ORIGINAL ARTICLE

METABOLIC SYNDROME IN YOUNG RHEUMATOID ARTHRITIS PATIENTS

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Background: Metabolic Syndrome is strongly associated with Rheumatoid Arthritis, which significantly increases cardiovascular complications and hence morbidity and mortality. Treating Metabolic Syndrome decreases cardiovascular related disease flares and deaths. This study evaluates prevalence of metabolic syndrome in young Rheumatoid Arthritis patients. **Methods:** This Cross-sectional study was conducted in rheumatology department of a tertiary care hospital in Karachi. All diagnosed cases of rheumatoid arthritis from April to August 2018 were consecutively included. Disease activity of rheumatoid arthritis assessed by Clinical Disease Activity Index (CDAI). Associate determinants of rheumatoid arthritis were measured along with outcome variables. **Results:** Out of 104 rheumatoid arthritis patients, 34 (32.7%) found to have metabolic syndrome in whom 20 (58.8%) of patients were seropositive. A significant association of metabolic syndrome was found with age (*p*-value 0.023), BMI (*p*-value 0.006), waist circumference (*p*-value 0.002), FBS (*p*-value <0.001), SBP (*p*-value <0.001), DBP (*p*-value <0.001), TG (*p*-value <0.001), HDL (*p*-value 0.022), and Methotrexate drug history (*p*-value 0.030). **Conclusion**: We conclude that metabolic syndrome is highly prevalent in young rheumatoid patients with rheumatoid arthritis. Treating Metabolic Syndrome decreases cardiovascular related disease flares and deaths. This young population base study will help out to estimate the exact burden of Metabolic Syndrome to decrease overall morbidity and mortality.

Keywords: Rheumatoid Arthritis; Metabolic Syndrome; Cardiovascular disease

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INTRODUCTION

A chronic disease associated with increased disability, morbidity, and death is rheumatoid arthritis.[1,2] Rheumatoid arthritis is characterized by a systemic inflammatory state involving multiple organs.[3] Studies reported that, compared to the general population, people with rheumatoid arthritis have increased mortality, partly due to high cardiovascular morbidity.[4,5]

The findings of a recent systematic review showed that rheumatoid arthritis is associated with an increased risk of mortality associated with CV disease.[6] Several risk factors have been reported for the high risk of CV disease related mortality which include dyslipidaemia, diabetes mellitus (DM), hypertension, higher body mass index (BMI) and high waist-to-hip ratio (WHR). In addition to this, late diagnosis and management of the risk factors also reported as the major causes.[7]

Longer duration of the disease, whether the patient is positive and/or anti - cyclic citrullinated peptide IgM - rheumatoid factor (RF), and whether certain extra articular manifestations appear to be associated with increased risk of CV disease due to rheumatoid arthritis.[4]

It seems likely that the inflammatory process and disease severity also increases the risk of CV disease.[8,9] The core elements of metabolic syndromes like dyslipidaemia, high density lipoproteins (HDL), blood pressure acceleration, and maladaptive homeostasis of glucose have gained increased consideration as the syndrome's core incarnations.[10]

Rheumatoid Arthritis is a rapidly progressive inflammatory arthritis which leads to significant disability if left untreated. Metabolic syndrome is strongly associated with rheumatoid arthritis. Parameters of Metabolic syndrome such as increase TG, cholesterol and LDL, low HDL, increasing blood pressure and blood sugar significantly increases cardiovascular complications and hence morbidity and mortality. Treating Metabolic syndrome decreases cardiovascular related deaths and disease flares in rheumatoid arthritis patients. General population-based studies confirmed that Metabolic syndrome is prevalent in Asian naïves especially south Asia like Pakistan, while data shows there is no single research been done in young adult population especially in our country for the estimation of this preventable and morbid entity.

MATERIAL AND METHOD

This cross-sectional study conducted in the Rheumatology department of Medical units II of JPMC, Karachi from April to August 2018. It included all the young patients (age <40 years) who were diagnosed Rheumatoid Arthritis.

Data were collected from 104 patients of age 16–40 years presenting with the seronegative or

seropositive rheumatoid arthritis diagnosed according to American College of Rheumatology (ACR 2010) criteria.

Metabolic syndrome was labelled according the NCEP ATP III criteria for metabolic syndrome More than 102 cm waist in men and more than 8 cm waist in women were labelled as increased waist circumference. More than equal to 150 mg/dl triglycerides were labelled as elevated triglycerides, less than 40 mg/dl HDL in men and less than 50 mg/dl HDL in women were labelled as low HDL, more than equal to 130 systolic blood pressure, and more than equal to 85 mmHg diastolic blood pressure was labelled as elevated blood pressure. Whereas, presence of more than equal to 100 mg/dl FBS was labelled as impaired fasting glucose.

Patients with Co-morbid conditions, such as Hypertension, Diabetes Mellitus, Ischemic Heart Disease, Chronic Kidney Disease, Familial Hypercholesterolemia, hypothyroidism or stroke, malignancies, such as Pancreatic Carcinoma, primary or secondary carcinoma of liver, patients with associated other autoimmune diseases, such as Systemic Lupus Erythematosus or mixed connective tissue disease and patients who were taking statins and patients who did not given consent were excluded from the study. A detailed history and thorough examination especially examination of the Musculoskeletal system to assess the severity of the disease by clinical disease activity index (CDAI) and disease activity score-28 joints (DAS-28) was done.

After an overnight fasting of at least 10 hours, 5 ml of blood samples were taken from the peripheral vein, 2ml was collected in the standard bottle for the fasting blood sugar, while remaining 3 ml was used for the measurement of fasting lipid profile especially for Triglycerides (TGs), High Density Lipoproteins (HDL), Low Density Lipoproteins (LDL) and total cholesterol (TC) from standardized laboratory.

Blood pressure of each patient was measured by standard blood pressure method by same researcher. Two readings were taken on same day with one hour apart. Waist circumference was taken with measuring tap and measurement was noted in centimetres.

A total of 120 patients registered for the study but 16 patients were excluded, as 10 has systemic lupus erythematosus overlap, 4 has Sjogren syndrome and 2 were taking statins. Thus, 104 patients include in the final analysis. Pre-approved Performa was used to collect and document data.

SPSS version 20.0 was used for analysis of data. Descriptive statistics like frequency, percentage proportion will be computed for presentation of qualitative variables like gender, disease activity of rheumatoid arthritis by DAS-28 or CDAI etc. Mean and standard deviation was calculated for presentation of numeric variables like age, blood pressure and waist circumference, fasting blood sugar (FBS), triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL) and low-density lipoprotein (LDL).

The data were collected after taking permission from Ethical review committee, Karachi. Written informed consent was obtained from patients while ensuring that the data was kept confidential.

RESULTS

The mean age of patients with Rheumatoid Arthritis 33.35±5.4 years. The female to male ratio in our study 9.4:1. Out of 104 Rheumatoid arthritis patients 34 (32.7%) of patients were found to have metabolic syndrome. (Figure-1) A significant association of metabolic syndrome was found with age (*p*-value 0.023) and BMI categories of the patients (*p*-value 0.006). (Table-1)

Fasting blood sugar was raised in 36 (34.6%) out of 104 patients. Triglycerides were increased in 18 (17.3%) of patients. LDL was increased in 10 (9.6%) of patients. Total no of patients with low HDL were 28 (26.9%). Total no of seropositive patients was 80 (76.9%). The mean duration of Disease was found to be 3.105±4.169 years. Total no of patients who were on very low dose of steroid not more than one month was 52 (50.0%). The disease severity was assessed by Clinical Disease Activity Index which showed Remission in 2 (1.9%) of the patients, Low Activity was found in 34 (32.7%). Moderate Activity was seen in 56 (53.8%) patients with High Activity were 12(11.5%). A significant association of metabolic syndrome was observed with waist circumference (*p*-value 0.002), FBS (*p*-value <0.001), SBP (*p*-value <0.001), DBP (*p*-value <0.001), TG (*p*-value <0.001), and HDL (*p*-value 0.022). (Table 2)

Total no of patients who were on Methotrexate are 34 (32.7%), those who were kept on Leflunomide 20 (19.2%) patient treated with Salazopyrine 16 (15.4%). HCQ was given to 56(53.8%) of patients. Only 2 (1.9%) of patients were treated with biologics. A significant association of metabolic syndrome was observed among patients with Methotrexate drug history (*p*-value 0.030). (Table-3)

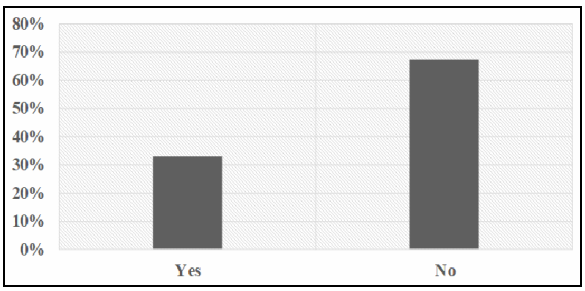

Figure-1: Frequency of metabolic syndrome

Table-1: Comparison of metabolic syndrome with demographic characteristics

Variables	Total	Metabolic Syndrome		*p*-value
		Yes	No	
		n (%)	n (%)	
Age, years				
≤30	34	6 (17.6)	28 (82.4)	
>30	70	28 (40)	42 (60)	0.023
Gender				
Male	10	4 (40)	6 (60)	0.604
Female	94	30 (31.9)	64 (68.1)	
BMI, kg/m2				
Normal	26	2 (7.7)	24 (92.3)	0.006
Overweight	56	22 (39.3)	34 (60.7)	
Obese	22	10 (45.5)	12 (54.5)	
Duration of disease				
1 year or less	48	16 (33.3)	32 (66.7)	0.897
More than 1 year	56	18 (32.1)	38 (67.9)	
Chi-square test applied, *p*-value <0.05 taken as significant				

Table-2: Comparison metabolic syndrome with clinical characteristics

Variables	Total	Metabolic Syndrome		*p*-value
		Yes	No	
		n (%)	n (%)	
Waist circumference				
Increased	86	34 (39.5)	52 (60.5)	0.002
Normal	18	0 (0)	18 (100)	
Fasting Blood Sugar, gm/dL				
Increased	36	20 (55.6)	16 (44.4)	<0.001
Normal	68	14 (20.6)	54 (79.4)	
SBP, mm/Hg				
Increased	38	28 (73.7)	10 (26.3)	<0.001
Normal	66	6 (9.1)	60 (90.9)	
DBP, mm/Hg				
Increased	38	26 (68.4)	12 (31.6)	<0.001
Normal	66	8 (12.1)	58 (87.9)	
TG				
Increased	18	14 (77.8)	4 (22.2)	<0.001
Normal	86	20 (23.3)	66 (76.7)	
LDL				
Increased	10	4 (40)	6 (60)	0.604
Normal	94	30 (31.9)	64 (68.1)	
HDL				
Normal	76	20 (26.3)	56 (73.7)	0.022
Decreased	28	14 (50)	14 (50)	
Seropositivity				
Positive	80	28 (35)	52 (65)	0.36
Negative	24	6 (25)	18 (75)	
CDAI Score				
Remission	2	2 (100)	0 (0)	0.131
Low activity	34	12 (35.3)	22 (64.7)	
Moderate activity	56	18 (32.1)	38 (67.9)	
Hight activity	12	2 (16.7)	10 (83.3)	
RA Factor				
Positive	50	20 (40)	30 (60)	0.126
Negative	54	14 (25.9)	40 (74.1)	
Anti CCP				
Positive	52	16 (34.6)	34 (65.4)	0.676
Negative	52	18 (34.6)	34 (65.4)	
Chi-square test applied, *p*-value <0.05 taken as significant				

Table-3: Comparison of metabolic syndrome with drug history

Variables	Total	Metabolic Syndrome		*p*-value
		Yes	No	
		n (%)	n (%)	
Methotrexate				
Yes	70	18 (25.7)	52 (74.3)	0.03
No	34	16 (47.1)	18 (52.9)	
Leflunomide				
Yes	84	30 (35.7)	54 (64.3)	0.178
No	20	4 (20)	16 (80)	
Salfasalazine				
Yes	88	32 (36.4)	56 (63.6)	0.061
No	16	2 (12.5)	14 (87.5)	
HCQ				
Yes	48	18 (37.5)	30 (62.5)	0.333
No	56	16 (28.6)	40 (71.4)	
Biologics				
Yes	102	34 (33.3)	68 (66.7)	0.320
No	2	0 (0)	2 (100)	
Chi-square test applied, *p*-value <0.05 taken as significant				

DISCUSSION

Metabolic syndrome, with a suggested ethnic predisposition in Asians, is highly prevalent in the adult population worldwide.[11] The finding of our study has reported that metabolic syndrome was observed in 32.7% patients with rheumatoid arthritis. Various studies from South East Asia has reported that metabolic syndrome prevalence ranges from 24.3–34.83%.[12,13]

The association of metabolic syndrome in Rheumatoid arthritis has been seen in many studies with high prevalence. In our study 34 (32.7%) of patients were found to have metabolic syndrome. which is almost compatible with several studies. The mean total duration of disease in our study was 3.105 years with minimum of 0.6yrs and maximum of 20 years. Metabolic syndrome, association was found even in those patients who have disease duration of less than 3 years. Which is supported by another study by Dao *et al*[14] they assessed the presence of Metabolic syndrome in women with RA. When individual component was assessed the highest frequency of waist circumference was found 86 (82.7%) this was observed due to low Asian cut off for BMI and waist circumference. Then body Mass Index with overweight were 56 (53.8%), obese were 22 (21.2%) followed by Hypertension in 48 (46.2%) of patients. According to our study estimates, a significant association of metabolic syndrome was observed with waist circumference, FBS, SBP, DBP, TG, and HDL.

Various studies have reported metabolic syndrome as a significantly prevalent long-standing rheumatoid arthritis in the Americans.[16,17] In a study risk of metabolic syndrome was also reported significantly higher in patients with rheumatoid arthritis and was associated with disease activity.[18]

In our study, a significant association of metabolic syndrome was observed among patients with Methotrexate drug history. Numerous studies have shown that the use of disease-modifying anti - rheumatic drugs and biological agents that affect these cytokines in patients with rheumatoid arthritis reduces inflammation and may be associated with decreased CVD potential risk.[19,20] In addition, studies have also shown that lipid - lowering therapy can be beneficial in reducing disease activity and the number of swollen ankles in rheumatoid arthritis.[21–23]

The European League Against Rheumatism's evidence - based and expert - opinion - based recommendations for screening and managing rheumatoid arthritis patients include annual CV risk assessment, management of identified CV risk factors, and aggressive suppression of the inflammatory process to further reduce the CV risk.[4]

One study conducted in Morocco found that, according to the definition used, the frequency of metabolic syndrome varied from 18%-48.6% in rheumatoid arthritis and was significantly higher than controls.[23]

CONCLUSION

Metabolic syndrome is highly prevalent in patients with rheumatoid arthritis which is evident by several studies. Abdominal obesity was observed in much higher number of patients. After completion of this study we conclude and recommend early recognition of Metabolic syndrome in rheumatoid arthritis patients irrespective of seropositivity, disease duration, their gender, age, BMI, so that treating Metabolic syndrome along with rheumatoid arthritis eventually decrease the cardiovascular related deaths in rheumatoid arthritis patients.

AUTHORS' CONTRIBUTION

SS: Study conception and design, Analysis and interpretation of data, drafting of manuscript.AD: Drafting of manuscript, Analysis and interpretation of data. SRA: Study conception and design. Critical revision. FK: Acquization of data

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