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Original research article

TO STUDY METABOLIC SYNDROME AND RHEUMATOID ARTHRITIS INTERRELATIONSHIP: CASE CONTROL STUDY

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Abstract

Background and Objectives: Rheumatoid Arthritis is closely linked to Metabolic Syndrome, which greatly enhances the risk of cardiovascular problems and consequently, morbidity and mortality. Managing Metabolic Syndrome reduces the occurrence of cardiovascular events and fatalities. This study assesses the frequency of metabolic syndrome in young patients diagnosed with Rheumatoid Arthritis.

Material and Methods: This case-control study was carried out in two different groups. The study was conducted at the Department of General Medicine, NRI Medical College and Hospital, Mangalagiri, Andhra Pradesh, India. This study was conducted from October 2022 to November 2023. Total 100 participants are used in this study and were selected from the outpatient departments.

Results: This study aimed to assess the impact of metabolic syndrome on the severity of rheumatoid arthritis, as well as the prevalence of metabolic syndrome in individuals with RA compared to those without RA. The frequencies of various components of Metabolic Syndrome were also assessed in Rheumatoid Arthritis. We also endeavoured to investigate the risk associated with illness biomarkers and disease severity in the development of Metabolic Syndrome. The study also evaluated the link between specific components of Metabolic Syndrome and disease biomarkers of Rheumatoid Arthritis. The incidence of Metabolic Syndrome in patients of Rheumatoid Arthritis was determined to be 41.6% in the population of northern India.

Conclusion: The results of this study demonstrate that TNF-α speeds up the development of MetS by increasing insulin resistance. MetS worsens RA symptoms. More research is required to ascertain the mechanism by which insulin resistance and metabolic syndrome are caused by high TNF-α levels and other markers.

Keywords: Interrelationship, metabolic syndrome, rheumatoid arthritis

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Introduction

Rheumatoid Arthritis (RA) is a widespread condition marked by severe damage and distortion of the joints, often accompanied by additional effects on important organs outside of the joints. Rheumatoid arthritis is linked to a higher likelihood of developing atherosclerotic vascular disease, which is responsible for around 50% of all deaths in this group, including heart attacks, strokes and heart failure. Patients with RA exhibit an increased prevalence of many cardiovascular risk factors [1, 2].

Furthermore, the presence of chronic inflammation, the utilisation of pharmaceutical interventions in treatment protocols, and a sedentary way of life may significantly contribute to the heightened susceptibility of cardiovascular disease in individuals with rheumatoid arthritis [3]. Epidemiological statistics indicate that rheumatoid arthritis is a distinct risk factor for atherosclerotic vascular illnesses, even while the higher rates cannot be attributed to established risk factors, the use of steroids or non-steroidal anti-inflammatory medicines, or shared genetic characteristics. The likelihood of developing cardiovascular disease is increased by both the inflammatory process and the severity of the condition. The fundamental components of metabolic syndromes, such as dyslipidaemia, high density lipoproteins, accelerated blood pressure, and impaired glucose homeostasis, have garnered greater attention as the central manifestations of the syndrome [4-6].

Rheumatoid Arthritis is an inflammatory arthritis that progresses quickly and can cause substantial disability if not managed. Rheumatoid arthritis exhibits a robust correlation with metabolic syndrome. Elevated levels of triglycerides, cholesterol, and LDL, along with low levels of HDL, as well as elevated blood pressure and blood sugar, greatly enhance the risk of cardiovascular problems, leading to increased morbidity and death. Managing metabolic syndrome reduces cardiovascular mortality and exacerbations of illness in people with rheumatoid arthritis [7-9].

The objective of this study was to assess the association between metabolic syndrome and the severity of rheumatoid arthritis, and therefore, the clinical status and overall health of individuals with RA. We conducted a study to determine if the coexistence of Metabolic Syndrome and Rheumatoid Arthritis exacerbates the severity of the disease, as shown by the blood levels of RA biomarkers such as TNF-α, anti-CCP, RF, CRP, and ESR. Additionally, we investigated the prevalence of MetS in the RA population in North India.

Material and Methods

This case-control study was carried out in two different groups. The study was conducted at the Department of General Medicine, NRI Medical College and Hospital, Mangalagiri, Andhra Pradesh, India. This study was conducted from October 2022 to November 2023. Total 100 participants are used in this study and were selected from the outpatient departments.

Statistical analysis

The gathered data was subjected to statistical analysis using the SPSS-16 software. The categorical measurements were provided as percentages and frequencies, whereas the continuous measurements were presented as mean ± standard deviation (SD). The chi-square test was used to compare categorical measurements between two groups,

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whereas the unpaired t-test was used to examine continuous measurements.

Results

The occurrence of metabolic syndrome (MetS) and its distinct components in instances of rheumatoid arthritis and control subjects. The prevalence of MetS in cases of RA was 41.6%. The levels of each individual component of Metabolic Syndrome were considerably elevated in the cases group compared to the controls group. However, the prevalence of hypertension and elevated triglyceride levels were the most frequent and noteworthy. While glycated haemoglobin is not a constituent of MetS, it was found to be more commonly present at lower levels in patients with RA. The study compares the demographic and routine biochemical markers of individuals with rheumatoid arthritis who have or do not have metabolic syndrome.

Table 1: Mets prevalence and components in RA patients and controls

	Group I (60)	%	Group II (40)	%
MetS	10	16.66	6	15.00
Central obesity	12	20.00	7	17.50
Hypertension	18	30.00	8	20.00
High triglycerides	5	08.33	7	17.50
Low HDL-C	5	08.33	2	05.00
Fasting Hyperglycemia	6	10.00	4	10.00
HbA1c	4	06.66	6	15.00

Table 2 shows the demographic and routine biochemical data of RA cases with and without MetS, compared. When comparing RA cases with and without MetS, the mean age is much older for the former. Cases of RA presenting with MetS also had a considerably longer disease duration than RA cases without MetS. Cases with RA with MetS were reported to have significantly lower HDL-C levels and significantly higher triglycerides and systolic and diastolic blood pressures.

Table 2: Standard biochemical data

Sr. No.	Parameters	Group I RA (n=60)	Group II RA + MetS (n=40)
1.	Age (years)	44.46 ± 11.45	54.44 ± 9.88
2.	Disease duration	5.09 ± 3.41	7.92 ± 2.66
3.	Waist circumference (cm)	92.12 ± 18.03	98.23± 19.22
4.	Fasting blood glucose (mg/dl)	99.20 ± 18.33	102.55 ± 22.45
5.	Total cholesterol (mg/dl)	197.61±22.55	205.22±32.19
6.	Triglycerides(mg/dl)	143.12±38.32	183.55±82.97
7.	LDL-C (mg/dl)	107.46±32.78	120.44±39.55
8.	HDL-C(mg/dl)	51.24±7.82	38.57±8.66

The risk linked with several parameters in the development of Metabolic Syndrome was depicted in Table 3.

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Table 3: Potential hazards linked to RA biomarkers in the progression of MetS

Sr. No.	Parameters	Odds ratio	Confidence Interval
1.	Disease duration	2.857	1.033-2.289
2.	EULAR score	1.065	0.784-2.367
3.	DAS-28	6.958	2.257-32.354
4.	CRP (mg/L)	2.324	2.058-2.254
5.	Anti-CCP (u/ml)	2.436	2.023-3.852

Discussion

This study aimed to assess the impact of metabolic syndrome on the severity of rheumatoid arthritis, as well as the prevalence of metabolic syndrome in individuals with RA compared to those without RA. The frequencies of various components of Metabolic Syndrome were also assessed in Rheumatoid Arthritis [10]. We also endeavoured to investigate the risk associated with illness biomarkers and disease severity in the development of Metabolic Syndrome. The study also evaluated the link between specific components of Metabolic Syndrome and disease biomarkers of Rheumatoid Arthritis. The incidence of Metabolic Syndrome in patients of Rheumatoid Arthritis was determined to be 41.6% in the population of northern India. We have taken into account the revised ATP-III Criteria of Metabolic Syndrome specifically for adult Asian Indians. In this criteria, the recognised threshold for fasting blood glucose is set at 100mg/dl instead of 110mg/dl. A study conducted in northern India has found that the prevalence of Metabolic Syndrome is marginally lower than 35.1% when using modified ATP-III criteria [11-13].

Nevertheless, the prevalence of rheumatoid arthritis in the south Indian population was found to be 57.4%, which is greater than what was observed in our cases. Our findings further validates the observation that the Indian population has a higher susceptibility to metabolic syndrome, as the global prevalence of MetS is considerably lower, at roughly 30.65% [14, 15].

Upon evaluating the frequency of several components of Metabolic Syndrome (MetS) in individuals with Rheumatoid Arthritis, it was found that elevated blood pressure exhibited the highest prevalence [16]. This aligns with the research carried out by Panoulas VF, Douglas KM *et al*. The presence of a greater proportion of metabolic syndrome (MetS) cases in individuals with rheumatoid arthritis who are over 55 years old and have had the disease for a longer period of time suggests the importance of the inflammatory burden in the development of metabolic abnormalities. Established cases of rheumatoid arthritis (RA) with metabolic syndrome had a higher prevalence of elevated triglyceride levels and decreased high-density lipoprotein cholesterol [17, 18].

The disease-specific, severity, and activity scores, as well as the levels of the inflammatory cytokine TNF-α, were compared in Table 3. TNF-α, due to its pro-inflammatory properties, induces insulin resistance, dyslipidaemia, and endothelial dysfunction, ultimately resulting in a chronic inflammatory state that leads to Metabolic Syndrome (MetS). Pro-inflammatory cytokines play a significant role in the formation of atherosclerosis, which in turn contributes to the development of cardiovascular disease [19, 20]. TNF-α also enhances the synthesis of acute phase reactants, specifically CRP; our findings further corroborate this notion. Greater levels of anti-CCP, together

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with elevated DAS-28 Score and EULAR score, are linked to joint deformity and the severity of the disease. Reports indicate that Infliximab and Methotrexate have a favourable effect on reducing anti-CCP levels in patients with rheumatoid arthritis (RA) and it has been discovered that TNFα is responsible for the production of anticitrullinated peptide antibodies [21, 22]. The association between various biomarkers of rheumatoid arthritis and the development of metabolic syndrome. The elevated odds ratio of TNF-α in the development of Metabolic Syndrome in Rheumatoid Arthritis sufferers is evident and easily understood. While previous research have found no link between DAS-28 and the development of MetS in instances of rheumatoid arthritis, our investigation has identified a substantial risk associated with DAS-28 [23-25].

The correlation analysis of disease biomarkers of rheumatoid arthritis with specific components of metabolic syndrome revealed a substantial positive association between the inflammatory cytokine TNF-α and fasting blood glucose and triglyceride levels. TNF-α stimulates the breakdown of fat in adipose tissue and also impacts the absorption of glucose in skeletal muscle. The exacerbation of insulin resistance is caused by the heightened liberation of free fatty acids from adipocytes. There was an inverse correlation between the anti-CCP and HDL-c. Citrullinated epitopes were detected in the atherosclerotic plaques that were specifically recognised by anti-CCP antibodies. Therefore, the presence of high anti-CCP levels combined with low HDL-c levels indicates an increased risk of cardiovascular disease in individuals with rheumatoid arthritis, regardless of the presence of metabolic syndrome [26-29].

Conclusion

This study illustrates that the pro-inflammatory cytokine TNF-α contributes to the development of Metabolic Syndrome (MetS) by exacerbating insulin resistance. An advantageous feedback loop is occurring between the development of rheumatoid arthritis (RA) and metabolic syndrome (MetS) via inflammatory cytokines and disease biomarkers. Rheumatoid arthritis (RA) with metabolic syndrome (MetS) is linked to heightened disease severity. A comprehensive investigation is necessary to determine the relationship between elevated levels of TNF-α and other illness biomarkers and the development of insulin resistance, which subsequently leads to metabolic syndrome.

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Conflict of Interest: None.

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