents have metabolic syndrome, and the rest (42.73%) of them are free of the syndrome.

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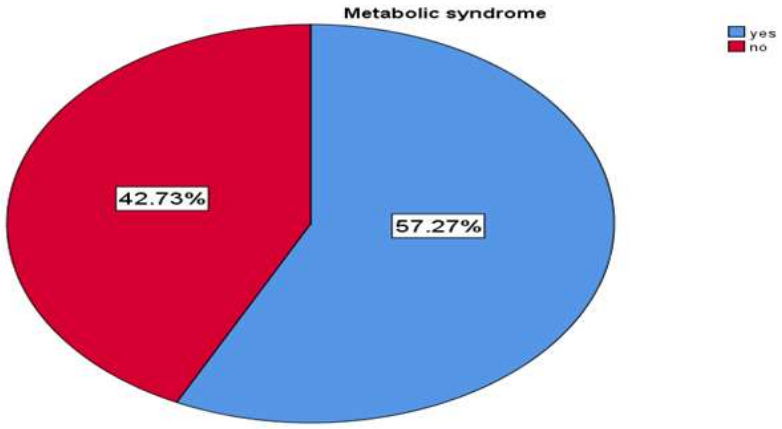

Figure (1): The percentage distribution of metabolic syndrome between the studied patients

Findings of Table (2) reveal that there was a non-significant statistical association between metabolic syndrome and proteinuria, p-value of (0.185). A statistically significant association was found between metabolic syndrome and BMI, most of the participants with MetS had obesity class 1(71.2%), compared to those without MetS (28.8%), with a p-value < (0.001). MetS and other comorbidities were shown to be statistically significantly correlated; the majority of MetS (59.4%) had hypertension compared to patients without MetS (40.6%), with a p-value of (0.019). The relationship between metabolic syndrome and bDMARDs was statistically significant; the majority of patients without MetS (55%) were on bDMARD medications, whereas about 45% of patients with MetS were on bDMARDs, a p-value of (0.049).

Table (2): Association between metabolic syndrome and other variables

Variable	**Categories**	Metabolic syndrome		**P-value**
		Yes	No	
Proteinuria	None	53(54.1%)	45(45.9%)	0.185
	1+	7(77.8%)	2(22.2%)	
	2+	3(100%)	0(0%)	
BMI	Normal	1(33.3%)	2(66.7%)	< 0.001
	Over-weight	7(23.3%)	23(76.7%)	
	Obesity class 1	52(71.2%)	21(28.8%)	
	Obesity class 2	3(75%)	1(25%)	
Comorbidities	None	14(37.8%)	23(62.2%)	0.019
	Diabetes mellitus	5(55.6%)	4(44.4%)	
	Hypertension	19(59.4%)	13(40.6%)	
	Hypothyroidism	6(85.7%)	1(14.3%)	
	More than one	19(76%)	6(24%)	
bDMARDs	No	45 (64.3%)	25 (35.7%)	0.049
	Yes	18 (45%)	22 (55%)	
Total			100%	

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Table (3) shows that, there was a significant difference between patients with and without metabolic syndrome. The mean values for weight (84.17), waist circumference (95.33), SBP (134.44) DBP (83.41), FBS (103.56), triglyceride (196.75), HDL (48.09), cholesterol (218.05), and BMI (32.16) for patients with metabolic syndrome were significantly higher than those without MetS, (78.26), (90.38), (123.30), (73.62), (87.23), (143.96), (55.76) , (195.11) ,(29.59) respectively, with a p-value of (less than 0.005) for each. There was no significant difference in mean value of ESR between patients with (20.54) and without (18.96) metabolic syndrome, p-value of (0.376).

Table (3): Difference of numerical variables between patients with and without metabolic syndrome

Variables	Metabolic syndrome	N	Mean	Std. Deviation	p-value	t-test
Weight	Yes	63	84.17	6.883	< 0.001	significant
	No	47	78.26	7.203		
Waist circumference	Yes	63	95.33	6.513	< 0.001	significant
	No	47	90.38	7.482		
SBP	Yes	63	134.44	11.644	< 0.001	significant
	No	47	123.30	9.514		
DBP	Yes	63	83.41	9.106	< 0.001	significant
	No	47	73.62	8.451		
FBS	Yes	63	103.56	15.639	< 0.001	significant
	No	47	87.23	5.939		
Triglyceride	Yes	63	196.75	68.184	< 0.001	significant
	No	47	143.96	29.303		
HDL	Yes	63	48.09	4.714	< 0.001	significant
	No	47	55.76	4.171		
Creatinine	Yes	63	0.794	0.184	0.041	significant
	No	47	0.728	0.133		
ESR	Yes	63	20.54	9.622	0.376	Non-significant
	No	47	18.96	8.685		
Cholesterol	Yes	63	218.05	44.544	0.004	significant
	No	47	195.11	33.426		
BMI	Yes	63	32.16	2.251	< 0.001	significant
	No	47	29.59	2.734		

Discussion

There are two studies with the highest proportion of female participants were conducted in Brazil and University of Naples-Italy, with 97 and 93 percent, respectively[14,18]. In our study, the prevalence of MetS was 57.27 %, which is approximately equals to the rates of 53.4% and 55.5 % in Brazil and Italy studies, respectively [14,18]. A study in Vietnam showed that 40.5% patients (IDF definition), only female patients with RA were included, which is lower than our results. We assumed the reason for this variation is to be the diagnostic criteria (They used ACR 1987) [19]. We compared this study with Ismail et al.'s study which was carried out in Erbil among a sample of population with no

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history of acute or chronic diseases (except for hypertension, diabetes and hyperlipidemia) [12]. We may assume that the risk of MetS may rise by 1.25 times in people with rheumatoid arthritis compared with those in the general population.

Two-thirds of the participants, in our study, had obesity class 1, and 71% of them had MetS. Obesity in RA is associated with increased inflammatory activity, decreased functional capacity and quality of life [20]. These two chronic inflammatory conditions are a risk factor for accelerated atherosclerosis and cardiovascular events [21,22].

In addition to the MetS, we found that the prevalence of proteinuria in patients with RA is 10.9%, which is consistent with the findings of Abubaker *et al* 10.2%(23), and Oweis et al study 9.4% [24]. But our study shows no significant association between proteinuria in RA patients with or without MetS. To our knowledge, this is the first study that showed this association in Asian countries. Increased cardiovascular mortality is linked to proteinuria in both the general population [25] and RA patients [26]. Renal involvement in RA may be brought on by the disease process or therapeutic lines with nephrotoxic effects, which may further increase the incidence of cardiovascular events with morbidity and mortality [27].

Similar pathogenic processes exist in both RA and atherosclerotic vascular disease, including the presence of autoreactive T cells and proinflammatory cytokines like TNF(28). TNF-alpha causes a wide range of atherogenic consequences in RA[29] in addition to its role in the development of insulin resistance. TNF-alpha antagonists, a class of drugs designed to inhibit TNF's effects, have been linked to a reduction in the course of joint destruction in RA patients who had not responded to traditional DMARD treatment [30]. More significantly, a decrease of systemic inflammation has been linked to an improvement in patients' CV prognosis(31). TNF-alpha, according to Gonzalez et al., may be effective in improving insulin resistance, a component of the metabolic syndrome, which may reduce the risk of MetS [32]. Our study has shown the same results that participants who receive bDMARDs are at lower risk for MetS.

Finally, hypothyroidism in RA patients, appears to be a significant additional risk factor for cardiovascular risk [33], with three times more common than in the general population [34]. The total number of patients who have hypothyroidism in our study is 7 (6.36%), which is comparable to Raterman et al.'s study 6.8% [35], but much lower than Mahagna *et al*.'s study 16% [36], This can be explained by variations in dietary iodine consumption dependent on geographic location, availability and quality of medical care, and using TNF- alpha inhibitors may assist clinically hypothyroid patients with their thyroid function [37].

Limitations of study

Our study is a cross-sectional study which lacks a control group without RA. Although a prevalence of 57% in patients may appear high, we cannot say that MetS occurs more often in RA patients than in people without RA, yet if we compare this study with other studies conducted in the same city by different authors, we come to conclusion that the rate of MetS shown in this study was greater than the rate in the general population

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(46%). The study's sample size was another drawback, which may have contributed to certain comparisons' statistical significance.

Conclusions

Metabolic syndrome is common in RA patients, and it increases the risk of other comorbidities (hypertension, diabetes, and hypothyroidism) as well as CVD. Patients on bDMARDs are at a lower risk of MetS.

Recommendations

We recommend additional laboratory testing for inflammatory markers, thyroid and renal function, as well as better clinical examination of RA patients, for early CVD identification. Other studies with a larger number of participants and different definitions of metabolic syndrome are recommended for comparison.

Source of funding: The current study was funded by our charges with no any other funding sources elsewhere.

Ethical clearance: The study was approved by the scientific and ethical committee of Kurdistan Higher Council of Medical Specialties (KHCMS). This study was explained to each patient, verbal consent was obtained from each patient or her caregiver. Confidentiality and anonymity of data were ensured.

Conflict of interest: Nil

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انتشار متلازمة التمثيل الغذائي فى النساء المصابات بالتهاب المفاصل الرثوي في مدينة أربيل

مصطفى عباس عثمان[١] ، محمد قادر مينه [٢]

الملخص

خلفية الدراسة: لا يرتبط التهاب المفاصل الرثوي ومتلازمة التمثيل الغذائي ارتباطا وثيقا، مما يزيد بشكل كبير من خطر حدوث مضاعفات القلب والأوعية الدموية ، وبالتالي الامراض والوفيات. يقلل علاج متلازمة التمثيل الغذائي من الوفيات والمراضة وأمراض القلب والأوعية الدموية.

اهداف الدراسة: لتقييم مدى انتشار متلازمة التمثيل الغذائي في مجموعة من المرضى الإناث المصابات بالتهاب المفاصل الرثوي، والارتباط بالأمراض المصاحبة والأدوية المضادة للرثوي المعدلة للمرض.

المرضى والطرائق: أجريت هذه الدراسة التحليلية المستعرضة في مدينة أربيل ، وتم تضمين ١١٠ مريضات تم تشخيص إصابتهن بالتهاب المفاصل الرثوي من تموز ٢٠٢١ إلى آذار ٢٠٢٢. تم التحقق في مؤشرات القياسات البشرية وضغط الدم وسكر الدم الصائم وملف الدهون والبيلة البروتينية. تم تطبيق معايير تحديد متلازمة التمثيل الغذائي من (الاتحاد الدولي للسكري).

النتائج: من بين ١١٠ مريضا ، وجد أن ٦٣(٥٧,٣%) يعانون من متلازمة التمثيل الغذائي ، وكان معظمهم ٥٢ (٧١,٢٪) يعانون من السمنة المفرطة من الفئة ١. تم العثور على ارتباط كبير من متلازمة التمثيل الغذائي مع الأمراض المصاحبة (ارتفاع ضغط الدم والسكري وقصور الغدة الدرقية) ف القيمة ٠,٠١٩ ، وأظهرت الأدوية المثبطة TNF ألفا أن ترافقا مع انخفاض خطر متلازمة التمثيل الغذائي.

الاستنتاجات: متلازمة التمثيل الغذائي شائعة في مرضى التهاب المفاصل الرثوي، وتزيد من خطر الإصابة بأمراض مصاحبة أخرى (ارتفاع ضغط الدم والسكري وقصور الغدة الدرقية) وكذلك أمراض القلب والأوعية الدموية. المرضى الذين يستخدمون الأدوية البيولوجية هم أقل عرضة للإصابة بمتلازمة التمثيل الغذائي.

الكلمات المفتاحية: متلازمة التمثيل الغذائي ، التهاب المفاصل الرثوي، السمنة ، قصور الغدة الدرقية

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تاريخ استلام البحث: ٢ آب ٢٠٢٢

تاريخ قبول البحث: ١٤ آب ٢٠٢٢

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