Assessment of Insulin Resistance and Metabolic Changes in Rheumatoid Arthritis: A Cross-Sectional Analysis

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ABSTRACT:

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with well-recognized systemic effects, including an increased risk of metabolic and cardiovascular complications. Insulin resistance (IR) is considered a central mechanism contributing to this risk; however, the reliability of surrogate markers such as the homeostatic model assessment of insulin resistance (HOMA-IR) remains uncertain in RA populations.

Methods: A cross-sectional study was conducted involving 180 participants, including 90 patients diagnosed with RA and 90 age-matched healthy individuals. Clinical characteristics such as body mass index (BMI) and disease activity assessed by the Disease Activity Score in 28 joints (DAS28) were recorded. Fasting blood samples were analyzed for glucose and insulin levels, and HOMA-IR was calculated. Statistical analyses included group comparisons and correlation assessments.

Results: Patients with RA demonstrated significantly higher BMI, fasting glucose, fasting insulin, and HOMA-IR levels compared to controls ($p < 0.001$ for all).

Conclusion: Although RA is associated with measurable metabolic disturbances, These findings confirm increased insulin resistance in RA patients as reflected by elevated HOMA-IR levels.

Keywords: AI-driven marketing; digital real estate; Bangalore; residential housing; market dynamics.

Introduction:

Rheumatoid arthritis (RA) is a long-standing autoimmune disorder characterized by persistent inflammation of synovial joints, frequently resulting in progressive joint damage and disability [1,2]. In addition to musculoskeletal involvement, RA is increasingly recognized as a systemic condition with multiple extra-articular manifestations that significantly influence morbidity and mortality [1].

One of the major concerns in RA is the elevated prevalence of cardiovascular and metabolic disorders compared to the general population [3,4]. This increased risk, estimated to be up to twofold higher, is largely attributed to chronic systemic inflammation and its downstream metabolic consequences [3,5]. Importantly, this excess risk cannot be fully explained by conventional factors such as smoking or hypertension, indicating the contribution of disease-specific mechanisms [5,6].

Persistent inflammation promotes metabolic abnormalities, including altered lipid profiles and impaired glucose metabolism, which are central features of metabolic syndrome [2,6]. Among these, insulin resistance plays a pivotal role in linking inflammatory activity with cardiometabolic outcomes.

Pro-inflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 are known to interfere with insulin signaling pathways, thereby reducing glucose uptake in peripheral tissues [4,7]. As a result, assessing insulin resistance has become an important component in evaluating metabolic health in RA patients.

The homeostatic model assessment of insulin resistance (HOMA-IR) is widely used in clinical research due to its simplicity and feasibility when compared to gold-standard techniques like the hyperinsulinemic-euglycemic clamp [9,10]. However, existing studies have reported inconsistent findings regarding its utility in RA populations. While some demonstrate a clear association between inflammation and insulin resistance, others suggest that factors such as adiposity may play a more dominant role [10,12].

Given these discrepancies, further investigation is required to clarify the metabolic profile of RA patients. The present study aims to evaluate insulin resistance using HOMA-IR and explore its relationship with disease activity and metabolic variables. This study also contributes to the ongoing discussion regarding the clinical reliability of HOMA-IR in inflammatory conditions.

Methodology:

Study Design and Setting

This cross-sectional study was carried out at IMS and SUM Hospital, Bhubaneswar, India, between January 2024 and March 2025. Ethical clearance was obtained from the institutional review board, and informed consent was obtained from all participants prior to enrollment.

Study Population

A total of 180 individuals were included in the study, consisting of 90 patients diagnosed with RA and 90 healthy controls matched for age.

Inclusion criteria for RA patients were:

- Age ≥18 years
- Diagnosis based on 2010 ACR/EULAR criteria
- Disease duration ≥6 months

Exclusion criteria included:

- Known diabetes mellitus or metabolic disorders

- Use of medications affecting glucose metabolism

Healthy controls had no history of chronic illness or medication affecting insulin sensitivity.

Data Collection

Baseline demographic data, including age, sex, and BMI, were recorded for all participants. For RA patients, disease-specific parameters such as disease duration and DAS28 score were also documented. Medication history was obtained where relevant.

Biochemical Analysis

Fasting blood samples were collected after an overnight fast. Plasma glucose levels were measured using the glucose oxidase method, and serum insulin levels were determined using ELISA.

Insulin resistance was calculated using the following formula:

$$HOMA\text{-}IR = \frac{(Fasting\ Insulin\ [\mu IU/mL] \times Fasting\ Glucose\ [mg/dL])}{405}$$

A HOMA-IR value greater than 2.5 was considered indicative of insulin resistance.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables were presented as frequencies and percentages.

Comparisons between groups were performed using independent sample t-tests and chi-square tests. Pearson's correlation coefficient was used to assess relationships between variables. Normality was evaluated using the Shapiro-Wilk test. A p-value less than 0.05 was considered statistically significant.

Results:

Table 1 compares baseline and biochemical parameters between the control and rheumatoid arthritis (RA) groups. Patients with rheumatoid arthritis demonstrated significantly higher BMI, fasting glucose, fasting insulin, and HOMA-IR levels compared to controls ($p < 0.001$ for all). Corticosteroid use was also significantly more frequent among RA patients ($p < 0.001$). No significant differences were observed in age or gender distribution between the groups.

Table 1: Comparison of parameters between study groups

Parameter	Control (n = 90)	RA (n = 90)	p-value
Age (years)	58.99 ± 17.65	59.59 ± 16.80	0.769
Gender (Male/Female)	45/45	45/45	1.000
BMI (kg/m²)	25.80 ± 3.35	29.35 ± 4.28	<0.001
Duration of Disease (months)	—	65.47 ± 34.75	—
DAS28 Score	—	2.90 ± 0.28	—
Corticosteroid Use (Yes/No)	0 / 90	29 / 61	<0.001
Fasting Glucose (mg/dL)	84.53 ± 8.63	100.02 ± 11.25	<0.001
Fasting Insulin (µIU/mL)	9.54 ± 2.88	19.60 ± 5.90	<0.001
HOMA-IR	**1.99 ± 0.60**	**4.84 ± 1.20**	**<0.001**

*Independent samples t-test; #Chi-square test; NA: Not applicable

Table 2 presents the univariate analysis of factors associated with RA. BMI, fasting glucose, and

fasting insulin were significant predictors ($p < 0.001$), showing positive associations. HOMA-IR demonstrated an increased odds ratio but did not reach statistical significance ($p = 0.100$). Age and gender were not significantly associated.

Table 2: Univariate Analysis

Parameter	B	OR	95% CI for OR	p-value
Age	0.002	1.002	0.988–1.016	0.768
Gender [Female vs Male]	-0.000	1.000	0.623–1.605	1.000
BMI	0.228	1.256	1.171–1.348	<0.001
Fasting Glucose (in mg/dL)	0.149	1.161	1.121–1.202	<0.001
Fasting Insulin (in μIU/mL)	0.615	1.850	1.584–2.161	<0.001
HOMA IR	1.064	2.898	0.815–10.310	0.100

Table 3 shows Pearson's correlation of HOMA-IR with clinical and biochemical variables. No statistically significant correlations were identified. Weak positive trends were observed for DAS28 score and fasting insulin, but they did not reach significance.

Table 3: Pearson's r Correlation

	Pearson's r	Lower 95% CI	Upper 95% CI	p-value
Age	-0.001	-0.106	0.102	0.983
Gender	-0.05	-0.155	0.051	0.335
BMI	0.049	-0.044	0.138	0.345
Duration of Disease	0.047	-0.055	0.148	0.361
DAS28 Score	0.092	-0.005	0.190	0.073
Use of Corticosteroids	0.023	-0.084	0.120	0.658
Fasting Glucose (in mg/dL)	0.072	-0.025	0.170	0.159
Fasting Insulin (in μIU/mL)	0.079	-0.025	0.178	0.122

Figure 1 illustrates the correlation between DAS28 score and HOMA-IR in the RA group. A weak positive relationship is observed; however, the correlation is not statistically significant, indicating no clear association between disease activity and insulin resistance in this cohort.

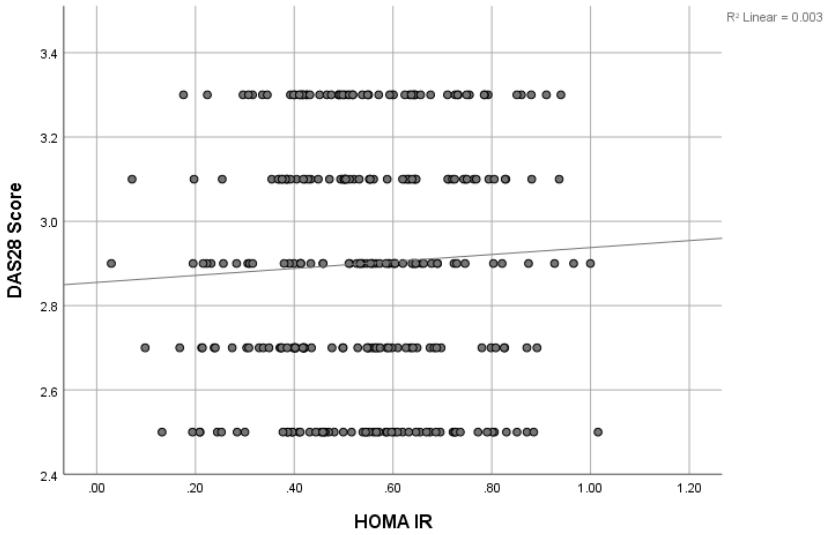

Figure 1: Correlation between DAS28 Score and HOMA-IR in RA Group

Discussion:

The findings of this study demonstrate that individuals with rheumatoid arthritis exhibit significant metabolic alterations, including elevated BMI, fasting glucose, fasting insulin, and HOMA-IR levels compared to healthy controls. The significantly higher HOMA-IR values observed in the RA group indicate increased insulin resistance, supporting the role of chronic inflammation in metabolic dysregulation. Previous research has reported conflicting results regarding insulin resistance in RA populations. While several studies have documented elevated HOMA-IR levels and a strong association with inflammatory markers [2,4], others have reported weaker or inconsistent relationships [10]. The findings of the present study are more aligned with the latter, indicating that the relationship between systemic inflammation and insulin resistance may not be uniform across different patient groups. Variations in demographic characteristics, treatment regimens, and disease duration may account for these discrepancies. From a mechanistic perspective, chronic inflammation is known to disrupt insulin signaling pathways through the action of cytokines such as tumor necrosis factor-alpha and interleukin-6 [4,7]. These mediators contribute to impaired glucose uptake in peripheral tissues. However, HOMA-IR primarily reflects hepatic insulin resistance and may not adequately represent peripheral insulin sensitivity. This limitation could explain why significant differences in glucose and insulin levels were observed without corresponding changes in HOMA-IR values. The results of the present study also suggest that traditional metabolic factors, particularly adiposity, may play a more dominant role in determining insulin sensitivity than inflammatory disease activity. This is supported by the univariate analysis, where BMI, fasting glucose, and insulin levels were significantly associated, whereas HOMA-IR and disease activity scores were not. These findings indicate that metabolic risk in RA may persist independently of disease activity and should be addressed as a separate clinical concern. From a clinical standpoint, these observations emphasize the importance of comprehensive metabolic evaluation in patients with RA. Reliance on a single surrogate marker such as HOMA-IR may lead to underestimation of insulin resistance and associated cardiovascular risk. Instead, a broader assessment incorporating multiple biochemical and clinical parameters may provide a more accurate representation of metabolic health in this population. The strengths of this study include the use of a well-defined study population and standardized biochemical measurements, which enhance the reliability of the findings. However, certain limitations should be acknowledged. The cross-sectional design restricts the ability to establish causal relationships. Additionally, the

sample size, although adequate for preliminary analysis, may limit the generalizability of the results. The absence of detailed information on lifestyle factors and body composition further limits the interpretation of metabolic risk. Furthermore, the use of HOMA-IR as a surrogate marker rather than a direct measure of insulin sensitivity represents an inherent methodological limitation. Overall, the findings of this study differ from some earlier reports that have shown significant elevations in HOMA-IR among patients with RA. These differences may reflect variability in study populations, treatment exposure, and methodological approaches. Further longitudinal studies using more sensitive techniques are required to better understand the relationship between inflammation and metabolic dysfunction in RA.

Conclusion:

In conclusion, patients with rheumatoid arthritis demonstrated significant metabolic alterations, including higher body mass index, fasting glucose, and fasting insulin levels compared to healthy controls, indicating an increased metabolic risk profile. However, HOMA-IR values were significantly higher in patients with rheumatoid arthritis compared to controls ($p < 0.001$), indicating increased insulin resistance. These findings highlight the complexity of metabolic dysfunction in rheumatoid arthritis and underscore the need for a comprehensive assessment beyond surrogate indices. Early identification and targeted management of metabolic abnormalities may play an important role in reducing long-term cardiovascular risk in these patients.

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