INCREASE FREQUENCY OF METABOLIC SYNDROME AMONG THE CASES OF RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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ABSTRACT

In view of the increased prevalence of vascular risk factors in patients with chronic inflammatory arthritis the present study was conducted to assess the prevalence of metabolic syndrome according to NCEP-ATP III definition in patients with rheumatoid arthritis.

METHODS AND MATERIALS

A cross-sectional observational controlled study among the patients attending Rheumatology clinic in Assam Medical College and Hospital has been enrolled; 72 cases fulfilling the ACR/EULAR 2010 criteria above 12 years of both genders were included in the test group. Patient's age less than 12 and pregnant women, and cigarette smokers were excluded; 72 patients without any history of rheumatoid arthritis were included in the control group for study. Metabolic syndrome was diagnosed as per NCEP ATP III guidelines.

RESULTS

The study shows that metabolic syndrome was seen in 12 (16.7%) patients compared to 5 (6.9%) patients in the control groups. When cases and controls of metabolic syndrome were compared, it is found that case with Rheumatoid arthritis have much earlier presentation with metabolic syndrome than control.

CONCLUSION

The study shows that there is a definite earlier presentation of metabolic syndrome among the cases of rheumatoid arthritis.

KEYWORDS

Rheumatoid Arthritis, Metabolic syndrome, Hypertension, Dyslipidemia.

INTRODUCTION

It is well established that Rheumatoid Arthritis is associated with decreased life expectancy. While the absolute increase in mortality risk varies between studies, most found that majority of deaths result from cardiovascular disease. Traditional cardiovascular disease risk factors associated with atherosclerosis include age, smoking, hypertension and dyslipidemia.[1] Raised levels of systemic inflammation have also been shown to predispose both insulin resistance and type 2 Diabetes Mellitus (DM).[2] The metabolic syndrome which includes a constellation of metabolic abnormalities like central obesity, insulin resistance, glucose intolerance, dyslipidemia and hypertension. Each of these features is known to augment the risk of developing diabetes mellitus and cardiovascular disease. In view of the increased prevalence of vascular risk factors in patients with chronic inflammatory arthritis, the study was conducted to assess the prevalence of Metabolic Syndrome in patients with Rheumatoid Arthritis.[3]

METHODS AND MATERIALS

The present study is a cross-sectional observational study done in Assam Medical College and Hospital, Dibrugarh. The study was carried over a period of 1 year from 1st May 2011 to 30th April 2012. We have included all the patient of rheumatoid arthritis attending rheumatology OPD or admitted in the ward fulfilling the ACR/EULAR 2010 criteria and equal number of otherwise asymptomatic age and sex matched controls from the general population.

A total of 144 patients and healthy controls were enrolled in the study and were randomised into test and control groups. All patients of Rheumatoid Arthritis more than 12 yrs. of age, diagnosed by 2010 Rheumatoid Arthritis Classification Criteria An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative who attended Rheumatology clinics or admitted in Medicine Department of Assam Medical College and Hospital, Dibrugarh were included in the study. During the predetermined study period, 72 patients of Rheumatoid Arthritis were recruited for the study. Another 72 age and sex matched controls (1:1) were also included in the study. The statistical analysis was carried out using Statistical Package of Social Science (SSPS Inc., Chicago, IL, version 16.0 for window). All quantitative variables were estimated using measures of central location (Mean) and measures of dispersion (Standard deviation).

Categorical variables were compared by Chi Square test. Unpaired Student 't' test and ANOVA was applied for calculation of significance in difference of means. Pearson correlation was also calculated as appropriate. All statistical tests were two sided and performed at a significance level of α=0.05.

RESULTS

The present study was conducted among 72 cases of Rheumatoid Arthritis who attended Rheumatology OPD or admitted in Dept. of Medicine of Assam Medical College and 72 age and sex matched comparable controls. Both the case and control groups were screened for presence of central obesity, hypertension, hyperglycemia and dyslipidemia. Metabolic syndrome was diagnosed in both study groups as per NCEP ATP III guidelines. The results are as follows:

Sex	Cases	Percentage
Female	66	91.6
Male	6	8.4
Total	**72**	**100**
Table 1: Sex Distribution of the Study		

The study population is comprised of 91.6% (n=66) female and 8.4% (n=6) male. The male:female in the study population is 1:11.

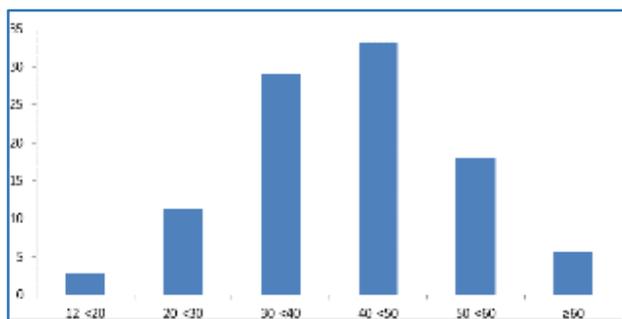| Age Group	No. of Cases	Percentage
12-<20	2	2.8
20-<30	8	11.2
30-<40	21	29.1
40-<50	24	33.3
50-<60	13	18.0
≥60	4	5.6
Total	**72**	**100%**
Table 2: Age Distribution in the Cases		

Fig. 1: Age Distribution in the Cases

The study shows that majority of the participant group (33.33%) belonged to age group 40-<50 yrs. The mean age of the study population was 41.5 yrs.

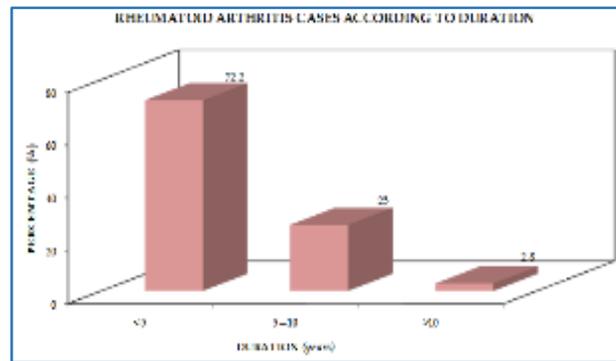| Duration (Years)	Cases	Percentage
< 5	52	72.2
5—10	18	25.0
>10	2	2.8
TOTAL	**72**	**100%**
Table 3: Rheumatoid Arthritis Cases According To Duration		

Fig. 2: Rheumatoid Arthritis Cases According to Duration

The above table shows most of the patient (72.2%) in the study group has disease duration of less than 5 yrs. Out of which only 4 (5.6%) have early Rheumatoid Arthritis, i.e. ≤6 months in duration. The mean duration is 3.8 yrs.

CRITERIA	CASES	CONTROL	P VALUE
SIGNIFICANT FAMILY HISTORY	15 (20.8%)	11 (15.2%)	0.383
BODY WT (KG)	55.4 ± 8.4	56.3±6.3	0.422
BMI			
<18.4	2 (2.8%)	0 (0%)	0.15
18.4-22.9	27 (37.5%)	23 (31.9%)	0.48
23-24.9	20 (27.8%)	35 (48.6%)	0.01
≥25	23 (31.9%)	14 (19.4%)	0.08
WAIST	51 ±14.6	52.9±14.6	0.436
SYSTOLIC BP ≥130	142±13.8	134.4±5	<0.000
DIASTOLIC BP≥85	92.9±5.7	89±4.6	<0.000
HIGH DENSITY LIPOPROTEIN	47±14.6	37.8±19	0.001
TRIGLYCERIDES	111±40	99.9±39.7	0.967
Table 4: Comparison of History, Clinical, Laboratory Characteristics of Cases and Controls			

(Results are expressed in mean±standard deviation and in percentage as applicable). The history, clinical and laboratory characteristics of Rheumatoid Arthritis patients and controls are demonstrated in the above table. Patients with Rheumatoid Arthritis has surprisingly more HDL levels than the control group. The BMI when compared between two groups heavy weight (Prevention and Management of Obesity and Metabolic Syndrome in India; October 2008) subjects are found to be significantly high in the control group. There is significant difference seen in relation to systolic blood pressure, diastolic blood pressure in between the cases and controls.

NCEP CRITERIA	CASES (n=72)	CONTROL (n=72)	P VALUE
WAIST CIRCUMFERENCE	6 (8.3%)	1 (1.3%)	0.05
HYPERTENSION	41 (56.9)	26 (36.1%)	0.01
HYPERGLYCEMIA	18 (25%)	17 (23.6%)	0.87
LOW HDL	43 (59.7%)	59 (81.9%)	0.006
HYPERTRYGLYCERIDEMIA	4 (5.5%)	9 (11.1%)	0.09
METABOLIC SYNDROME	12 (16.7%)	5 (6.9%)	0.07
Table 5: Frequencies of Metabolic Syndrome and Its Criteria in Cases and Control			

Based on the NCP ATP III criteria 12(16.7%) patients and 5 (6.9%) controls has metabolic syndrome (p=0.07), Rheumatoid Arthritis patients and control groups are found to be different in hypertension (p=0.003) and low HDL (p=0.006) significantly, as hypertension was more common in cases whereas low HDL in controls.

DETERMINANTS	WITH METABOLIC SYNDROME	WITHOUT METABOLIC SYNDROME (n=60)	P VALUE
AGE	39.25±12.5	41.9±11	0.458
DURATION	3.6±3	3.8±3.9	0.730
DAS28	4.2±0.83	4.3±1.4	0.602
ESR	55.83±19	54.9±22.1	0.891
RF POSITIVE	8(66%)	35(58.3%)	0.589
DURATION OF STEROID	2.5±2.3	2.7±2.7	0.811
Table 6: Determinants of Rheumatoid Arthritis among Patients with Metabolic Syndrome and Without Metabolic Syndrome			

There is no significant difference of the determinants of the disease process i.e. Rheumatoid arthritis in between the cases with metabolic syndrome and without metabolic syndrome.

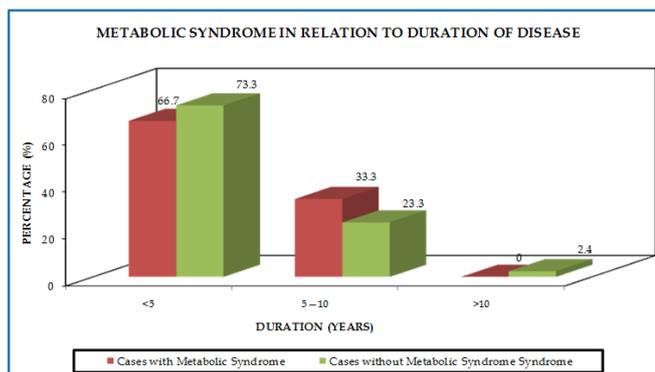| DURATION (YRS)	CASES WITH METABOLIC SYNDROME	CASES WITHOUT METABOLIC SYNDROME	TOTAL
<5	8 (66.7%)	44 (73.3%)	52
5—10	4 (33.3%)	14 (23.3%)	18
>10	0	2 (3.4%)	2
TOTAL	12	60	72
Table 7: Metabolic Syndrome in Relation to Duration of Disease			

Fig. 3: Metabolic Syndrome in Relation to Duration of Disease

From the above table it is found that the metabolic syndrome is more common among the Rheumatoid arthritis cases with disease duration <5yrs. However, there was no correlation found between metabolic syndrome and the duration of the disease (p=0.65).

DISCUSSION
The present study was done among the cases of Rheumatoid arthritis and their age, sex matched controls to find out the prevalence of metabolic syndrome in both groups and significant difference between them.

The interest in identifying metabolic syndrome in patients with Rheumatoid Arthritis has emerged recently, justified by the need to better understand the determinant factors of Cardiovascular Disease (CVD) in these patients.

In the present study, the sex ratio was 1:11 which is much higher than the normal (1:3), as it was not a population based study so this cannot be depicted as real sex ratio of Rheumatoid Arthritis. The age of maximum incidence in the study population was in between 40-<50 years, which is similar to the study by Alamanos Y et al. 2006.[4] where disease incidence appeared to be greatest for women between 40 and 50 years of age and for men somewhat late. The minimum and maximum duration of Rheumatoid Arthritis in the present study was around 2 months and maximum was 25 years. Maximum number of the patient in the present study had disease duration less than 5 yrs. and mean duration was 3.8 years.

The prevalence of metabolic syndrome in Rheumatoid Arthritis patients is 16.7% compared to 6.9% patients in the control groups as per NCEP-ATPIII guidelines, though the prevalence of metabolic syndrome in Rheumatoid Arthritis cases is two folds higher than the age and sex matched controls still it is not significant. This finding is in accordance with the results observed by Dessein et al. 2006.[5] La Montagna et al. 2007.[6] Marjenahkarimi et al. 2011.[7] In the present study one of the prominent finding was higher and significant prevalence of hypertension in Rheumatoid Arthritis patients as compared to controls, which was also observed by Antonio Naranjo et al. 2008 (QUEST RA Study).[8] and Mehmet Karakoca et al. 2012.[9] The prevalence of hypertension in the present study is 56.9%, which is very close to the observations made by Antonio Naranjo et al. 2008 (QUEST RA study).[8] where the prevalence for CV risk factors was 62.9% for hypertension.

Another striking observation made during the study is low HDL in controls (81.9) as compared to patients (61.1), which is recently supported by McMahon and colleagues.[10] They showed that pro-inflammatory HDL was detected more often in RA patients (n = 48) than in control subjects, (n = 72), i.e. 20% versus 4% respectively.[11] The most common form of dyslipidaemia in Rheumatoid Arthritis patients is the reduction of total HDL, LDL cholesterol and triglycerides. The use of corticosteroid independent of doses increases HDL levels. Endogenous glucocorticoid hormones regulate HDL concentration in the plasma by increasing synthesis and secretion of HDL by liver, therefore high level of exogenous glucocorticoid hormone, similar to those used in Rheumatoid Arthritis patients, probably accelerate this pathway. Thus in Rheumatoid Arthritis, the levels of HDL which were previously reduced increases, as a result a less atherogenic profile is induced may be due to the indirect effect of glucocorticoids.

The case with metabolic syndrome and without metabolic syndrome was compared and no significant difference is seen; however, a significant observation that was made during the study was, components of metabolic syndrome were manifested much earlier among the cases (39.25 years) as compared to controls (46.5 years). Around 7 years early, which is in consistent to certain extent with the findings of QUEST-RA.[8] study where around one decade early there was appearance of cardiovascular risk factors. The body weight of the controls with metabolic syndrome were significantly higher than the cases with metabolic syndrome,

thus the occurrence of metabolic syndrome in controls can be attributed to adipose tissue.

While studying the relation between disease duration and prevalence of metabolic syndrome in Rheumatoid arthritis patients, there was no significant difference was seen when compared with cases without metabolic syndrome, which was in accordance with Mehmet Karakoc, et al. 2012.[9] This may be attributed to the fact that 72.2% of the present study population has a disease duration less than 5 yrs.

No significant difference were found regarding DAS28 index or other disease related factors and the presence or absence of metabolic syndrome in the present study even after taking disease activity as categorical variable, which is similar to Marjaneh Karimi et al. 2011 observation.[7] More ever relation between DAS 28 and prevalence of metabolic syndrome is conflicting. Study done by Mehmet Karakoca et al.[9] found that the prevalence of metabolic syndrome is higher in low disease activity group, whereas according to the study done by SA Karvounaris et al.[11] it is more common in high disease activity. It may be due to the masking of the inflammatory process by the ongoing drug treatment.

CONCLUSION
The present study was an initiative to know the complex interplay between Rheumatoid Arthritis and metabolic syndrome in this part of India where a pilot study is still lacking. The study observation shows that though there is no significant prevalence of metabolic syndrome among the cases of Rheumatoid Arthritis comparison to age and sex matched controls, but there is definite earlier presentation of metabolic syndrome among the cases, which has some implications as rheumatoid arthritis has less life expectancy than general population and the most common cause of death is cardiovascular diseases.

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