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FREQUENCY OF CARDIAC INVOLVEMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract

OBJECTIVE: *To determine the frequency of cardiac involvement in patients with rheumatoid arthritis.*

METHODOLOGY: *This cross-sectional study was conducted at JPMC Karachi on 96 RA patients, diagnosed per 2010 ACR/EULAR criteria. Patients ≥20 years old with RA for ≥6 months were included, while those with cardiovascular diseases, systemic illnesses, or infections were excluded. ECG and ECHO assessed cardiac abnormalities, while ESR, CRP, RF, and anti-CCP evaluated inflammation. Data was analyzed by SPSS version 26.*

RESULTS: *Among 96 RA patients (mean age 48.85 ± 12.84 years, 76% female, 24% male), electrocardiographic abnormalities were observed in 32.29%, while echocardiographic abnormalities were more prevalent at 73.95%. Pericardial involvement was noted in 47.9% of cases. Cardiac symptoms, including dyspnea (38.5%), chest pain (40.6%), tachycardia (50%), orthopnea (10.4%), syncope (14.6%), and murmurs (17.7%), were significantly associated with abnormal findings.*

CONCLUSION: *The present study demonstrates a strong relationship between cardiac findings and rheumatoid arthritis which should be considered in relation to clinical findings, sex and BMI. The results underline the necessity of regular cardiovascular screening among RA patients to diagnose subclinical changes as early as possible and provide early treatment. Incorporating ECG and echocardiography to the standard of care for RA can prevent complications and improve patient outcomes.*

INTRODUCTION

Rheumatoid arthritis (RA) is a long-term, systemic autoimmune disorder characterized by continuous inflammation of the synovial membrane, primarily impacting peripheral joints on both sides of the body [1]. An aberration of immune activation and regulation sets forth an autoimmune assault on synovium that leads to chronic joint inflammation, progressive joint destruction, and serious disability if untreated [2,3]. Genetic predisposition, environmental factors and immune dysfunction contribute significantly to disease initiation, although the precise etiology of this illness is still unidentified. It affects around 1% of the global population, with a higher prevalence observed in women, especially middle-aged women [4]. The disease has a clinically heterogeneous presentation which includes mild

oligoarticular forms as well as aggressive progressive polyarthritis with joint deformities or loss of function, and extra-articular systemic effects [5, 6].

But RA extends beyond joint involvement, presenting as a systemic condition with various extra-articular manifestations that can impact skin, lungs, eyes, blood vessels, and heart, among many organ systems [7]. Of these, cardiovascular complications are the most alarming, as they are a significant contributor to both illness and death in individuals with RA [8]. Cardiac damage in RA has been confirmed and usually occurs in forms of pericarditis, myocarditis, valvular heart disease, coronary artery disease (CAD), conduction abnormalities [9]. The most common cardiac manifestation is pericarditis, which, in most cases, is subclinical and diagnosed only by echocardiography; however, symptomatic pericardial effusion resulting in cardiac tamponade is uncommon [10]. Myocarditis is, albeit rare, another form of inflammatory damage to the myocardium that may also lead to heart failure [11]. Valvular heart disease, especially mitral and aortic valve regurgitation, results from valvular inflammation and fibrosis, which predispose the risk of infective endocarditis [12]. The most notable risk is accelerated coronary artery disease (CAD); RA promotes chronic inflammation that increases plaque formation and leads to early myocardial infarction and abrupt cardiac death due to impaired blood vessel function and increased arterial rigidity [13,14]. In addition to accelerated atherosclerosis, another contributor to cardiovascular morbidity in RA is the high incidence of arrhythmias (eg, atrial fibrillation) and conduction disturbances.

Since cardiac involvement has a significant part in the prognosis of RA patients, early diagnosis and treatment is essential to prevent adverse cardiovascular outcomes. Electrocardiography (ECG) and echocardiography are widely used to perform cardiac screening regularly, thus helping in early detection of subclinical cardiac abnormalities, which can be effectively managed and risk intervention strategies can be applied [15]. As pharmacological treatment should ideally control RA disease activity, aggressive cardiovascular risk management (including lipid lowering therapy, control of blood pressure, smoking cessation and weight management and risk factor modification) is also necessary.

This research aims to assess the prevalence and types of cardiac abnormalities in RA patients using ECG and echocardiography to improve the understanding of cardiovascular risks associated with RA. By identifying subclinical cardiac involvement at an early stage, this research may help guide clinical decision-making, improve risk stratification, and minimize cardiovascular-related disease and death in the RA population.

METHODOLOGY

This cross-sectional study was conducted in the Rheumatology and Cardiology Departments of Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan, a tertiary-care referral hospital. We employed a non-probability consecutive sampling approach to recruit 96 patients diagnosed with rheumatoid arthritis (RA). Their diagnosis was confirmed according to the 2010 ACR/EULAR Classification Criteria, which require a minimum score of 6 out of 10 based on factors including joint involvement, serologic markers, levels of acute-phase reactants, and the duration of symptoms.

Patients included were adults (≥20 years old) of either gender who had RA for at least six months, allowing assessment of chronic cardiac involvement, and who provided written informed consent. Cases with a history of ischemic heart disease, uncontrolled hypertension, diabetes mellitus, renal failure, thyroid dysfunction, smoking, pregnancy, or other systemic diseases that could independently contribute to cardiac abnormalities were excluded. At the same time, patients with active upper respiratory tract infections or acute inflammatory conditions were also excluded.

This study secured ethical clearance from the JPMC Karachi Institutional Review Board, adhering to Good Clinical Practice standards and the Declaration of Helsinki. Written informed consent was obtained from every participant prior to their involvement.

We obtained demographic data, disease duration, medication history, and cardiovascular symptoms. DAS-28 was used to measure RA severity. Electrocardiography (ECG) was done for all the patients to assess for arrhythmias, conduction abnormalities, ST-T wave change and ischemic pattern. Echocardiography (ECHO) was performed using a Philips Ultrasound MOD iE33 device by an

experienced cardiologist to evaluate left ventricular ejection fraction (LVEF%), diastolic dysfunction, pericardial involvement, valvular lesions, and pulmonary hypertension.

To confirm the diagnosis and assess inflammation severity, laboratory evaluations were conducted, including measurements of the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti-cyclic citrullinated peptide (anti-CCP) antibodies. SPSS 26.0 was used for statistical analysis. Categorical variables are expressed as frequencies and percentages, while continuous variables are summarized as means with their corresponding standard deviations. The Chi-square test was employed, considering a p-value below 0.05 as indicative of statistical significance.

RESULTS

Table I presents the demographic and clinical characteristics of the 96 patients included in the study. The mean age of the participants was 48.85 ± 12.84 years, with the majority (76.0%) being female and 24.0% being male. Most patients (68.8%) were over 40 years old, while 31.3% were between 20-40 years. The mean body mass index (BMI) was 26.06 ± 3.83 kg/m², with 69.8% of patients having a BMI greater than 24 kg/m², while 30.2% fell within the 18-24 kg/m² range. The mean duration of disease was 5.91 ± 2.26 years, with 63.5% of patients having the condition for 1-6 years, while 36.5% had it for more than 6 years.

Among the reported symptoms, tachycardia (50.0%) and chest pain (40.6%) were the most common, followed by dyspnea (38.5%). Other symptoms included syncope (14.6%), cardiac murmurs (17.7%), and orthopnea (10.4%). Electrocardiographic abnormalities were observed in some patients, with 15.6% showing ST interval changes and 14.6% exhibiting T wave abnormalities. Echocardiographic findings revealed that 47.9% of patients had pericardial involvement, while 45.8% showed signs of ventricular dysfunction. These findings highlight a significant prevalence of cardiovascular symptoms and abnormalities in the study population, with notable structural and electrical cardiac changes detected through electrocardiography and echocardiography.

Of these patients, 65 patients had a normal ECG, and 31 patients had electrocardiographic abnormalities (of whom 15 had ST changes, 12 had conduction disturbances, and 6 had arrhythmias). Those who had abnormal final ECG findings were significantly older than individuals with normal results (53.87 ± 11.30 vs. 46.46 ± 12.92 years; p = 0.008) and heavier based on mean body mass index (27.53 ± 4.90 vs. 25.36 ± 2.99 kg/m²; p = 0.009). The rate of abnormal ECG in men was significantly higher (69.6%) than that of women (20.5%) (p = 0.000). Patients with abnormal ECGs were more likely to have clinical symptoms such as dyspnea [p = 0.002], orthopnea [p = 0.000], syncope [p = 0.031] and cardiac murmurs [p = 0.045]. This experience also reported more chest pain (0.050) and tachycardia (0.049). At the same time, the disease duration was not significantly different between the two groups (p=0.497). (TABLE 2)

Echocardiographic abnormalities were noted in 71 of 96 patients and the remaining 25 patients had normal echocardiographic findings. Patients with abnormal echocardiography were older (51.63 ± 12.40 vs. 40.96 ± 10.82 years, p = 0.000) and had higher mean body mass index (26.56 ± 3.99 vs. 24.64 ± 2.98 kg/m2, p = 0.031). Echocardiographic abnormalities were more prevalent in males (91.3%) than females (68.5%) (p = 0.023). Patients with abnormal echocardiographic findings had more frequent dyspnea (p = 0.027), chest pain (p = 0.000), tachycardia (p = 0.011), and orthopnea (p = 0.041) as clinical symptoms. As for other clinical markers, syncope and cardiac murmurs were also more prevalent in patients with abnormal echocardiography, but these associations reached only trend levels of statistical significance (p=0.071 and p=0.117, respectively). No significant difference was evident with respect to disease duration between the groups (p = 0.133). (TABLE 3)

DISCUSSION

Cardiovascular disease (CVD) remains a leading contributor to illness and death in RA, mainly because of systemic inflammation and conventional cardiovascular risk factors [16]. Study of Crowson et al. clearly showed that both RA-specific and conventional risk factors are implicated in the increased cardiovascular threat in RA patients [16]. Endothelial dysfunction inherent in RA is worsened by the inflammatory burden, promoting progression

of atherosclerosis and increased cardiovascular events. Baghdadi et al. reinforced the influence of classical cardiovascular contributors to risk on outcomes in RA patients, arguing for focused cardiovascular risk evaluation and management [17]. Smoking is considered a significant factor linked to higher disease activity and an increased risk of cardiovascular disease in RA, one of the major variable risk factors. Gianfrancesco et al. and Graf et al. reports smoking being a contributor towards improved RA disease activity, which leads to increasing susceptibility to adverse cardiovascular events in RA patients [18,19]. This suggests that smoking cessation should be included in the RA management to help slow disease progression and lower the risk of cardiovascular conditions.

Moreover, irritative markers and disease activity scores have an essential importance for cardiovascular risk stratification in RA patients. Hansen et al. criticized the overestimation of disease activity by using subjective parameters of the DAS28, and, in particular the use of CRP levels [20]. Such an overestimation may cause the misclassification of disease severity and thus an overestimation of cardiovascular risk. A thorough evaluation including objective and subjective measures is therefore fundamental for a risk assessment and a management of RA patients and the diseases accordingly.

This research highlights a significant incidence of cardiac involvement in RA individuals, reinforcing findings from previous research [2-3]. Notably, electrocardiographic abnormalities were observed in 32.29% of patients, echocardiographic abnormalities in 73.95%, and pericardial involvement in 47.9%, consistent with prior studies reporting similar trends [4]-5].

Several cardiac symptoms showed strong associations with abnormal findings. Dyspnea (38.5%), chest pain (40.6%), tachycardia (50%), orthopnea (10.4%), syncope (14.6%), and cardiac murmurs (17.7%) were significantly more prevalent in patients with abnormal ECG and echocardiographic findings ($p < 0.05$). These connections imply that subclinical cardiac involvement is prevalent in individuals with RA, supporting the need for routine cardiovascular screening [6]. Similar trends were reported in research by Coşkun et al. and Kumar et al., where echocardiographic abnormalities were noted to be 67% and 48.9% in RA patients, respectively [7-8].

The main strengths of this investigation relate to the inclusion of multiple different cardiovascular manifestations of RA, combining ECG-detected abnormalities with echocardiographic features of RA patients. We strengthen the reported findings by including multiple clinical parameters. Furthermore, we were able to juxtapose our estimates with the existing literature which also corroborated the associations we observed. P-values afford statistical power to our results and make sure that our results are significant. This research has certain restrictions. The amount of local sample population may restrict the finding to perceived population of RA broadly. Thirdly, cross-sectional design of the research restricts us to determine causal association between RA complications and cardiovascular complications. Finally, we consider clinical and imaging findings at a single time point, while long-term progression of disease and cardiovascular outcomes are not assessed. In order to improve cardiovascular outcomes in RA patients, cardiovascular screening, should be performed regularly in routine RA management. Longer-term studies based on larger specimen are needed to establish causation and the longer-term effects of cardiovascular manifestations in RA. Moreover, smoking cessation measures should be highly promoted in RA treatment to reduce CVD risks. Furthermore, risk prediction models targeted at RA should be improved for early preventive intervention in future studies. Our study adds weight to the accumulating evidence that RA is associated with excess cardiovascular morbidity. The common occurrence of cardiovascular manifestations, electrocardiographic and echocardiographic abnormalities, and pericardial involvement highlights the importance of early detection and management. Because inflammation is a central driver of cardiovascular pathology in RA, aggressive disease control through anti-inflammatory and DMARD therapies could reduce cardiovascular risk. In RA care, lifestyle measures (smoking cessation and cardiovascular risk factors) should also come first. Our study strengthens the argument to intensify the cardiovascular follow-up of patients with RA. Research in this area needs to address the refinement of cardiovascular risk prediction models tailored to

RA; and the evaluation of whether a more aggressive approach to managing cardiovascular risk factors can decrease cardiovascular-related illness and death in RA, a high-risk group.

CONCLUSION

The present study demonstrates a strong relationship between cardiac findings and rheumatoid arthritis which should be considered in relation to clinical findings, sex and BMI. The results underline the necessity of regular cardiovascular screening among RA patients to diagnose subclinical changes as early as possible and provide early treatment. Incorporating ECG and echocardiography to the standard of care for RA can prevent complications and improve patient outcomes.

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Table I: Demographic Characteristics of the Patients (n=96)	
Variable	**Frequency (%)**
Gender	
Male	23 (24.0)
Female	73 (76.0)
Age, Mean ± SD= 48.85 ± 12.84 years	
20-40 Years	30 (31.3)
>40 Years	66 (68.8)
Body Mass Index, Mean ± SD= 26.06 ± 3.83 kg/m^2	
18-24 Kg/m^2	29 (30.2)
>24 Kg/m^2	67 (69.8)
Duration of Disease, Mean ± SD= 5.91 ± 2.26 years	
1-6 years	61 (63.5)
>6 years	35 (36.5)
Signs and Symptoms	
Dyspnea	37 (38.5)
Chest Pain	39 (40.6)
Tachycardia	48 (50.0)
Orthopnea	10 (10.4)
Syncope	14 (14.6)
Cardiac Murmurs	17 (17.7)
Electrocardiographic Abnormalities	
ST Intervals	15 (15.6)

T Waves	14 (14.6)
Echocardiographic Abnormalities	
Pericardial Involvement	46 (47.9)
Ventricular Dysfunction	44 (45.8)

Table II: Comparison of Patients with and without electrocardiographic abnormalities (n=96)

Variables, *n (%)*		***Normal ECG*** *(n = 65)*	***Abnormal ECG*** *(n = 31)*	**P-Value**
Age (years)		46.46 ± 12.92	53.87 ± 11.30	0.008*
Duration of Disease (years)		6.02 ± 2.33	5.68 ± 2.13	0.497
Body Mass Index (kg/m^2)		25.36 ± 2.99	27.53 ± 4.90	0.009*
Gender	Male	7 (30.4)	16 (69.6)	0.000*
	Female	58 (79.5)	15 (20.5)	
Dyspnea		18 (48.6)	19 (51.4)	0.002*
Chest Pain		22 (56.4)	17 (43.6)	0.050*
Tachycardia		28 (58.3)	20 (41.7)	0.049*
Orthopnea		1 (10.0)	9 (90.0)	0.000*
Syncope		6 (42.9)	8 (57.1)	0.031*
Cardiac Murmurs		8 (47.1)	9 (52.9)	0.045*

Table III: Comparison of Patients with and without echocardiographic abnormalities (n=96)

Variables, *n (%)*		***Normal Echocardiography*** *(n = 25)*	***Abnormal Echocardiography*** *(n = 71)*	**P-Value**
Age (years)		40.96 ± 10.82	51.63 ± 12.40	0.000*
Duration of Disease (years)		5.32 ± 2.17	6.11 ± 2.27	0.133
Body Mass Index (kg/m^2)		24.64 ± 2.98	26.56 ± 3.99	0.031*
Gender	Male	2 (8.7)	21 (91.3)	0.023*
	Female	23 (31.5)	50 (68.5)	
Dyspnea		5 (13.5)	32 (86.5)	0.027*
Chest Pain		3 (7.7)	36 (92.3)	0.000*
Tachycardia		7 (14.6)	41 (85.4)	0.011*
Orthopnea		0 (0.0)	10 (100.0)	0.041*
Syncope		1 (7.1)	13 (92.9)	0.071
Cardiac Murmurs		2 (11.8)	15 (88.2)	0.117