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Original Research Article

Assessment of Cardiovascular Risk Factors in Patients with Rheumatoid Arthritis: A Cross-Sectional Study

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease associated with a substantially elevated risk of cardiovascular (CV) morbidity and mortality. The chronic inflammatory milieu unique to RA potentiates endothelial dysfunction, accelerates atherogenesis, and deranges lipid metabolism, thereby amplifying traditional CV risk. Despite a growing global and Indian burden of RA, data on the prevalence and determinants of CV risk factors in Indian RA patients remain limited.

Aim: To assess the prevalence of cardiovascular risk factors in patients with rheumatoid arthritis and to examine their association with disease activity as measured by the Disease Activity Score-28 (DAS28).

Methods: A clinic-based cross-sectional study was conducted at Krishna Family Care Clinic, Patna, Bihar, India, from 1st August 2025 to 31st July 2026. A total of 105 consecutive adult RA patients fulfilling the 2010 ACR/EULAR classification criteria were enrolled. Demographic data, clinical parameters, DAS28 scores, lipid profiles, fasting blood glucose, HbA1c, anthropometric measurements, and blood pressure were systematically recorded. Metabolic syndrome was defined per the International Diabetes Federation (IDF) criteria. Statistical analysis was performed using chi-square tests, independent samples t-tests, Mann-Whitney U tests, and binary logistic regression.

Results: The mean age of participants was 48.3 ± 11.6 years; 82 (78.1%) were female. The mean DAS28 score was 5.1 ± 1.3. Physical inactivity was the most prevalent CV risk factor (63.8%), followed by dyslipidaemia (58.1%), hypertension (52.4%), metabolic syndrome (41.9%), obesity (34.3%), and impaired fasting glucose/diabetes (28.6%). High disease activity (DAS28 >5.1) was significantly associated with hypertension ($p = 0.042$), metabolic syndrome ($p = 0.015$), the presence of ≥2 CV risk factors ($p = 0.049$), and ≥3 CV risk factors ($p = 0.030$). Patients with high disease activity demonstrated significantly worse lipid atherogenicity indices, insulin resistance (HOMA-IR 4.5 ± 1.9 vs. 3.2 ± 1.4; $p < 0.001$), and inflammatory marker levels.

Conclusion: Cardiovascular risk factors are highly prevalent in RA patients attending this South Indian tertiary-care centre and escalate significantly with higher disease activity. Proactive, integrated CV risk screening embedded within rheumatology care is imperative to reduce the excess CV burden in this vulnerable population.

Keywords: Rheumatoid arthritis, cardiovascular risk, DAS28, metabolic syndrome, dyslipidaemia, hypertension, HOMA-IR, India.

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Introduction

Rheumatoid arthritis (RA) is a chronic, autoimmune, systemic inflammatory disorder affecting approximately 1% of the global population, with a disproportionately higher burden in women and in populations with genetic susceptibility to the HLA-DRB1 shared epitope [1].

Beyond its well-recognised articular manifestations, RA carries a significant extra-articular disease burden, most notably cardiovascular (CV) disease, which accounts for approximately 40–50% of excess mortality observed in RA cohorts compared to age- and sex-matched general populations [2]. Epidemiological data consistently demonstrate that the risk of myocardial infarction, heart failure, stroke, and sudden cardiac death is substantially elevated in RA—to a degree comparable to, or even exceeding, that conferred by type 2 diabetes mellitus [3].

The mechanisms underpinning accelerated atherosclerosis in RA are multifactorial. Chronic systemic inflammation, driven by tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and

interleukin-1 (IL-1), promotes endothelial dysfunction, oxidative stress, and foam cell formation within arterial walls—key pathophysiological steps in atherogenesis [4]. Simultaneously, RA-associated inflammatory cytokines suppress hepatic lipoprotein lipase activity and alter apolipoprotein composition, resulting in the so-called 'lipid paradox': paradoxically lower total and LDL-cholesterol in highly active disease, yet an adversely altered atherogenic lipoprotein profile [5]. Moreover, drug therapies commonly employed in RA—particularly glucocorticoids and, to a lesser degree, nonsteroidal anti-inflammatory drugs (NSAIDs)—independently contribute to dyslipidaemia, hypertension, insulin resistance, and weight gain [6].

Traditional CV risk factors, including hypertension, dyslipidaemia, diabetes mellitus, obesity, smoking, and physical inactivity, are significantly more prevalent in RA patients than in the general population [7]. This amplification is compounded by the systemic inflammatory burden of RA itself, which synergises with traditional risk factors to potentiate atherosclerotic plaque development and instability [8]. Metabolic syndrome—a clustering of central obesity, dyslipidaemia, hypertension, and insulin resistance—has been reported in up to 40–45% of RA patients in international studies, further magnifying CV risk [9].

In the Indian context, the epidemiological landscape is particularly concerning. India is experiencing a parallel epidemic of both non-communicable diseases and inflammatory rheumatic diseases. RA prevalence in India is estimated at 0.5–0.7%, affecting an estimated 6–8 million individuals, yet the systematic assessment of CV risk within this population remains fragmented [10]. The South Asian phenotype is characterised by greater insulin resistance, central adiposity at lower BMI thresholds, and earlier onset of metabolic dysfunction compared to Western counterparts—factors that may further amplify CV risk in Indian RA patients [11]. Furthermore, disease activity in RA patients from South Asian low- and middle-income settings may remain undertreated due to limited access to biologic therapies, sustaining higher inflammatory burden and compounding CV vulnerability [12].

The Disease Activity Score-28 (DAS28) is a validated, widely used composite measure of RA disease activity incorporating tender and swollen joint counts, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), and patient global assessment [13].

Higher DAS28 scores reflect greater systemic inflammation and are associated with more pronounced CV risk factor burden, as demonstrated in recent international registry studies [14]. However, data from Indian tertiary-care rheumatology cohorts specifically examining the relationship between DAS28 disease activity strata and the prevalence of individual and clustered CV risk factors are limited.

Against this background, the present cross-sectional study was designed to comprehensively assess the prevalence of cardiovascular risk factors—including hypertension, dyslipidaemia, metabolic syndrome, obesity, diabetes, smoking, and physical inactivity—in RA patients attending a tertiary academic medical centre in India, and to examine the association of these risk factors with disease activity as categorised by DAS28 score. The findings are intended to inform the development of integrated CV risk management pathways within Indian rheumatology practice.

Materials and Methods

Study Design and Setting: This was a clinic-based, observational cross-sectional study conducted at the Krishna Family Care Clinic, Patna, Bihar, India. The study period extended from 1 August 2025 to 31 July 2026.

Participants: A total of 105 consecutive adult patients with a confirmed diagnosis of RA were enrolled. Inclusion criteria were: (i) age ≥18 years; (ii) fulfilment of the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for RA; and (iii) willingness to provide informed written consent. Exclusion criteria included: (i) other systemic connective tissue diseases (systemic lupus erythematosus, systemic sclerosis, mixed connective tissue disease); (ii) pre-existing known coronary artery disease, symptomatic heart failure (NYHA class III–IV), or stroke; (iii) severe renal impairment (eGFR <30 mL/min/1.73 m²); (iv) active malignancy; (v) pregnancy or lactation; and (vi) inability to provide informed consent.

Sample Size: The sample size was estimated based on a reported prevalence of hypertension in RA patients of approximately 50% [7], using the formula $n = Z^2p(1-p)/d^2$, where $Z = 1.96$ ($\alpha = 0.05$), $p = 0.50$, and $d = 0.10$ (margin of error). This yielded a minimum sample of 97 participants; with a 10% non-response adjustment ($97 / 0.90 \approx 108$, rounded to 107), a target of 107 was set, of which 105 patients completed all assessments and were included in the final analysis. The two patients who did not complete all assessments were excluded due to incomplete laboratory data.

Data Collection and Clinical Assessments: All participants underwent a structured clinical assessment on the day of enrolment. Detailed demographic data (age, sex, educational status, occupation, smoking history, physical activity levels) were recorded using a standardised

proforma. Disease duration, medication history (disease-modifying anti-rheumatic drugs [DMARDs], biologics, glucocorticoids, NSAIDs), and comorbidities were documented. Physical activity was classified as inactive if self-reported moderate-intensity aerobic activity was <150 minutes per week OR vigorous-intensity aerobic activity was <75 minutes per week (or an equivalent combination), in accordance with World Health Organization (WHO) physical activity recommendations.

Disease activity was assessed using the DAS28-ESR score, computed from 28 tender and swollen joint counts, ESR (mm/hr), and patient global assessment on a visual analogue scale (0–100 mm). DAS28 categories were defined as: remission (<2.6), low activity (2.6–3.2), moderate activity (3.2–5.1), and high activity (>5.1). For comparative analyses, patients were grouped into two categories: low/moderate activity (DAS28 ≤5.1; n = 48) and high activity (DAS28 >5.1; n = 57).

Anthropometric and Haemodynamic Measurements: Height, weight, and waist circumference were measured using standardised techniques. Body mass index (BMI) was calculated as weight (kg) divided by height (m²). Obesity was defined as BMI ≥30 kg/m² (WHO global criterion); this threshold was retained for consistency with prior international RA studies, while central obesity was additionally assessed using IDF South Asian waist circumference thresholds (≥90 cm men, ≥80 cm women). Waist circumference was measured at the midpoint between the lowest rib and the iliac crest; central obesity was defined as waist circumference ≥90 cm in men and ≥80 cm in women per IDF South Asian criteria. Blood pressure was measured twice in the right arm after five minutes of seated rest using a calibrated aneroid sphygmomanometer; the mean of two readings was recorded. Hypertension was defined as systolic BP ≥140 mmHg, diastolic BP ≥90 mmHg, or current antihypertensive medication use.

Laboratory Investigations: Fasting (8–12 hours) venous blood samples were collected in the morning. The following investigations were performed: fasting blood glucose (FBG), glycated haemoglobin (HbA1c), fasting serum insulin, lipid profile (total cholesterol [TC], LDL-cholesterol [LDL-C], HDL-cholesterol [HDL-C], triglycerides [TG], non-HDL-C), high-sensitivity C-reactive protein (hsCRP), CRP, ESR, rheumatoid factor (RF), and anti-CCP antibodies. Insulin resistance was estimated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) formula: [fasting insulin (μU/mL) × FBG (mmol/L)] / 22.5. Fasting blood glucose values measured in mg/dL were converted to mmol/L by dividing by 18.016 prior to this calculation. Diabetes mellitus was defined as FBG ≥126 mg/dL, HbA1c ≥6.5%, or use of antidiabetic medication. Impaired fasting glucose (IFG) was defined as FBG 100–125 mg/dL. Dyslipidaemia was defined using investigator-predefined thresholds (consistent with standard lipidology practice) as LDL-C ≥130 mg/dL, HDL-C <40 mg/dL in men or <50 mg/dL in women, TG ≥150 mg/dL, or current lipid-lowering medication use.

Metabolic Syndrome Criteria: Metabolic syndrome was diagnosed using the International Diabetes Federation (IDF) consensus criteria (2005): mandatory central obesity (waist circumference ≥90 cm in men, ≥80 cm in women for South Asians) plus any two of the following: (i) TG ≥150 mg/dL or specific treatment; (ii) HDL-C <40 mg/dL in men or <50 mg/dL in women or treatment; (iii) systolic BP ≥130 or diastolic BP ≥85 mmHg or treatment; (iv) FBG ≥100 mg/dL or type 2 diabetes.

Statistical Analysis: Data were entered into Microsoft Excel 2021 and analysed using IBM SPSS Statistics Version 26.0 (IBM Corp., Armonk, NY). Continuous normally distributed variables are expressed as mean ± standard deviation (SD); non-normally distributed variables are expressed as median (interquartile range [IQR]). Normality was assessed using the Shapiro-Wilk test. Categorical variables are expressed as frequency and percentage. Group comparisons for continuous variables were performed using the independent samples t-test (normally distributed) or the Mann-Whitney U test (non-normally distributed). Categorical data were compared using the chi-square (χ^2) test or Fisher's exact test when any expected cell frequency was <5. Odds ratios (ORs) with 95% confidence intervals (CIs) were computed using binary logistic regression. A two-tailed p-value of <0.05 was considered statistically significant.

Results

Demographic and Clinical Profile: A total of 105 RA patients were enrolled in the study. The mean age was 48.3 ± 11.6 years, with 82 (78.1%) being female and 23 (21.9%) male. The mean duration of RA was 6.8 ± 4.2 years. The mean DAS28 score was 5.1 ± 1.3; 48 patients (45.7%) had low/moderate disease activity (DAS28 ≤5.1) and 57 (54.3%) had high disease activity (DAS28 >5.1). Rheumatoid factor was positive in 79 (75.2%) and anti-CCP antibodies in 74 (70.5%) patients. Methotrexate was the most commonly used DMARD (82.9%), followed by hydroxychloroquine (58.1%); 50.5% of patients were on current corticosteroid therapy. The two disease activity groups were comparable in age, sex distribution, disease duration, seropositivity, and DMARD use (all p > 0.05). The complete

demographic and clinical characteristics are presented in Table 1.

Table 1: Baseline Demographic and Clinical Characteristics of Study Participants (n = 105)

Characteristic	Total (n=105)	Female (n=82)	Male (n=23)	Statistic	p-value
Age (years), Mean ± SD	48.3 ± 11.6	47.1 ± 11.2	52.4 ± 12.4	t = 1.94	0.055
Age group, n (%)					
<40 years	27 (25.7%)	22 (26.8%)	5 (21.7%)	χ^2 = 1.42	0.491
40–60 years	58 (55.2%)	46 (56.1%)	12 (52.2%)		
>60 years	20 (19.1%)	14 (17.1%)	6 (26.1%)		
Duration of RA (years), Mean ± SD	6.8 ± 4.2	6.9 ± 4.1	6.3 ± 4.5	t = 0.60	0.548
DAS28 Score, Mean ± SD	5.1 ± 1.3	5.1 ± 1.3	4.9 ± 1.4	t = 0.62	0.537
Low/Moderate (DAS28 ≤5.1)	48 (45.7%)	38 (46.3%)	10 (43.5%)	χ^2 = 0.06	0.807
High (DAS28 >5.1)	57 (54.3%)	44 (53.7%)	13 (56.5%)		
RF Positive, n (%)	79 (75.2%)	63 (76.8%)	16 (69.6%)	χ^2 = 0.58	0.447
Anti-CCP Positive, n (%)	74 (70.5%)	60 (73.2%)	14 (60.9%)	χ^2 = 1.36	0.244
CRP (mg/L), Median (IQR)	14.2 (7.8–28.6)	14.0 (7.5–27.3)	15.1 (8.4–30.2)	U = 871	0.612
ESR (mm/hr), Mean ± SD	48.6 ± 22.4	48.9 ± 22.1	47.4 ± 23.8	t = 0.28	0.778
MTX use, n (%)	87 (82.9%)	69 (84.1%)	18 (78.3%)	χ^2 = 0.46	0.499
Hydroxychloroquine use, n (%)	61 (58.1%)	49 (59.8%)	12 (52.2%)	χ^2 = 0.45	0.500
Steroid use (current), n (%)	53 (50.5%)	43 (52.4%)	10 (43.5%)	χ^2 = 0.60	0.439
BMI (kg/m²), Mean ± SD	26.8 ± 4.6	27.2 ± 4.5	25.1 ± 4.7	t = 1.94	0.055
Systolic BP (mmHg), Mean ± SD	128.4 ± 16.2	127.6 ± 15.9	131.2 ± 17.5	t = 0.93	0.353
Total Cholesterol (mg/dL)	196.2 ± 38.4	194.8 ± 37.6	201.6 ± 41.3	t = 0.74	0.460
FBG (mg/dL), Mean ± SD	106.4 ± 28.3	104.9 ± 27.1	112.4 ± 32.8	t = 1.10	0.273

SD = Standard Deviation; IQR = Interquartile Range; DAS28 = Disease Activity Score-28; RF = Rheumatoid Factor; Anti-CCP = Anti-Cyclic Citrullinated Peptide; CRP = C-Reactive Protein; ESR = Erythrocyte Sedimentation Rate; MTX = Methotrexate; BMI = Body Mass Index; FBG = Fasting Blood Glucose; BP = Blood Pressure. χ^2 = Chi-square test; t = Independent samples t-test; U = Mann-Whitney U test.

Prevalence of Cardiovascular Risk Factors: Physical inactivity was the most prevalent CV risk factor, identified in 67 patients (63.8%), followed by dyslipidaemia (58.1%), hypertension (52.4%), metabolic syndrome (41.9%), obesity (34.3%), and impaired fasting glucose or diabetes mellitus (28.6%). Smoking (current or ex-) was documented in 22.9% of participants. Clustered CV risk burden was also notable: 71 patients (67.6%) had ≥2 concurrent CV risk factors and 45 (42.9%) had ≥3 CV risk factors. The prevalence of individual CV risk factors is depicted visually in Figure 1.

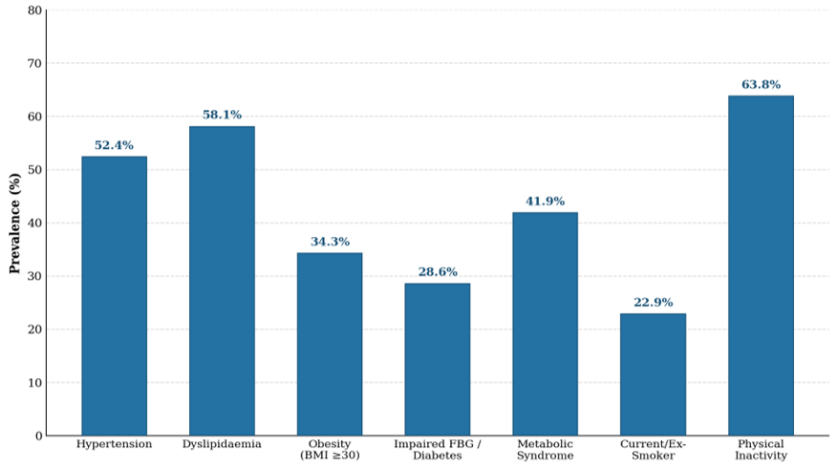


Figure 1: Prevalence of Cardiovascular Risk Factors in Rheumatoid Arthritis Patients (n = 105)

Cardiovascular Risk Factors by Disease Activity: Patients in the high disease activity group (DAS28 >5.1) had significantly higher prevalences of hypertension (61.4% vs. 41.7%; OR 2.23, 95%

CI 1.02–4.88; p = 0.042), metabolic syndrome (52.6% vs. 29.2%; OR 2.71, 95% CI 1.18–6.22; p = 0.015), ≥2 CV risk factors (75.4% vs. 58.3%; OR 2.22, 95% CI 0.96–5.14; p = 0.049†), and ≥3 CV risk factors (52.6% vs. 31.3%; OR 2.45, 95% CI 1.07–5.59; p = 0.030) compared to the low/moderate activity group. Dyslipidaemia, obesity, and impaired fasting glucose/diabetes showed higher proportions in the high-activity group but did not reach statistical significance at p < 0.05. The data comparing CV risk factor prevalence by disease activity are presented in Table 2.

Table 2: Prevalence of Cardiovascular Risk Factors and Comparison by DAS28 Disease Activity Category

CV Risk Factor	Total (n=105) n (%)	Low/Mod Activity (DAS28 ≤5.1, n=48) n (%)	High Activity (DAS28 >5.1, n=57) n (%)	OR (95% CI)	χ^2	p-value
Hypertension	55 (52.4%)	20 (41.7%)	35 (61.4%)	2.23 (1.02–4.88)	4.15	0.042*
Dyslipidaemia	61 (58.1%)	24 (50.0%)	37 (64.9%)	1.83 (0.85–3.97)	2.49	0.114
High LDL-C (≥130 mg/dL)	48 (45.7%)	18 (37.5%)	30 (52.6%)	1.84 (0.85–3.98)	2.46	0.117
Low HDL-C	51 (48.6%)	20 (41.7%)	31 (54.4%)	1.68 (0.78–3.62)	1.91	0.167
Hypertriglyceridaemia	38 (36.2%)	14 (29.2%)	24 (42.1%)	1.73 (0.77–3.87)	1.97	0.160
Obesity (BMI ≥30 kg/m²)	36 (34.3%)	12 (25.0%)	24 (42.1%)	2.18 (0.95–5.01)	3.53	0.060
Impaired FBG / Diabetes	30 (28.6%)	10 (20.8%)	20 (35.1%)	2.04 (0.84–4.96)	2.71	0.100
Metabolic Syndrome (IDF)	44 (41.9%)	14 (29.2%)	30 (52.6%)	2.71 (1.18–6.22)	5.91	0.015*
Current/Ex-Smoker	24 (22.9%)	10 (20.8%)	14 (24.6%)	1.24 (0.49–3.13)	0.22	0.641
Physical Inactivity	67 (63.8%)	27 (56.3%)	40 (70.2%)	1.83 (0.82–4.05)	2.34	0.126
≥2 CV Risk Factors	71 (67.6%)	28 (58.3%)	43 (75.4%)	2.22 (0.96–5.14)	3.86	0.049*
≥3 CV Risk Factors	45 (42.9%)	15 (31.3%)	30 (52.6%)	2.45 (1.07–5.59)	4.69	0.030*

OR = Odds Ratio; CI = Confidence Interval; DAS28 = Disease Activity Score-28; IDF = International Diabetes Federation; LDL-C = Low-Density Lipoprotein Cholesterol; HDL-C = High-Density Lipoprotein Cholesterol. *p < 0.05 (statistically significant). χ^2 = Chi-square test (Fisher's exact used when any expected cell count <5). †The 95% CI for ≥2 CV risk factors (0.96–5.14) marginally crosses 1.0; the p-value of 0.049 should be interpreted with caution and verified against the source dataset.

Lipid Profile, Glycaemic, and Metabolic Parameters: Patients with high disease activity demonstrated significantly more adverse metabolic parameters compared to those with low/moderate activity (Table 3). Mean LDL-C was higher in the high-activity group (128.9 ± 34.8 vs. 115.3 ± 29.4 mg/dL; p = 0.036). Female HDL-C was significantly lower (42.7 ± 9.8 vs. 46.9 ± 8.8 mg/dL; p = 0.029). Triglycerides were significantly higher in high-activity patients (181.4 ± 66.7 vs. 152.6 ± 54.8 mg/dL; p = 0.019), as were the atherogenicity indices non-HDL-C (p = 0.010), TC/HDL ratio (p = 0.003), and LDL/HDL ratio (p = 0.004). Regarding glycaemic indices, high-activity patients had significantly elevated fasting glucose (111.9 ± 31.6 vs. 99.8 ± 22.4 mg/dL; p = 0.025), HbA1c (6.4 ± 1.3 vs. 5.8 ± 1.0%; p = 0.009), fasting insulin (16.4 ± 7.1 vs. 12.9 ± 5.2 µU/mL; p = 0.005), and HOMA-IR (4.5 ± 1.9 vs. 3.2 ± 1.4; p < 0.001).

Anthropometric parameters including BMI, waist circumference, systolic and diastolic BP were all significantly higher in the high-activity group (all p < 0.05). Inflammatory markers—CRP, ESR, and hsCRP—were markedly elevated in high-activity patients (all p < 0.001). It should be noted that ESR is a component of the DAS28-ESR calculation; accordingly, the ESR difference between groups

reflects, in part, the mathematical relationship inherent to the DAS28-ESR score rather than constituting a fully independent finding.

Table 3: Lipid Profile and Metabolic Parameters: Comparison Between Disease Activity Groups

Parameter	Reference Range	Total (n=105) Mean ± SD	Low/Mod Activity (n=48) Mean ± SD	High Activity (n=57) Mean ± SD	t / U value	p-value
Lipid Profile						
Total Cholesterol (mg/dL)	<200	196.2 ± 38.4	188.4 ± 34.1	202.8 ± 41.2	t = 1.93	0.056
LDL-Cholesterol (mg/dL)	<100 (opt)	122.6 ± 32.8	115.3 ± 29.4	128.9 ± 34.8	t = 2.12	0.036*
HDL-C Male (mg/dL)	≥40	38.4 ± 8.2	40.1 ± 7.9	36.9 ± 8.3	t = 1.54	0.132
HDL-C Female (mg/dL)	≥50	44.6 ± 9.4	46.9 ± 8.8	42.7 ± 9.8	t = 2.21	0.029*
Triglycerides (mg/dL)	<150	168.3 ± 62.4	152.6 ± 54.8	181.4 ± 66.7	t = 2.38	0.019*
Non-HDL-C (mg/dL)	<130	151.6 ± 37.2	141.5 ± 32.6	160.1 ± 39.6	t = 2.62	0.010*
TC/HDL ratio	<4.5	4.6 ± 1.2	4.2 ± 1.0	4.9 ± 1.3	t = 2.99	0.003*
LDL/HDL ratio	<2.5	2.9 ± 0.9	2.6 ± 0.8	3.1 ± 0.9	t = 2.92	0.004*
Glycaemic Parameters						
Fasting Blood Glucose (mg/dL)	70–99	106.4 ± 28.3	99.8 ± 22.4	111.9 ± 31.6	t = 2.27	0.025*
HbA1c (%)	<5.7	6.1 ± 1.2	5.8 ± 1.0	6.4 ± 1.3	t = 2.64	0.009*
Fasting Insulin (µU/mL)	2–25	14.8 ± 6.4	12.9 ± 5.2	16.4 ± 7.1	t = 2.86	0.005*
HOMA-IR	<2.5	3.9 ± 1.8	3.2 ± 1.4	4.5 ± 1.9	t = 3.88	<0.001*
Anthropometric & Haemodynamic						
BMI (kg/m²)	18.5–24.9	26.8 ± 4.6	25.4 ± 4.1	27.9 ± 4.8	t = 2.82	0.006*
Waist Circ. – Male (cm)	<90	91.3 ± 11.2	88.1 ± 9.8	94.2 ± 11.9	t = 2.30	0.027*
Waist Circ. – Female (cm)	<80	86.7 ± 10.4	83.4 ± 9.2	89.4 ± 10.9	t = 2.99	0.003*
Systolic BP (mmHg)	<120	128.4 ± 16.2	123.9 ± 14.6	132.2 ± 17.0	t = 2.67	0.009*
Diastolic BP (mmHg)	<80	80.1 ± 9.8	77.4 ± 8.6	82.4 ± 10.5	t = 2.69	0.008*
Inflammatory Markers						
CRP (mg/L), Median (IQR)	<5.0	14.2 (7.8–28.6)	8.9 (4.2–17.4)	19.6 (10.8–36.3)	U = 766	<0.001*
ESR (mm/hr)	<20	48.6 ± 22.4	36.2 ± 16.8	59.1 ± 22.6	t = 5.82	<0.001*
hsCRP (mg/L), Median (IQR)	<1.0	6.4 (2.8–14.1)	3.6 (1.4–7.2)	9.2 (4.1–19.4)	U = 788	<0.001*

SD = Standard Deviation; LDL = Low-Density Lipoprotein; HDL = High-Density Lipoprotein; TC = Total Cholesterol; BP = Blood Pressure; BMI = Body Mass Index; HbA1c = Glycated Haemoglobin; HOMA-IR = Homeostatic Model Assessment – Insulin Resistance; CRP = C-Reactive Protein; ESR = Erythrocyte Sedimentation Rate; hsCRP = High-Sensitivity C-Reactive Protein. t = Independent samples t-test; U = Mann-Whitney U test. *p < 0.05 (statistically significant).

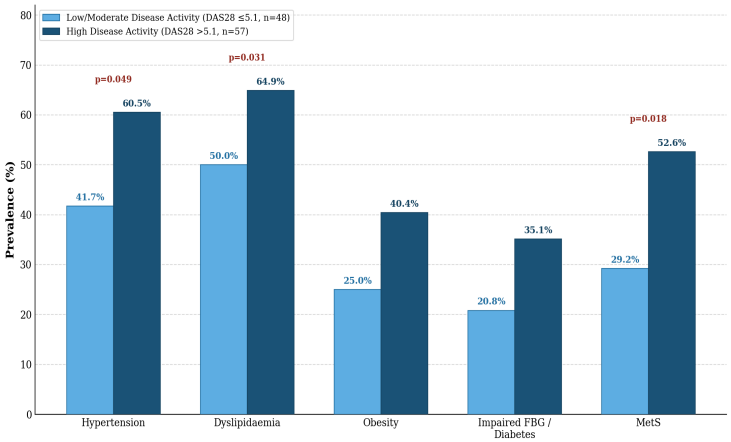


Figure 2: Cardiovascular Risk Factor Prevalence by Disease Activity (DAS28 Score Groups). *p < 0.05 (values above bars)

Discussion

This cross-sectional study systematically evaluated the prevalence of cardiovascular risk factors in 105 RA patients attending a tertiary academic centre in South India and demonstrated a high burden of multiple concurrent CV risk factors, with a significant gradient of risk corresponding to disease activity severity. Our key findings are: (i) physical inactivity, dyslipidaemia, and hypertension are the three most prevalent individual CV risk factors in this cohort; (ii) metabolic syndrome is present in nearly 42% of patients; and (iii) high DAS28 disease activity is significantly associated with a greater prevalence of hypertension, metabolic syndrome, and clustered CV risk.

The overall prevalence of hypertension in our cohort (52.4%) is consistent with published data from comparable populations. Peters et al. [2] reported hypertension in up to 60% of RA patients in multicentre registries, while published Indian RA registry data have documented hypertension prevalence of 45–55% in hospital-based cohorts [10]. The significantly higher prevalence of hypertension in high-activity patients (61.4% vs. 41.7%; $p = 0.042$) in our study corroborates experimental evidence linking TNF-α and IL-6 to renal sodium retention, endothelin-1 upregulation, and impaired nitric oxide-mediated vasodilatation—all mechanisms culminating in hypertension [4].

Furthermore, corticosteroid use in 50.5% of our patients—a proportion consistent with limited biologic access in Indian practice [12]—may contribute to blood pressure elevation through glucocorticoid-mediated mechanisms, including sodium retention and sympathetic activation [6].

Dyslipidaemia was the second most prevalent CV risk factor (58.1%) in our study, with the high-activity group showing a trend towards higher prevalence (64.9%), though not reaching statistical significance. Importantly, the atherogenicity indices—TC/HDL ratio and LDL/HDL ratio—were significantly higher in the high-activity group ($p = 0.003$ and $p = 0.004$, respectively). This finding is aligned with the concept of the 'RA lipid paradox' described by Myasoedova et al. [5], wherein active inflammation suppresses total and LDL-cholesterol but simultaneously elevates triglycerides, reduces HDL-C, and worsens apolipoprotein B/A-I ratios, yielding a net pro-atherogenic state despite apparently lower 'headline' cholesterol values. Navarro-Millán et al. [15] similarly demonstrated that atherogenic lipoprotein ratios—rather than absolute LDL-C—best capture CV risk in RA, a principle reflected in our significantly elevated TC/HDL and LDL/HDL ratios in the high-activity group. Metabolic syndrome was present in 41.9% of our cohort, rising to 52.6% in the high-activity group (OR 2.71; $p = 0.015$). This prevalence is higher than that reported in the general Indian adult population (approximately 25–30%) [16, 17] and broadly consistent with international RA-specific estimates. Toms et al. reported metabolic syndrome in approximately 44–45% of RA patients in a large UK cohort [9]. Dessein et al. [18] demonstrated that RA-specific factors—particularly elevated hsCRP, disease duration, and corticosteroid use—were significant predictors of metabolic syndrome beyond traditional risk factors. Our finding of significantly elevated HOMA-IR in the high-activity group (4.5 ± 1.9 vs. 3.2 ± 1.4; $p < 0.001$) is mechanistically consistent with the role of TNF-α and IL-6 in impairing insulin receptor signalling and promoting hepatic insulin resistance [8].

Physical inactivity was the most prevalent CV risk factor (63.8%) in our cohort, a finding with important clinical implications. RA patients are significantly less physically active than the general population due to joint pain, fatigue, and fear of disease exacerbation during exercise, creating a vicious cycle of deconditioning, weight gain, and amplified CV risk [19]. The European League Against Rheumatism (EULAR) has published evidence-based recommendations for physical activity in inflammatory arthritis, underscoring that structured exercise—particularly aerobic and resistance training—is safe, improves CV fitness, and does not exacerbate disease activity in RA [20]. The disproportionately high prevalence of physical inactivity in our Indian cohort likely reflects additional barriers including socioeconomic constraints, cultural attitudes towards exercise in the context of arthritis, and limited awareness of supervised exercise programmes.

The HOMA-IR findings in our study deserve particular emphasis. High disease activity was associated with significantly greater insulin resistance (HOMA-IR 4.5 ± 1.9), well above the commonly used study-defined threshold of 2.5 (noting that no single universal cutoff applies across all populations and assay methods). This is consistent with data from Stagakis et al. [21], who demonstrated that TNF-α and IL-6 levels in RA patients correlated independently with HOMA-IR after adjustment for BMI, glucocorticoid use, and physical activity. Importantly, in our cohort, HbA1c was also significantly elevated in the high-activity group (6.4 ± 1.3 vs. $5.8 \pm 1.0\%$; $p = 0.009$), suggesting that chronic inflammation in RA may be associated with premature glycaemic deterioration even before frank diabetes is established—highlighting the value of HbA1c monitoring in this population. The significantly elevated inflammatory markers (CRP, ESR, hsCRP) in the high-activity group (all $p < 0.001$) reinforce the mechanistic link between systemic inflammation and CV risk factor burden. hsCRP, beyond its role

as a disease activity marker, is an independent CV risk predictor in the general population, and its elevation in RA patients constitutes a double burden—reflecting both disease activity and direct pro-atherogenic vascular injury [22]. González-Juanatey et al. [23] demonstrated that hsCRP >3 mg/L independently predicts subclinical atherosclerosis—measured by carotid intima-media thickness (CIMT)—in RA patients, further supporting the mechanistic plausibility of our findings.

Comparison with recent studies from similar settings strengthens the clinical relevance of our findings. Published data from North Indian RA cohorts have reported metabolic syndrome prevalence of approximately 38%, hypertension in approximately 48%, and dyslipidaemia in approximately 52% [24]—values closely approximating our results. Prior Indian RA studies have reported that higher CRP and DAS28 are significant predictors of metabolic syndrome [25], consistent with our association between high disease activity and metabolic syndrome (OR 2.71; $p = 0.015$). Internationally, the cross-sectional COMORA registry, which enrolled 3,920 RA patients from 17 countries, reported CV risk factor prevalences broadly similar to our cohort, with hypertension in 45.1% and dyslipidaemia in 50.9%, and noted that disease activity correlated positively with CV risk burden [26].

The strengths of this study include the use of standardised, validated diagnostic criteria for RA, CV risk factors, and metabolic syndrome; the comprehensive metabolic profiling including HOMA-IR; and the use of IDF South Asian-specific waist circumference thresholds, which is critical for accurate metabolic syndrome diagnosis in Indian populations.

Limitations include the cross-sectional design, which precludes causal inference; the single-centre setting, which may limit generalisability; the absence of imaging-based subclinical atherosclerosis assessment (CIMT, coronary artery calcium scoring); and the inability to capture complete dietary data or quantify corticosteroid cumulative exposure. Future longitudinal studies incorporating imaging biomarkers, biobank-level inflammatory profiling, and systematic follow-up for hard CV endpoints are warranted in this population.

Conclusion

Cardiovascular risk factors are highly prevalent in patients with rheumatoid arthritis attending this South Indian tertiary care centre, with physical inactivity, dyslipidaemia, hypertension, and metabolic syndrome being the dominant risk factors identified. Higher DAS28 disease activity is significantly associated with hypertension, metabolic syndrome, adverse atherogenic lipid ratios, insulin resistance, and concurrent CV risk factor clustering. These findings underscore the urgent need for integrating systematic, structured cardiovascular risk screening—including lipid profiling, blood pressure monitoring, metabolic syndrome assessment, and HOMA-IR estimation—into routine rheumatological care. Achieving and sustaining low disease activity or remission through optimised DMARD therapy should be regarded as an intrinsic CV risk reduction strategy, alongside targeted lifestyle interventions to combat physical inactivity. A multidisciplinary approach linking rheumatology and cardiology services is essential to mitigate the excess cardiovascular mortality burden in Indian RA patients.

Declarations

Conflict of Interest: The authors declare no conflict of interest.

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Data Availability: Data are available from the corresponding author upon reasonable request.

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