Prevalence of Metabolic Syndrome in Rheumatoid Arthritis Patients: A Case Control Study from a Tertiary Care Centre in North India

GSRSNK Naidu¹, Nilesh Bhilave², Kusum Sharma³, Indu Verma⁴, Aman Sharma⁵*

Abstract

**Background:** Cardiovascular disease (CVD) is the leading cause of mortality in patients with rheumatoid arthritis (RA). Along with traditional cardiovascular risk factors and systemic inflammation, metabolic syndrome (MetS) contributes to CVD and increased mortality in patients with RA. In this study we determine the prevalence of MetS in RA patients presenting to a tertiary care centre in north India.

**Methods:** This is a case control study involving 114 patients of RA with disease duration of ≥1 year and 114 healthy controls who are age and sex matched. Components of MetS were assessed in all the subjects and disease activity of RA was determined by DAS28-ESR. MetS was defined according to modified ATP-III criteria and consensus definition of metabolic syndrome for adult Asian Indians.

**Results:** Women constituted 81.6% in RA group and 80.5% in control group. Mean age of subjects was 44.81±12.7 years in RA group and 43.27±12.6 years in control group. According to modified ATP-III criteria, 36 (31.6%) RA subjects and 17 (14.9%) controls had MetS (p=0.03). According to the consensus definition of metabolic syndrome for adult Asian Indians, 40 (35.1%) RA subjects and 18 (15.8%) controls had MetS (p=0.01). There was no significant difference in disease activity between subjects of RA with or without MetS (p=0.276).

**Conclusion:** The prevalence of MetS was higher in RA subjects compared to controls. There is no association of MetS with disease activity in our cohort. Larger studies are needed to determine the relation between MetS and disease activity.

Introduction

Rheumatoid arthritis (RA) is a chronic, symmetric, inflammatory arthritis of unknown etiology. Extra articular manifestations are seen in up to 50% of patients with RA.¹ Extra articular manifestations are in the form of rheumatoid nodules, skin ulcers, scleritis, episcleritis, neuropathy, interstitial lung disease, pleural involvement, pericarditis, myocarditis, coronary artery disease (CAD), sicca symptoms, glomerulonephritis, vasculitis and atherosclerotic disease. Cardiovascular disease (CVD) is a major cause of mortality in RA patients and about 50% of mortality in RA could be attributed to cardiovascular disease.² Apart from the traditional risk factors for CVD, systemic inflammation and metabolic syndrome (MetS) contribute to CVD risk and increased mortality in patients with RA.³

Metabolic syndrome (MetS) describes a constellation of atherosclerotic cardiovascular risk factors such as dyslipidemia, central obesity, insulin resistance, impaired glucose tolerance and hypertension.⁴ MetS is associated with approximately two fold increased risk for fatal cardiovascular disease (CVD) in men and nonfatal CVD in women in general population.⁵ Studies from India showed a high prevalence of MetS in general population, varying between 23.9% and 33.5%.⁶ ⁷ The estimated worldwide prevalence of MetS in RA was 30.65%.⁸ Two small studies from India, one from northeast India and the other from south India, showed the prevalence of MetS in RA to be 16.7% and 57.4% respectively.⁹ ¹⁰

The present study was done to determine the prevalence of MetS in patients with RA from north India and to explore the relationship between MetS and disease activity.

Materials and Methods

**Subjects**

This is a prospective case control study conducted in a tertiary care centre in north India. The cases included 114 patients diagnosed to have RA (according to 1987 ACR classification criteria for RA) and with a disease duration of more than 1 year.¹¹ The controls group included 114 healthy controls that were matched for sex and age (±5 years). Pregnant females, subjects not consenting to participate in the study were excluded from the study. This study was approved by the institute ethics committee and a written informed consent was obtained from all subjects before enrolling in the study.

**Patient assessment**

Patient assessment included a structured interview, physical examination, laboratory tests and review of medical records. Details regarding disease duration, extra-articular manifestations, co-morbid conditions (hypertension and diabetes mellitus) and treatment details were noted. Height (cm), weight (kg) and waist circumference (cm) were measured and body mass index was calculated. Blood pressure was determined as the average of two measurements obtained 5 min apart.

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after subjects had rested for at least 10 min. Subjects were considered hypertensive if they were taking antihypertensive agents or if they had a systolic blood pressure of more than 130mmHg or a diastolic pressure of more than 85mmHg. In patients, disease activity was measured using the Disease Activity Score-28 ESR (DAS28-ESR). DAS28-ESR of less than 2.6 was considered remission, score between 2.6 and 3.2 was considered low activity, score more than 3.2 and less than 5.1 was considered moderate activity and score more than 5.1 was considered high disease activity.

**Laboratory tests**

Blood was collected after an overnight fast (8-12 hours) for the measurement of a complete blood count, urea, creatinine, liver enzymes, serum bilirubin, serum total proteins, serum albumin, total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides and low-density lipoprotein (LDL) cholesterol. In patients with RA, CRP and ESR (by Westergren’s method) were measured at the umbilical level as MetS. Waist circumference was measured at the umbilical level according to the WHO guidelines, with the person breathing silently.

**Statistical analysis**

Data was analyzed using the statistical package SPSS for MS-windows (version 10, SPSS Inc, Chicago, IL). Continuous variables were expressed as mean and standard deviation, while categorical variables were expressed as percentages. Chi square test was used for comparison of categorical variables and Mann-Whitney U test or student’s t test were used for continuous variables. P value of <0.05 was considered as significant.

**Results**

**Demographic characteristics**

Out of 114 patients with rheumatoid arthritis, 93 (81.6%) were women and 21 (18.4%) were men, with a mean (±SD) age of 44.81±12.7 years. Among the controls, 92 (80.7%) were women and 22 (19.3%) were men, with a mean (±SD) age of 43.27±12.6 years. Age (p=0.36) and sex (p=0.866) were matched in both the groups. Rheumatoid factor was positive in 89 (78.1%) patients while CRP was elevated in 96 (86%) patients. Deformities were noted in 37 (32.5%) patients with RA while rheumatoid nodules were seen in only 7 (6.1%) patients with RA.

Compared to controls, patients with RA had significantly more BMI (25.5±5.2 kg/m² vs 24.2±3.5 kg/m², p=0.005) and waist circumference (92.1±20.1 cm vs 81.2±9.9 cm, p=0.001). The mean fasting blood glucose was 95.3±26.7 mg/dl in RA patients and 97.8±21.6 mg/dl in controls (p=0.079). In RA patients, mean serum triglycerides (152.2±67.2 mg/dl vs 135±50 mg/dl, p=0.039) and HDL cholesterol (47.4±11 mg/dl vs 41±12.6 mg/dl, p<0.001) were significantly more than the controls. Both the mean systolic blood pressure (124.9±16.7 vs 119.4±10.7 mmHg, p=0.018) and mean diastolic blood pressure (80.5±9.9 vs 75.3±7.4 mmHg, p<0.001) were significantly more in RA patients compared to controls. Baseline characteristics of RA patients and controls are shown in Table 2.

**Prevalence of metabolic syndrome**

According to modified ATP-III criteria, 36 (31.6%) RA subjects and 17 (14.9%) controls had MetS. The prevalence of MetS between the two groups was statistically significant (p=0.03). According to the consensus definition of metabolic syndrome for adult Asian Indian criteria, 40 (35.1%) patients with RA and 18 (15.8%) controls had MetS and the difference was statistically significant (p=0.01). The details of criteria fulfilled by patients of MetS are shown in Table 3.

**Correlation of disease activity and metabolic syndrome**

Among the 36 RA patients with MetS according to modified ATP-III criteria, 25 patients had very high disease activity (DAS28-ESR>5.1), 6 patients had moderate activity (DAS28-ESR 3.2-5.1) and 5 patients had low disease activity (DAS28-ESR 2.6-3.2). There was no significant difference in disease activity between patients of RA with or without MetS (p=0.276). Out of 40 patients with RA and MetS according to consensus definition of metabolic syndrome for adult Asian Indians criteria, 29 patients had very high disease activity, 6 patients had moderate activity and 5 patients had low disease activity. None of the patients with MetS were in remission (DAS28-ESR<2.6) at the time of assessment. There was no significant difference in disease activity

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**Table 1: Definitions of metabolic syndrome used in the study**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NCEP ATP-III definition modified for asians</th>
<th>Consensus definition of MetS for adult Asian Indians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference</td>
<td>≥80 cm for men ≥80 cm for women</td>
<td>≥80 cm for men ≥80 cm for women</td>
</tr>
<tr>
<td>Serum triglycerides</td>
<td>≥150 mg/dl</td>
<td>≥150 mg/dl</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>&lt;40 mg/dl for men &lt;50 mg/dl for women</td>
<td>&lt;40 mg/dl for men &lt;50 mg/dl for women</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>≥110 mg/dl</td>
<td>≥100 mg/dl</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>≥130 mmHg systolic pressure ≥85 mmHg diastolic pressure</td>
<td>≥130 mmHg systolic pressure ≥85 mmHg diastolic pressure</td>
</tr>
</tbody>
</table>

**Table 2: Baseline characteristics of RA patients and controls**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases (n=114)</th>
<th>Controls (n=114)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD) years</td>
<td>44.81±12.7</td>
<td>43.27±12.6</td>
<td>0.361</td>
</tr>
<tr>
<td>Female: Male</td>
<td>93:21</td>
<td>92:22</td>
<td>0.866</td>
</tr>
<tr>
<td>Deformities</td>
<td>32.5% (n=37)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rheumatoid nodules</td>
<td>6.1% (n=7)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Skin rash</td>
<td>2.6% (n=3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sicca symptoms</td>
<td>5.3% (n=6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RF positivity</td>
<td>78.1% (n=89)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>High CRP</td>
<td>86% (n=96)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.9±7.3</td>
<td>156.8±7.8</td>
<td>0.895</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>60.8±12.2</td>
<td>59.1±9.9</td>
<td>0.244</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>25.5±5.2</td>
<td>24.2±3.5</td>
<td>0.005</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>92.1±20.1</td>
<td>81.2±9.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FBG (mg/dl)</td>
<td>95.3±26.7</td>
<td>97.8±21.6</td>
<td>0.079</td>
</tr>
<tr>
<td>Sr. triglycerides (mg/dl)</td>
<td>152.2±67.2</td>
<td>135±50</td>
<td>0.039</td>
</tr>
<tr>
<td>Cholesterol LDL (mg/dl)</td>
<td>98.7±29.7</td>
<td>100.9±27.7</td>
<td>0.320</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>47.4±11</td>
<td>41±12.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total (mg/dl)</td>
<td>168.2±39.2</td>
<td>164.8±39.2</td>
<td>0.526</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>124.9±16.7</td>
<td>119.4±10.7</td>
<td>0.018</td>
</tr>
<tr>
<td>DBP (mg/Hg)</td>
<td>80.5±9.9</td>
<td>75.3±7.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI: Body Mass Index; CRP: C-Reactive Protein; HDL: High Density Lipoproteins; LDL: Low Density Lipoproteins; RF: Rheumatoid Factor.</td>
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</tbody>
</table>
Indian criteria for MetS, which takes fasting blood glucose of >100 mg/dl as the cutoff instead of >110 mg/dl in the modified ATP-III criteria. 12,13 In a meta-analysis by Hallajadze et al., the worldwide pooled prevalence of MetS in RA was 31.55% according to the NCEP ATP-III criteria, which is similar to that seen in our cohort of patients. 14

MacMohan et al. have shown previously that patients of RA had higher levels of pro-inflammatory HDL levels compared to the controls. 14 Similar results were also noted in the Indian patients of RA by Dihingia et al. 9 Even though we have not measured pro-inflammatory HDL levels in our cohort, the mean total HDL cholesterol levels were higher in RA patients compared to controls (47.4±11 mg/dl vs 41±12.6 mg/dl, p=0.001). Pro-inflammatory HDLs enhance the inflammatory responses by their inability to prevent oxidation of LDL in vessel wall which leads to recruitment of monocytes in to the vessel wall subendothelial space. 15

We did not find any significant difference in the disease activity, as measured by DAS28-ESR, among RA patients with or without MetS. Even, Dihingia et al. from India and Rostom et al. from Morocco have shown no association between presence of MetS and disease activity in RA patients. 16 However, Tantayakom et al. from Thailand have shown that low cumulative disease activity significantly reduced the risk of having MetS. 17 Karvounaris et al. from Greece also showed that prevalence of MetS was higher in patients with high disease activity. 18

The major limitation of our study is that it is a case control study involving a less number of patients and controls. A larger cohort of RA patients needs to be prospectively followed up to determine the incidence and the cumulative prevalence of MetS in RA patients and to know their long term cardiovascular outcomes.

In conclusion, prevalence of MetS among RA patients from north India is higher than that seen in controls. However, there is no association of MetS with disease activity in our cohort. More studies with large number of patients of RA needs to be conducted to determine the association between MetS and disease activity scores.

References


