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Association between Metabolic Syndrome and Rheumatoid Arthritis

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Abstract: ***Background and Objectives: To assess prevalence of MetS in RA patients and compare with that of normal subjects. Methods: A cross sectional study was conducted in Government Medical College Kozhikode in 200 subjects of which 100 were Rheumatoid Arthritis patients and 100 were age and sex matched healthy controls. All the subjects who satisfied the inclusion and exclusion criteria and who gave informed consent were included in a consecutive manner till the sample size was achieved. Waist circumference was measured using measuring tape, BP by mercury sphygmomanometer, Fasting Blood Sugar by Glucose oxidase-peroxidase method, Triglycerides by GPO Trinder method and HDL Cholesterol by Phosphotungstic method. The data were analyzed using statistical package for social sciences (SPSS) version 18. Results: p value of this study is <0.05 which is statistically significant. Conclusion: The frequency of Metabolic Syndrome in RA was significantly higher compared to controls. The physicians should screen for Metabolic syndrome in patients with RA to control its components.***

1. Introduction

RA is a chronic inflammatory disease associated with increased disability, morbidity and mortality (1) The initial point of inflammation is the production of proinflammatory cytokines such as tumor necrosis factor-α, Interleukin (IL)-6 and IL-1 in the tissues within joints (1).The secretion of these mediators into systemic circulation produces inflammatory responses like Arteriosclerosis that increases the risk of CV disease (2)and contributes indirectly to cardiometabolic risk factors such as insulin resistance, atherogenic lipid profile and sarcopenic obesity, all features of chronic active RA (3).

Insulin Resistance has also been found to be significantly more frequent in established RA in addition to chronic inflammation (1). Recently, many studies suggested that TNFα which plays major role in the pathogenesis of autoimmune diseases and inflammatory disorders might be an important mediator of insulin resistance in animal models (5) Since IR is associated with inflammatory markers and cluster of metabolic disorders, including type 2 diabetes, obesity, hypertension and lipid abnormalities it increases the risk for atherosclerotic CVD (6)

Systemic inflammation and insulin resistance (IR) which are linked has its impact on atherosclerosis in rheumatoid arthritis (7).Patients with RA are at increased risk of CVD, including myocardial infarction (MI) and heart failure (HF), as well as CV mortality (8)Given that Rheumatoid arthritis and metabolic syndrome are considered to be diseases with common traits that can increase the risk of cardiovascular disease incidence, screening of metabolic syndrome in patients with RA to control its components will help to reduce the risk of cardiovascular disease in these patients (2).

2. Review of Literature

Rheumatoid arthritis is a common idiopathic inflammatory arthritis, affecting approximately 0.8% of the population, and is two to four times more common in women than in men (9). It mainly affects the lining of the synovial joints and can cause progressive disability, premature death, and socioeconomic burdens. The clinical manifestations of symmetrical joint involvement include arthralgia, swelling, redness, and even limiting the range of motion. (10) Rheumatoid arthritis not only target joints, but also causes a systemic inflammatory response in the lungs, heart, and kidneys (2).

- According to a study by Avina-Zubieta et al., the mortality rate from cardiovascular disease was 1.5 times higher in rheumatoid arthritis patients than in the general population (11)
- Karvounaris et al found a frequency of metabolic syndrome (defined according to the NCEP ATP III criteria) in RA patients (40%),comparable with their control population (12).
- Dodani and al found that the frequency of metabolic syndrome was 13.3% and 40% respectively, according to WHO and NCEP ATP III criteria (13).
- Research in Asia has reported the prevalence of MetS to be 45.2% among RA patients using the NCEP-ATP III criteria (14).
- Based on the NCEP-ATP III criteria, Oliveira et al. found that the prevalence of MetS among RA patients in South American was 51.4%

3. Methodology

Study design:
A cross sectional study

Setting:
This study was carried out in the departments of physiology and medicine, Govt medical college, Kozhikode, after clearances from research committee and ethics committee.

Rheumatoid arthritis patients with the age group of 25-75 years were taken from the medicine op and Rheumatology clinic.

Age and sex matched healthy controls were taken from the bystanders of the patients, medical and paramedical staffs.

Sampling:

Sample size:
Hundred participants in each group.

Sampling procedure:
The sample size was calculated using the formula:
$n= 2 (Z\alpha+Z\beta)^2 pq\times 2/d^2$
(p=40.9%)
Prevalence of metabolic syndrome in RA was found to be 40.9% by Dao et al, the sample size required is 100 in each group.

Study duration
One year (from February 2018 – March 2019)

Inclusion criteria

Group 1:
100 Rheumatoid arthritis patients belonging to both the sexes.

Group 2:
100 age and sex matched healthy subjects which includes bystanders of the patients, medical and paramedical staff of the hospital.

Exclusion criteria:
- Patients with other inflammatory diseases, Cardiovascular diseases and malignancies.
- Patients with drug abuse, alcohol and acute illness.

Data collection:
Study was conducted after obtaining their informed consent.

Waist circumference was measured in centimeters using a tape kept midway between lower costal margin and the upper border of iliac crest.

Blood Pressure was recorded using sphygmomanometer

Collection of blood samples
Blood samples were collected by venous puncture using disposable syringes and needles under aseptic precautions and transferred into clean dry bottles. Samples were taken after 8 -12 hours fasting.1ml of blood was transferred into a bottle containing oxalate fluoride mixture as an anticoagulant for fasting blood sugar estimation.2 ml was transferred into another clean dry bottle without any anticoagulant for estimating lipid profile.
The parameters assayed were:
Fasting blood sugar
Serum lipid profile

Statistical Analysis
The present study was designed as a cross sectional comparative study. Statistical analysis was done to determine the differences between the two groups. The data were analysed using statistical package or social sciences (SPSS) version 18.The results were expressed as Mean±SD. The mean value of each parameter was obtained by summing up all the individual values in the groups and dividing it by number of subjects in the groups. The mean differences between the groups were analysed using Independent sample 't' test. For all statistical tests a p value ≤0.05 was taken as the level of significance.

4. Results

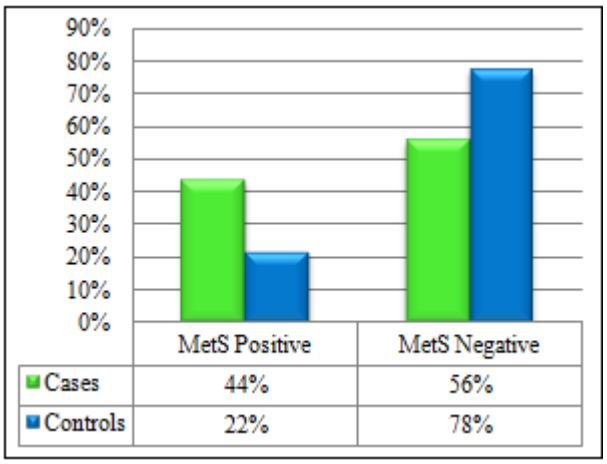
Data were analyzed using Statistical Package for Social Sciences (SPSS) version 18. Results were expressed as Mean ± SD. The p value of <0.05 will be taken as the level of significance. The results are summarized in tables and figures.

Mean levels of FBS, SBP, DBP, HDL, TG and waist circumference in the study groups

Table 9

	Healthy subjects	RA patients
FBS (mg/dl)	102.59±14.72	113.04±33.36
SBP (mm of Hg)	122.68±15.52	127.92±15.98
DBP (mm of Hg)	79.24±7.95	82.44±7.98
HDL (mg/dl)	45.61±9.33	42.04±5.15
TG (mg/dl)	114.31±33.75	118.02±21.95
Waist circumference (cm)	81.42±5.94	89.41±7.38

Comparison of Metabolic Syndrome in RA patients and healthy controls



P value=0.001

There was a significant rise of metabolic syndrome in RA patients when compared with the control group.

5. Discussion

Rheumatoid arthritis (RA) is an inflammatory rheumatic disease with progressive course affecting articular and extra-articular structures resulting in pain, disability and mortality (15). The risk of cardiovascular disease (CVD) in patients with RA is comparatively higher than the general population (16-18) and it increases the mortality in RA. The underlying inflammation in RA plays an essential role in increased cardiovascular risk. It is related to the fact that atherosclerosis also has an inflammatory etiology that is accelerated by RA. Inflammation also increases insulin resistance which is an important contributor to the metabolic syndrome.

The clustering of cardiovascular risk factors including diabetes, obesity, dyslipidemia and hypertension is referred to as metabolic syndrome. Metabolic syndrome increases CVD risk by 2 fold in general population (19).Therefore the development of accelerated atherosclerosis and increased risk of CV disease in patients with RA maybe influenced by the occurrence of MS (20)

The present study was conducted to find out the association between metabolic syndrome and rheumatoid arthritis. The study was conducted in 2 groups of 100 subjects each: rheumatoid arthritis patients and normal subjects. The various components of metabolic syndrome assayed in the both groups were compared.

In the present study the frequency of metabolic syndrome in rheumatoid arthritis patients is 44% compared to the control population 22%.The frequency of metabolic syndrome has varied markedly between different studies (21). Da Cunha et al. reported that 39% of RA patients met criteria for MS while these criteria were only fulfilled in 19% of controls (p=0.001) (22)

In the study, the BMI values were found to be high in rheumatoid arthritis patients than the normal subjects..Body mass index (BMI) (defined as weight in kilograms divided by the square of the height in meters) was calculated. High BMI (obesity) was defined as >30 kg/m2 and low BMI as <20 kg/m2. Waist circumference was found to be increased in rheumatoid arthritis patients than in normal subjects in the present study. The findings were similar in studies by Da Cunha et al, Crowson et al. Obesity is highly prevalent in patients with RA (23). Studies by Hotamisligil and Spiegelman postulated that the enhanced production of tumor necrosis factor-α by adipocytes in obese rodents would induce systemic IR (24).Changes in body composition have been found in patients with RA, with reduced fat-free mass and increased fat mass and , thus, with little or no weight loss or with a maintained body mass index. This condition has been named ‘rheumatoid cachexia’ and is believed to accelerate morbidity and mortality in RA and has also been linked to MS.

Compared to normal subjects, RA patients had lower HDL values in this study. Patients with inflammatory arthritis, particularly those with active disease have low HDL-c levels resulting in a higher that is, unfavourable, TC/HDL-c ratio, and high TG levels.

The disease duration in RA patients with and without metabolic syndrome was compared.No significant differences were seen between the two groups according to disease duration. Similarresults were obtained in Sahebari et al and Maryam Sahebari et al but in contrary to Karimi et al., in which duration of RA was associated with MS.

The disease activity was significantly increased in Rheumatoid arthritis patients with Metabolic Syndrome compared to RA patients without metabolic syndrome. Da cunha et al., Karvounaris et al., studied disease activity and showed that disease activity is associated with MS.

The rheumatoid arthritis patients had higher systolic and diastolic blood pressure values than the normal (p=0.01).In this study the hypertension in RA patients is 56% and in normal subjects 39%. Similar rise in blood pressure values were obtained for RA patients in studies by Da Cunha et al., Karimi et al., Crowson et al., This may be attributed by inflammation, physical inactivity, and drugs (25).

The present study showed a significant rise in Fasting blood sugar in RA patients compared to the normal subjects. There was no significant rise in Triglycerides in RA patients when compared with those of normal controls

So the current study emphasizes the need for monitoring and treatment of metabolic syndrome in RA patients to prevent the cardiovascular risk which is increased by the presence of metabolic syndrome.

6. Conclusion

The present study was undertaken to determine the association between metabolic syndrome and rheumatoid arthritis.200 subjects were included in the study out of which 100 were patients with rheumatoid arthritis and 100 age and sex matched controls.

The following results were obtained in the current study:

- Mean levels of Fasting blood sugar, Systolic blood Pressure, Diastolic blood pressure, waist circumference were higher in rheumatoid arthritis patients when compared to controls and mean HDL levels were lower.
- The disease activity was found to be significantly higher in RA patients with metabolic syndrome compared to the patients without Metabolic syndrome.
- No significant differences were seen between the two groups according to disease duration.

The following conclusions were made:

- Metabolic syndrome was found to be significantly higher in rheumatoid arthritis patients when compared with that of normal controls.
- These findings suggest that clinicians should screen for metabolic syndrome in patients with RA to control its components and therefore reduce the risk of cardiovascular disease in these patients.

7. Limitations of the Study

The limitations of the current study should be addressed. The study population was comprised of only 100 cases and 100 controls. A larger study population is needed to get a more reliable data.

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