Metabolic Syndrome Among Patients with Rheumatoid Arthritis and the Correlation with Disease Activity

CRISTINA GABRIELA ENE[1#], MIHAELA MITROI[2*], IONELA MIHAELA VLADU[3#], LUCRETIU RADU[4], TIBERIU STEFANITA TENEA COJAN[5], ANCA MIHAELA PREDESCU[6], MARIUS GABRIEL BUNESCU[7]

[1]University of Medicine and Pharmacy of Craiova, Pharmacology Department, Emergency Clinical Hospital of Craiova, 2-4 Petru Rares Str.,200349, Craiova, Romania

[2]University of Medicine and Pharmacy, Craiova Department of Otorhinolayngology, County Hospital Craiova, 2-4 Petru Rares Str., 200349,Craiova, Romania

[3]University of Medicine and Pharmacy of Craiova, Department of Metabolism and Nutrition Diseases, Filantropia Clinical Hospital of Craiova, 1 Filantropiei Str., 200143, Craiova, Romania

[4]University of Medicine and Pharmacy of Craiova, Department of Hygiene, Filantropia Clinical Hospital of Craiova, 1 Filantropiei str., 200143, Craiova, Romania

[5]University of Medicine and Pharmacy of Craiova, Department of Surgery, CFR Hospital of Craiova, Stirbei-Voda Str., 200374,Craiova, Romania

[6]University of Medicine and Pharmacy of Craiova, Faculty of Dentistry Medicine, Histology Department, 2-4 Petru Rares Str., 200349, Craiova, Romania

[7]University of Medicine and Pharmacy of Craiova, Occupational Medicine Department, 2-4 Petru Rares Str., 200349, Craiova, Romania

Rheumatoid arthritis is a systemic inflamatory disease that affects primarily the synovial joints and it is associated with a progressive disability and a important socio-economic burden. [1] Although the main characteristic is the joint involvement, it is important to remember that RA is a disorder with systemic involvement mainly due to it's chronic inflamation. Patients with RA have a higher risk of cardio-vascular mortality that in general population. There are numerous studies that sugest that inflamation plays a key"role in the develompent of aterosclerosis and heart disease, therefore a better understanding of the inflamatory response in RA may lead to better outcomes for patients with RA. Metabolic Syndrome is described as a congregate of major risk factors for cardiovascular diseases (CVD): Diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood presure[2]. The clustering of CVD risk factors that typifies the metabolic syndrome is now considered to be the driving force for a new CVD epidemic [3]. The conducted study aims to assess and evaluate the presence of metabolic syndrome (MetS) in RA patients. 120 patients with RA (89 women and 31 men) and 120 (85 women and 35 men) patients without RA were included in the study. The prevalence of MetS in RA patients was 39.16% and 22.5% for the control group. RA patients with MetS had significantly higher disease activity score of 28 joints index (DAS28-ESR) than patients without MetS (3.70 ± 0.644 vs. 3.35 ±0.725; p=0.006).

Keywords: Rheumatoid arthritis, Metabolic Syndrome, inflamation, disease activity, cardiovascular risk

Rheumatoid arthritis (RA) is an autoimmune condition characterized by a systemic aberrant inflammatory response whose main feature is joint damage especially to the small joints of the hands and feet.

The character of systemic disease is demonstrated by multiple extraarticular affections and numerous studies have demonstrated that approximately between 50% and 80% of RA patients present extraarticular manifestations during the course of the disease and their presence is associated with a more aggressive disease status.

Patients with RA have a higher risk of cardio-vascular mortality that in general population. There are numerous studies sugesting that inflamation plays a *key* role in the develompent of atherosclerosis and heart disease, therefore a better understanding of the inflamatory response in RA may lead to better outcomes for patients with RA.

Metabolic syndrome is a group of major risk factors for type 2 diabetes and cardiovascular diseases (CVD), including insulin resistance, abdominal obesity, dyslipidemia, hypertension, and impaired fasting glucose, incorporated into a single disease group [4].

Experimental part

Aim of the study

The present study aims to evaluate the prevalence of MetS and it's components in patients with RA. Correlation between disease activity, inflamation response in RA and the presence of MetS among patients with RA could identify subjects at an aditional higher risk of cardio-vascular events in order to provide a better outcome in management of patients with RA.

Material and methods

The conducted study was a prospective longitudinal study and included 120 patients previously diagnosed with RA undergoing different type of Disease-modifying antirheumatic drugs (DMARDs) in the Medical Clinic of the Railway Clinical Hospital of Craiova from January 2017 to January 2019 and a control group consisting of 120 patients comparable to age and sex without RA that were hospitalized in the same clinical service.

For all the patients included in the study, RA diagnosis was according to the 2010 American College of

**e-mail address: mhlmitroi@yahoo.com; Phone: 0744395269;* *# Authors contributed equally to the manuscript and share first authorship.*

Table 1

INTERNATIONAL DIABETES FEDERATION - NATIONAL CHOLESTEROL EDUCATION PROGRAMME ADULT TREATMENT PANEL III (IDF - NCEP ATP III) GUIDELINES FOR METABOLIC SYNDROME

Central obesity* If Body Mass Index (BMI) >30kg/m^2 , central obesity can be assumed and waist circumference does not need to be measured.	Male	Female
	≥ 102cm	≥ 88cm
Reduced HDL cholesterol (HDL-C) or specific treatment for this lipid abnormality	Male	Female
	<40mg/dl	<50mg/dl
Raised triglycerides or specific treatment for this lipid abnormality	≥ 150mg/dl	
Raised blood presure or treatment of previously diagnosed hypertension	systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg	
Raised fasting plasma glucose or previously diagnosed type 2 diabetes	≥ 100mg/dl (5.6mmol/L)	

Rheumatology (ACR)/ European League Against Rheumatism (EULAR) classification criteria [5].

The assessment of MetS was made for all the patients included in the study. MetS was defined according to International Diabetic Federation - National Cholesterol Education Programme Adult Treatment Panel III (IDF - NCEP ATP III) guidelines where a minimum of 3 criteria must be fulfilled for the diagnosis of Metabolic Syndrome (table 1).

For all the patients included in this study, demographic data regarding sex and age were collected, blood preasure (systolic and diastolic) was measured each, day during their hospitalisation and anthropometric measurements were taken (weight, height, waist circumference). Blood samples were collected from which we tested total cholesterol, high density lipoprotein cholesterol (HDL-C), triglycerides, serum glucose concentration.

Additionally, for the patients with RA, the erythrocyte sedimentation rate (ESR), rheumatoid factor (RF), C-reactive protein (CRP), and anticyclic citrullinated peptide (anti-CCP) were measured and the assessment of disease activity was made using the Disease activity score of 28 joints (DAS28-ESR) (table 2).

Table 2

DISEASE ACTIVITY CLASSIFICATION ACCORDING TO DAS28-ESR

Disease activity score of 28 joints with ESR (DAS28-ESR)	
Disease activity	**DAS28 ESR**
Remission	< 2.6
Low disease activity	< 3.2
Moderate disease activity	< 5.1
High disease activity	> 5.1

The study was conducted according to the Declaration of Helsinki and local regulations. Ethical approval for the study was obtained from the local ethics commitee and also, patients in both groups signed an informed consent.

Statiscal analysis were made using IBM Statistical Package for Social Science (IBM SPSS) V 20.0 where a *p* value < 0.05 was considered significant.

Results and discusions

The analisys of the demographic data showed no statistically significant differences between the studied groups. Among the RA patients 89 (74.16%) were women and 31 (25.83%) were men, while in the control group 85 were women (70.83%) and 35 (29.16%) were men (fig. 1). Patients in RA group were aged between 26 and 72 years old with a mean age of 52.77 ± 10.40, while in the control group, patients were aged between 23 and 75 years old with a mean age of 53.55 ± 11.49 (p=0.585) (table 3).

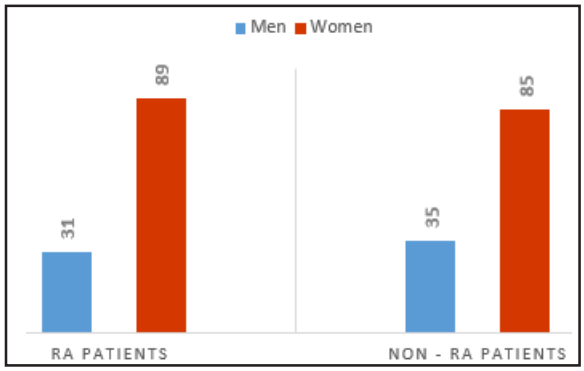

Fig. 1. Sex distribution among both studied groups

Regarding the prevalence of MetS in both groups, we found that this was higher in the RA group comparing to the control group (p=0.005)(fig. 2). Thus, in the presented study we found 74 patients with MetS (30.83% from all the patients enrolled in the study. Among the group of patients with RA, 47 patients (39.16%) had MetS while, in the control group, only 27 patients fulfilled the criteria for MetS (22.5%) (table 4).

Regarding the metabolic syndrome components as defined in table1, the conducted study showed that central obesity was found in 45 RA patients (37.5%) vs. 22(18.33%) patients from the control group (p=0.001) . Regarding low levels of HDL-C, we found no significant differences between both groups (p=0.112), while high triglyceride levels were found in 65 (54.16%) RA patients vs. 36 (30%) Non-RA patients. High blood presure was accounted in 48 (38.33%) RA patients and in 29 (24.16%) patients from control group. Regarding high glucose levels, 30 patients had RA while 17 where Non-RA patients (p=0.035) (table 5).

Variables		RA patients (n=120)		Non- RA patients (n=120)	
Sex	Women	89	74.16%	85	70.83%
	Men	31	25.83%	35	29.16%
		P=0.565			
Age	Mean age	52.77		53.55	
	Std. Deviation	± 10.40		± 11.49	
		P=0.585			

Table 3
DEMOGRAPHIC ASSESSMENT OF THE PATIENTS INCLUDED IN THE STUDY

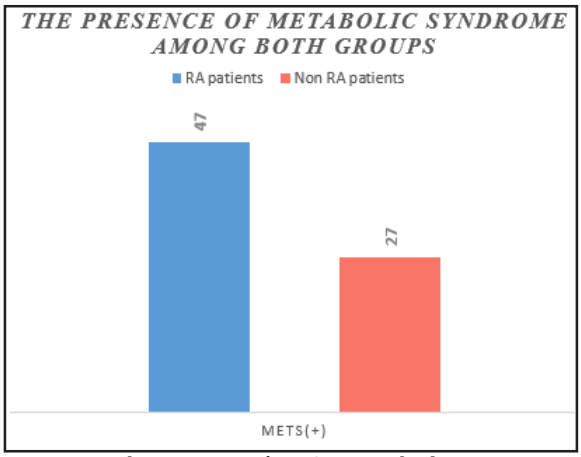

Fig. 2. The presence of MetS among both groups

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	RA patiens (n=120)		Non-RA patients (n=120)	
	Women (n=89)	Men (n=31)	Women (n=85)	Men (n=35)
MetS (+)	33 (37.07%)	14 (45.16%)	18 (21.17%)	9 (25.71%)
MetS (-)	56 (62.92%)	17 (54.83%)	67 (78.82%)	26 (74.28%)
	P=0.005			

Table 4
METABOLIC SYNDROME IN PATIENTS AMONG BOTH GROUPS

IDF - NCEP ATP III guidelines for MetS	RA patients	Non-RA patients	P value
Central obesity	45 (37.5%)	22 (18.33%)	P=0.001
Low HDL-C	70 (58.33%)	58 (48.33%)	P=0.112
High trglycerides levels	65 (54.16%)	36 (30%)	P=0.0001
Raised blood presure	48 (38.33%)	29 (24.16%)	P=0.008
Raised fasting plasma glucose	30 (25%)	17 (14.16%)	P=0.035

Table 5
METABOLIC SYNDROME COMPONENTS AMONG BOTH GROUPS

	Patients	DAS28-ESR			
		Min	Max	Mean	Std. devaition
RA patients with MetS	47 (39.16%)	2.5	5.4	3.70	± 0.644
RA patients without MetS	73 (60.83%)	2.5	5.1	3.35	± 0.725
	P=0.006				

Table 6
CORRELATION BETWEEN THE PRESENCE OF METS IN RA PATIENTS AND DISEASE ACTIVITY

Disease activity was also evaluated in patients with RA. Our study showed that DAS28-ESR was significantly higher in RA patients with MetS (3.70± 0.644) than in RA patients without MetS (3.35 ± 0.725) (table 6).

The cardiovascular risk quantitation is a golden desideratum for clinical management [6-8] allowing a better and more accurate medical care for the patients.

Patients with RA are known to have an increased risk of cardiovascular events early in life [9] than in general populations. Meune C et al on a meta-analysis over 50 years showed that RA is associated with a increased morbidity and mortality by up to 50% compared with general population [10].

Atherosclerosis in considered to be responsable for CVD but traditional risk factors for CVD do not entirely explain the increased risk of CVD in patients with RA.[11] The inflamatory response in RA is known to act on adipose tissue and the endangium resulting in a increased insulin resistance and destruction of endangium. Due to chronic pain percieved by patients with RA, low levels of physical activity are common in this patients resulting in increased

adipose tissue. Obesity is known as one of the most important risk factor for cardiovascular disease.[12-15] The prevalence of obesity has increased by 10-40% over the past ten years with an estimated number of 302.1 million adult with obesity worldwide (8.2% of the world's population) [16]. Many studies sugest that adipose tissue represents a source of proinflamatory cytokines - like interleukin 6 (IL-6) or tumour necrosis factor α (TNF α). [17-19] TNF α interferes with insulin signaling inducing insulin resistance which Eckel R H et al consider to be the basic metabolic disturbance of MetS [20-23].

Conclusions

The presented study showed a significant higher prevalence of metabolic syndrome in patients with rheumatoid arthritis coparable with control group.

Comparing the prevalence of metabolic syndrome components in both group, we observed that each component of metabolic syndrome had a significantly higher prevalence among patients with rheumatoid arthritis comparable to control group.

A correlation between disease activity of rheumatoid arthritis and metabolic syndrome showed that patients with both rheumatoid arthritis and metabolic syndrome had higher values of DAS28-ESR index comparable with patients with rheumatoid arthritis without metabolic syndrome.

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