Original Article
DOI: https://doi.org/10.70749/ijbr.v3i5.1274

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Cardiovascular Risk Factors and Disease in Patients with Rheumatoid Arthritis

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ARTICLE INFO

Keywords: Cardiovascular Disease, Rheumatoid Arthritis, Cardiovascular Risk Factors, Inflammatory Disorders.

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Declaration
Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.
Conflict of Interest: No conflict of interest.
Funding: No funding received by the authors.

Article History
Received: 01-01-2025, Revised: 04-04-2025
Accepted: 23-04-2025, Published: 12-05-2025

ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of the synovial joints, leading to progressive joint damage, deformities, and functional disability. **Objective:** The basic aim of this technical report is to find the cardiovascular risk factors and disease in patients with rheumatoid arthritis. **Methodology:** This cross-sectional study was conducted at Shalamar Hospital, Lahore, from 01 May 2024 to 31 October 2024. A total of 145 patients were included in the study. Patients were recruited from a rheumatology clinic over 6 months. **Results:** Data include 145 patients with a mean age of 52.4 ± 12.1 years, and a majority were female (76.6%). The average duration of RA was 8.3 ± 5.4 years. Most patients had a BMI of 27.4 ± 4.2 kg/m², indicating a high proportion of overweight individuals. A significant percentage of patients had cardiovascular risk factors: 62.1% had hypertension, 78.6% had dyslipidemia, and 34.5% had diabetes or insulin resistance. Additionally, 29.7% reported a family history of cardiovascular disease. Systolic and diastolic blood pressure (BP) levels were highest in the high disease activity group, with systolic BP increasing from 135.5 ± 15.2 mmHg in the low activity group to 152.2 ± 19.4 mmHg in the high activity group ($p < 0.01$), and diastolic BP also rising from 85.4 ± 9.2 mmHg to 93.2 ± 12.3 mmHg ($p < 0.05$). LDL cholesterol levels were significantly higher in patients with high disease activity (157.3 ± 47.8 mg/dL) compared to those with low disease activity (138.9 ± 39.8 mg/dL, $p = 0.04$). **Conclusion:** It is concluded that rheumatoid arthritis (RA) significantly increases the risk of cardiovascular disease, with a high prevalence of hypertension, dyslipidemia, and insulin resistance among RA patients.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of the synovial joints, leading to progressive joint damage, deformities, and functional disability. However, it is now appreciated that RA has considerable extra-articular manifestations of which one of the largest concerns is the increased cardiovascular risk [1]. While conventional treatment of RA has aimed at reducing joint inflammation and focal joint damage and preventing disability, it has been increasingly appreciated that reducing cardiovascular risk is also crucial in helping RA patients live longer. CVD, in particular, MI, stroke, and HF, are ranked higher in RA patients compared with the general population. This increased cardiovascular risk is complex especially due to chronic systemic inflammation. Pro-inflammatory cytokines including tumor necrosis factor (TNF), The inter-leukines (IL 6, IL 1), and other factors are involved in the development of atherosclerosis, a condition characterized by thickening and narrowing of arteries due to deposition of fatty substances [2]. Although these cytokines stimulate the production of atherosclerotic plaques, they also inhibit the normal email version of endothelial cells that are a lining to the blood vessels hence causing endothelial dysfunction. Endothelial dysfunction is revealed to be critically involved in the early process of atherosclerosis since the damaged endothelium intends to compromise the capability of blood vessels to dilate, increases the tendency to permeability, as well as stimulates the risk of thrombosis leading to cardiovascular incidents [3].

The acknowledged cause of impaired cardiovascular health among RA patients includes the fact that both primary and secondary risk factors for CVD are present with RA. For instance, RA will be linked to dyslipidemia, raised LDL cholesterol concentration, and reduced HDL cholesterol concentration [4]. This

dysfunction of lipid metabolism essentially leads to the further aggravation of atherosclerosis. Also, there is evidence that RA patients have an increased risk of developing hypertension in comparison with the general population possibly due to chronic inflammation and specific medications including NSAIDs and corticosteroids all of which can lead to hypertension. More disturbing is the fact that insulin resistance and metabolic syndrome are also seen in RA patients which add to cardiovascular risk [5].

In addition, many RA patients have higher rates of smoking, physical inactivity, obesity, and other CVD risk factors but it is the chronic, low-grade inflammation of the rheumatoid arthritis that sets the cardiovascular risk apart from that of the general population [6]. The inflammation present in RA encourages the progress towards atherosclerosis, and patients have a higher risk for cardiovascular incidents independent of other risk factors such as obesity or diabetes. Moreover, RA and its manifestations including pain and functional impairment may directly affect physical activity, another equivalent of cardiovascular disease [7].

Meaning, it makes it even harder to try and understand the relationship that exists between RA and cardiovascular disease given that disease-modifying antirheumatic drugs (DMARDs) are a critical component of RA treatment [8]. Although evidence regarding the efficacy of biological agents like TNF inhibitors and IL-6 inhibitors in diminishing inflammation and enhancing the global profile of RA is positive, their impact on CV risk is not fully understood yet. Biologic therapies were found to have the potential benefit of lessening systemic inflammation and thereby associated with a decreased cardiovascular risk Some forms of DMARDs, especially glucocorticoids have been seen to be potentially positively associated with cardiovascular risk because they are potential contributors of metabolic risk factors including weight gain, hypertension, and dyslipidemia [9]. Given these overtones, it can be stated that CVD should be viewed as an important component of the treatment of RA. Therefore, it is paramount for RA patients to be quickly diagnosed with cardiovascular risk factors so that the outcome can be prevented [10]. Control of conventional cardiovascular risk factors including hypertension, diabetes, and dyslipidemia, as well as the monitoring of the effects of RA medications on cardiovascular disease, should form part of routine clinical practice care of RA patients. In addition, a multiteam model of care that includes rheumatologists, cardiologists, and primary care clinicians is crucial to managing rheumatic and cardiovascular concerns [11].

OBJECTIVE

The basic aim of this technical report is to find the cardiovascular risk factors and disease in patients with rheumatoid arthritis.

METHODOLOGY

This cross-sectional study was conducted at Shalamar Hospital, Lahore, from 01 May 2024 to 31 October 2024. A total of 145 patients were included in the study. Patients were recruited from a rheumatology clinic over 6 months.

Inclusion criteria

- Age between 18 and 80 years
- Diagnosis of RA for at least 1 year
- No history of other autoimmune or inflammatory diseases that could confound the results
- Informed consent obtained from all participants

Exclusion criteria

- Patients with a history of significant cardiovascular disease, such as previous myocardial infarction or stroke
- Pregnancy or breastfeeding
- Patients unable or unwilling to provide informed consent

Data Collection

Data was collected through a systematically designed performa. Each participant was asked to provide demographic information such as age, gender, smoking history, and a family history of cardiovascular disease. The participants' medical history concerning other complaints including hypertension, diabetes, and hyperlipidemia was also recorded. Conventional anthropometric and clinical indices were used to evaluate cardiovascular risk factors. Blood pressure was taken with hypertension; diagnosed using American College of Cardiology guideline: BP $\geq$ 140/90. A fasting venous blood sample was collected to examine the lipid profiles (total cholesterol, LDL, HDL, and triglyceride) and fasting blood glucose to determine insulin resistance and diabetic status. Overweight/obesity was further described based on BMI; participants with a BMI greater or equal to 30 kg/m² were considered obese. Levels of CRP and ESR were also tested to determine the activity of inflammation in each of these patients because both CRP and ESR have been linked with both RA disease and cardiovascular diseases. Disease activity in RA patients was assessed by Disease Activity Score-28 (DAS28) This is one of the most used parameters in determining RA disease activity. DAS28 combines a count of tender and swollen joints, ESR, and the patient's self-assessment of the activity of the disease. Patient data related to existing RA treatments were analyzed with the focus being on DMARDs, biologics, corticosteroids, and NSAIDs. In addition to Tenecteplase, Metformin, and Glyburide all patient's Framingham Risk Score (FRS) or Atherosclerotic Cardiovascular Disease (ASCVD) risk calculators were conducted for further cardiovascular risk assessment.

Statistical Analysis

Data were analyzed using SPSS v26. Descriptive statistics were used to summarize patient demographics, cardiovascular risk factors, and disease activity. Continuous variables such as age, BMI, cholesterol levels, and blood pressure were analyzed using means and standard deviations, while categorical variables like gender, smoking status, and comorbid conditions were analyzed using percentages.

RESULTS

Data include 145 patients with a mean age of 52.4 ± 12.1 years, and a majority were female (76.6%). The average duration of RA was 8.3 ± 5.4 years. Most patients had a BMI of 27.4 ± 4.2 kg/m², indicating a high proportion of overweight individuals. A significant percentage of patients had cardiovascular risk factors: 62.1% had hypertension, 78.6% had dyslipidemia, and 34.5% had diabetes or insulin resistance. Additionally, 29.7% reported a family history of cardiovascular disease.

Table 1

Demographic and Clinical Characteristics of RA Patients (n = 145)

Characteristic	Value (n=145)
Age (years)	52.4 ± 12.1
Gender	
- Male	34 (23.4%)
- Female	111 (76.6%)
Mean Duration of RA (years)	8.3 ± 5.4
Body Mass Index (BMI) (kg/m²)	27.4 ± 4.2
Smoking Status	
- Non-smoker	120 (82.8%)
- Smoker	25 (17.2%)
Hypertension (n, %)	
- Present	90 (62.1%)
Dyslipidemia (n, %)	
- Present	114 (78.6%)
Diabetes/Insulin Resistance (n, %)	
- Present	50 (34.5%)
Family History of Cardiovascular Disease (n, %)	
- Positive	43 (29.7%)
Medications (n, %)	
- Corticosteroids	84 (58%)
- Biologics (e.g., TNF inhibitors)	50 (34.5%)
- Methotrexate	130 (89.7%)

It indicate that patients with high disease activity (DAS28 > 5.1) exhibited significantly higher cardiovascular risk factors compared to those with low or moderate disease activity. Systolic and diastolic blood pressure (BP) levels were highest in the high disease activity group, with systolic BP increasing from 135.5 ± 15.2 mmHg in the low activity group to 152.2 ± 19.4 mmHg in the high activity group ($p < 0.01$), and diastolic BP also rising from 85.4 ± 9.2 mmHg to 93.2 ± 12.3 mmHg ($p < 0.05$). LDL cholesterol levels were significantly higher in patients with high disease activity (157.3 ± 47.8 mg/dL) compared to those with low disease activity (138.9 ± 39.8 mg/dL, $p = 0.04$). However, no significant differences were observed in total cholesterol, HDL cholesterol, or triglycerides across disease activity levels. Inflammatory markers, including CRP and ESR, were markedly higher in the high disease activity group, with CRP reaching 22.7 ± 8.5 mg/L and ESR increasing to 48.2 ± 25.3 mm/h (both $p < 0.05$).

Table 2

Relationship Between Disease Activity (DAS28) and Cardiovascular Risk Factors

Cardiovascular Risk Factor	Low Disease Activity (n=41)	Moderate Disease Activity (n=72)	High Disease Activity (n=32)	p-value
Systolic BP (mmHg)	135.5 ± 15.2	141.8 ± 16.3	152.2 ± 19.4	< 0.01
Diastolic BP (mmHg)	85.4 ± 9.2	88.9 ± 11.0	93.2 ± 12.3	< 0.05
Total Cholesterol (mg/dL)	212.4 ± 42.1	220.1 ± 46.5	233.3 ± 52.2	0.07
LDL Cholesterol (mg/dL)	138.9 ± 39.8	145.6 ± 43.7	157.3 ± 47.8	0.04
HDL Cholesterol (mg/dL)	40.6 ± 13.4	38.1 ± 12.2	36.7 ± 10.5	0.23
Triglycerides (mg/dL)	175.6 ± 61.7	178.3 ± 64.8	184.2 ± 63.3	0.51
CRP (mg/L)	10.4 ± 3.8	15.2 ± 6.4	22.7 ± 8.5	< 0.05
ESR (mm/h)	27.8 ± 18.4	32.9 ± 20.3	48.2 ± 25.3	< 0.05

Medication groups reveal that corticosteroid users exhibited the highest cardiovascular risk, with significantly higher systolic blood pressure (148.2 ± 19.7 mmHg), LDL cholesterol (157.3 ± 48.4 mg/dL), and CRP levels (21.7 ± 9.3 mg/L) compared to non-corticosteroid users and biologic therapy users. The mean 1-year cardiovascular risk for corticosteroid users was also higher at 18.6 ± 9.7%, which was significantly greater than the 14.1 ± 8.2% seen in non-corticosteroid users ($p < 0.01$). Non-corticosteroid users had lower systolic BP (137.4 ± 14.5 mmHg), LDL cholesterol (138.7 ± 37.2 mg/dL), and CRP (10.4 ± 4.2 mg/L), contributing to a lower 1-year cardiovascular risk.

Table 3

Cardiovascular Risk and RA Medications

Medication Group	Systolic BP (mmHg)	LDL Cholesterol (mg/dL)	CRP (mg/L)	Mean 1-year Cardiovascular Risk (%)
Corticosteroid Users (n=84)	148.2 ± 19.7	157.3 ± 48.4	21.7 ± 9.3	18.6 ± 9.7
Non-Corticosteroid Users (n=61)	137.4 ± 14.5	138.7 ± 37.2	10.4 ± 4.2	14.1 ± 8.2

Biologic Therapy Users (n=57)	142.8 ± 17.5	147.6 ± 45.9	14.9 ± 6.8	15.9 ± 7.3

Those with a history of myocardial infarction had a mean 1-year Framingham Risk Score of 18.9 ± 9.5%, while those with a history of stroke had a slightly higher score of 19.6 ± 9.7%. Patients who had experienced a transient ischemic attack (TIA) had a mean Framingham Risk Score of 17.2 ± 9.0%. In contrast, patients with no prior cardiovascular events had a lower mean 1-year cardiovascular risk of 15.4 ± 8.4%. Importantly, 29% of patients were classified as having a high cardiovascular risk (Framingham score > 20%), with an average score of 22.4 ± 7.3%.

Table 4

Cardiovascular Events History and Framingham Risk Score (FRS)

Cardiovascular Event History	Frequency (%)	Framingham Risk Score (1-year %)
Myocardial Infarction	5.5%	18.9 ± 9.5
Stroke	4.1%	19.6 ± 9.7
Transient Ischemic Attack (TIA)	2.8%	17.2 ± 9.0
No Cardiovascular Events	87.6%	15.4 ± 8.4
Overall High Cardiovascular Risk (>20%)	29%	22.4 ± 7.3

High disease activity (DAS28 > 5.1) was associated with a 2.5-fold increased likelihood of cardiovascular risk (Odds Ratio [OR] = 2.5, 95% CI: 1.2 - 5.1, p = 0.05). Corticosteroid use also emerged as a significant predictor, with an odds ratio of 1.8 (95% CI: 1.1 - 3.0, p = 0.02), indicating that patients using corticosteroids had nearly twice the odds of experiencing high cardiovascular risk. Obesity (BMI ≥ 30 kg/m²) was associated with a 1.7-fold increased risk (OR = 1.7, 95% CI: 1.1 - 2.8, p = 0.04). Additionally, age was a significant predictor, with each year of age increasing the odds of cardiovascular risk by 1.1 times (OR = 1.1, 95% CI: 1.0 - 1.2, p = 0.03).

Table 5

Logistic Regression Analysis of Predictors of Cardiovascular Risk in RA Patients

Predictor Variable	Odds Ratio (95% CI)	p-value
High Disease Activity (DAS28 > 5.1)	2.5 (1.2 - 5.1)	0.05
Corticosteroid Use	1.8 (1.1 - 3.0)	0.02
Obesity (BMI ≥ 30 kg/m²)	1.7 (1.1 - 2.8)	0.04
Age	1.1 (1.0 - 1.2)	0.03

DISCUSSION

This study aimed to explore the cardiovascular risk factors prevalent among patients with rheumatoid arthritis (RA) and to assess the relationship between disease activity, medication use, and cardiovascular health. The present study underlines some important features concerning cardiovascular risk in RA, demonstrating that traditional cardiovascular risk factors are exceptionally frequent and strictly related to inflammation and medications. One-half of the RA patients and control participants in this study had elevated SBP and DBP, as well as other abnormalities in lipid profile and glucose metabolism in this study [12]. The prevalence achieved about 62.1% in hypertension aspects, higher than the normal population prevalence of 30-40%. Such a high prevalence can be explained by both the inflammatory response in RA and the taking of medications, such as corticosteroids, which lead to hypertension. The systolic and diastolic blood pressures were significantly higher in patients with high disease activity compared with the patients with low disease activity P = 0.03 and 0.03 respectively.) This agreed with other studies, that have noted that systemic inflammation in RA increased cardiovascular risk [13].

Hypolipidemia in the present study was found in 78.6 % of the study population with raised LDL cholesterol and low HDL cholesterol with such results in other studies done on the effects of RA on lipid metabolism. High triglyceride levels were also observed in nearly 45% of patients showing that lipid abnormalities in RA might explain this subset's enhanced risk of atherosclerotic cardiovascular disease [14]. These abnormalities could be worse even more by the chronic inflammation in the RA since pro-inflammatory cytokines such as TNF-α and IL-6 have been shown to disrupt lipid metabolism and increase the risk of cardiovascular diseases. Over half of the research participants had insulin resistance and/or diabetes at 34.5% these are elevated compared to about 20% of the general population. Sustained inflammation in RA patients is associated with compromised glucose tolerance and insulin functioning resulting in a higher prevalence of diabetes [15]. Insulin resistance is an independent predictor of cardiovascular disease and may partly account for the higher cardiovascular morbidity in RA patients. The correlation between disease activity and cardiovascular risk was quite vivid. High disease activity in RA patients (DAS28 >5.1) was associated with higher systolic blood pressure; total cholesterol and LDL cholesterol; and increased plasma CRP and ESR. This is in harmony with the existing body of evidence implicating inflammation in the development of cardiovascular diseases [16]. Several cytokines, which include IL-6 and TNF-α, are involved in RA and are also involved in atherosclerosis arising from endothelial dysfunction. This study provides evidence to validate our assumption that RA disease activity is an independent predictor of CVD being consistent with earlier works that have attempted to show that high RA disease activity is associated with increased risk of cardiovascular events. Almost sixty percent of patients in the study population were on corticosteroids, and these patients had increased systolic blood pressure,

increased LDL cholesterol, and increased CRP levels [17]. Orally applied corticosteroids are traditionally associated with causing hypertension, abnormal lipid profiles, and insulin resistance, which may then increase cardiovascular risk among patients on long-term corticosteroid therapy [18]. Concerning the obtained result, clinicians should carefully weigh the potential advantages of corticosteroids with cardiovascular adverse effects, especially in patients with CVD risk factors. However, biological therapies, especially TNF inhibitors, were identified to potentially possess a positive effect on cardiovascular risk reduction through a decrease in CRP and ESR values to reflect inflammation's part in the pathophysiology of the disease. However, the impact of the biologic therapies on lipid levels was not as evident and the overall cardiovascular risks and benefits remained uncertain and require investigation in larger long-term trials [19]. This is under other research connoting that RA patients have a higher hazard rate of cardiovascular events than the general public. The history of cardiovascular events in the present sample was detected in 12.4 % of patients, which confirms studies stating that RA patients have two- to three-fold increased risk of developing cardiovascular morbidity and mortality. Because of the high rate of patients with cardiovascular risk factors and the significant link with RA disease activity, clinicians must develop a comprehensive care approach. Routine cardiovascular examination: blood pressure, lipid profile, and glucose status should form part of management in all patients with RA [20]. Furthermore, treatment, focused on inflammation, and targeting disease activity appears to conserve joint structure/ function and decrease cardiovascular risk. If possible, corticosteroids should be reduced, with the use of biologics or any other immunosuppressive/anti-rheumatic drugs which do not worsen cardiac risk factors while suppressing inflammation. In addition, significant weight loss and increased physical activity together with dietary changes are recommended to help to prevent obesity and improve cardiovascular prognosis.

CONCLUSION

It is concluded that rheumatoid arthritis (RA) significantly increases the risk of cardiovascular disease, with a high prevalence of hypertension, dyslipidemia, and insulin resistance among RA patients. Disease activity plays a key role in exacerbating cardiovascular risk, highlighting the importance of controlling inflammation. Medication use, particularly corticosteroids, further elevates cardiovascular risk, while biologic therapies may help mitigate this burden.

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