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Original Article

Internal Medicine Section

Clinical Profile of Patients with Ischaemic Heart Disease and its Correlation with Rheumatoid Factor: A Cross-sectional Study

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ABSTRACT

Introduction: Ischaemic Heart Disease (IHD) remains a leading cause of global mortality, with increasing evidence suggesting the role of inflammatory markers in its pathogenesis. While Rheumatoid Factor (RF) is traditionally associated with autoimmune conditions, its potential involvement in IHD has gained attention.

Aim: To evaluate the clinical profile of IHD patients and investigate its correlation with RF.

Materials and Methods: A cross-sectional study was conducted at Dr. D. Y. Patil Medical College and Research Centre, Pune, Maharashtra, India from November 2023 to October 2024, involving 100 IHD patients. Comprehensive clinical assessments, including detailed history, physical examination, laboratory investigations (including RF testing), Electrocardiography (ECG), and cardiac imaging, were performed. Statistical analysis was conducted using Epi Info software version 7.

Results: The study population (52% male, 48% female) showed a high prevalence of RF positivity (70%). Significant correlations were found between RF levels and cardiac parameters: a negative correlation with ejection fraction (r-value=-0.385, p-value=0.002) and positive correlations with the number of vessels involved (r-value=0.412, p-value=0.001) and C-Reactive Protein (CRP) levels (r-value=0.526, p-value <0.001). Traditional risk factors were prevalent: diabetes mellitus (52%), hypertension (40%) and dyslipidaemia (50%). Seventy-five percent of patients showed angiographic evidence of coronary artery disease, with 29% having triple vessel involvement. RF-positive patients demonstrated more severe disease manifestations across multiple parameters.

Conclusion: A significant correlation was found between RF and IHD severity, suggesting its potential utility as a marker for risk stratification. The findings support the integration of RF testing in the comprehensive evaluation of IHD patients, particularly for identifying those at risk for more severe disease manifestations.

Keywords: Autoimmunity, Cardiac biomarkers, Cardiovascular diseases, Coronary artery disease, Disease severity, Ejection fraction, Endothelial dysfunction, Immune complexes

INTRODUCTION

The IHD remains one of the leading causes of mortality and morbidity worldwide, accounting for approximately 16% of total global deaths [1]. The complex interplay between traditional cardiovascular risk factors and systemic inflammation has emerged as a crucial area of research in understanding the pathogenesis of atherosclerosis and subsequent IHD [2]. Recent evidence suggests that autoimmune mechanisms may play a significant role in the development and progression of coronary artery disease, particularly through inflammatory pathways [3]. An autoantibody commonly linked to rheumatoid arthritis, RF has garnered increasing attention in cardiovascular studies. Studies indicate that RF positivity may have a broader function than just in autoimmune disorders, as it can occur in individuals who do not have clinically evident rheumatoid arthritis [4-6]. One important component in the emergence of cardiovascular disorders is systemic inflammation, which has been linked to RF as a possible indicator. As a result, research into RF's potential as a stand-alone cardiovascular risk indicator has begun. Its effects on heart health are brought into question when RF is identified in patients who do not have rheumatoid arthritis. Therefore, in IHD, RF is being investigated as a potential biomarker for systemic inflammation.

The presence of RF has been associated with accelerated atherosclerosis, endothelial dysfunction and increased cardiovascular risk, even in the absence of clinically evident autoimmune disease [7]. The relationship between RF and IHD represents a fascinating intersection of autoimmunity and cardiovascular pathology [8]. Several mechanisms have been proposed to explain this association, including immune complex formation, complement activation and enhanced inflammatory responses within the vessel wall [9]. Understanding this relationship could potentially identify novel therapeutic targets and risk stratification strategies for patients with IHD. The clinical profile of patients with IHD who are RF-positive may differ from those who are RF-negative in terms of disease presentation, progression and outcomes [10]. This understanding becomes particularly relevant in the context of personalised medicine, where identifying specific patient subgroups could lead to more targeted therapeutic approaches and improved clinical outcomes.

This study comprehensively evaluates the clinical profile of IHD patients and investigates its correlation with RF status. By analysing clinical parameters, biochemical markers and outcomes, it explores the role of autoimmune mechanisms in IHD. This research enhances understanding of inflammation in IHD and may help identify novel therapeutic targets for better risk stratification and management. The aim of this study was to investigate the relationship between RF and IHD. The objectives include examining the clinical profile of IHD patients and exploring the correlation between RF levels and the severity of IHD.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of General Medicine, Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune, Maharashtra, India from November 2023 to October 2024. The study protocol was approved by the Institutional Ethics Committee (Approval number IESC/PGS/2023/20) and followed

the Declaration of Helsinki guidelines. Written informed consent was obtained from all participants prior to enrolment.

Inclusion criteria: Patients above 18 years with IHD, proven by echocardiography or angiography, were included in the study.

Exclusion criteria: Those with autoimmune diseases, autoimmune collagen vascular diseases, diagnosed rheumatoid arthritis, pregnancy and individuals below 18 years were excluded from the study.

Sample size: The study included 100 patients with IHD, with the sample size calculated using WINPEPI 11.3 software, considering a 50% prevalence of RF among men with IHD at a 95% confidence level and a 9% acceptable difference.

Study Procedure

A comprehensive clinical assessment was performed on all participants, including a detailed medical history and physical examination. RF titres were assessed using the serial dilution method, with titres greater than 1:80 considered significant. Cardiac evaluation comprised a 12-lead electrocardiogram, chest X-rays in the posterior-anterior view and two-dimensional echocardiography performed by experienced cardiologists to assess cardiac structure and function. All investigations were conducted in accredited laboratories following standard operating procedures, with strict quality control measures.

STATISTICAL ANALYSIS

Data was analysed using Epi Info software version 7. Quantitative data were presented as mean, median, standard deviation and ranges, while qualitative data were expressed as frequencies and percentages. Student's t-test (two-tailed) was used to test the significance of means, with a p-value of <0.05 considered significant.

RESULTS

[Table/Fig-1] demonstrates the demographic and clinical profile of the study population. The majority of patients (83%) were between 40 and 70 years of age, with a slight male preponderance (52%). Notably, 71% of patients were overweight or obese (Body Mass Index (BMI) >25 kg/m^2). Co-morbidities were highly prevalent, with a family history of IHD being the most common (62%), followed by diabetes mellitus (52%), dyslipidaemia (50%), and hypertension (40%).

Characteristics	Category	Frequency (%)
Age (years)	40-50	31 (31)
	51-60	26 (26)
	61-70	26 (26)
	>70	17 (17)
Gender	Male	52 (52)
	Female	48 (48)
Body Mass Index (BMI) (Kg/m^2)	18.5-24.9	29 (29)
	25-29.9	49 (49)
	>30	22 (22)
Co-morbidities	Diabetes mellitus	52 (52)
	Hypertension	40 (40)
	Dyslipidaemia	50 (50)
	Family H/O IHD	62 (62)

[Table/Fig-1]: Demographic and clinical characteristics (n=100).

[Table/Fig-2] reveals the cardiac assessment findings. Most patients (56%) maintained a normal ejection fraction (50-70%), while 41% showed a mild reduction (41-49%). ECG abnormalities were present in 72% of patients, with ST segment changes being the predominant finding (52%). Significantly, 75% of patients showed evidence of coronary artery disease on angiography, with 29% having triple vessel involvement.

Parameters	Category	Frequency (%)
Ejection fraction	50-70%	56 (56)
	41-49%	41 (41)
	<40%	3 (3)
ECG findings	Normal	28 (28)
	ST depression	26 (26)
	ST elevation	26 (26)
	Arrhythmia	20 (20)
Coronary vessels affected	0 vessel	25 (25)
	1 vessel	22 (22)
	2 vessels	24 (24)
	3 vessels	29 (29)

[Table/Fig-2]: Clinical parameters and cardiac assessment (n=100).

[Table/Fig-3] highlights the significant presence of RF in the study population, with 70% showing positivity. The mean laboratory values indicated elevated lipid profiles, with total cholesterol (226.5±39.5 mg/dL) and LDL (154.06±29.2 mg/dL) being above normal ranges. Inflammatory markers CRP and ESR were also elevated in the study population.

Parameters	Values	Normal value
RF status (n=100)		
RF positive	70 (70%)	Negative (typically <15 IU/mL)
Mean laboratory values (±SD)		
Total cholesterol (mg/dL)	226.5±39.5	<200
LDL (mg/dL)	154.06±29.2	<100
HDL (mg/dL)	52.5±10.7	≥40 (men), ≥50 (women)
Triglycerides (mg/dL)	173.4±72.7	<150
CRP (mg/L)	4.8±3.2	<3
ESR (mm/hr)	15.5±8.84	<15 (men), <20 (women)

[Table/Fig-3]: Rheumatoid Factor (RF) status and relevant laboratory investigations. LDL: Low density lipoprotein; HDL: High density lipoprotein; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate

[Table/Fig-4] demonstrates significant correlations between RF and cardiac parameters. A negative correlation was found with ejection fraction (r-value=-0.385, p-value=0.002), while positive correlations were observed with the number of coronary vessels involved (r=0.412, p-value=0.001) and CRP levels (r-value=0.526, p-value <0.001), suggesting that higher RF levels were associated with more severe cardiac involvement and increased inflammation.

Variable	Pearson's correlation	p-value
Ejection fraction	-0.385	0.002
Number of coronary vessels involved	0.412	0.001
CRP	0.526	<0.001

[Table/Fig-4]: Correlation of Rheumatoid Factor (RF) with key variables.

DISCUSSION

The present study revealed insights regarding the relationship between RF and IHD. Significant positive correlations were observed between the number of coronary vessels involved and RF. This study demonstrated a notably high prevalence of RF positivity (70%) among IHD patients, which was substantially higher than the findings reported by Edwards CJ et al., who found RF positivity in approximately 30% of their cardiac patients. This difference might be attributed to the study's more diverse patient population and potentially different RF detection methodologies [6]. The negative correlation between RF levels and ejection fraction (r-value=-0.385, p-value=0.002) observed in this study supports the findings of Maradit-Kremers H et al., who demonstrated that RF-positive individuals had a 1.5-fold higher risk of developing reduced ejection fraction compared to RF-negative individuals [4]. This association

suggests that RF might play a role in myocardial dysfunction, possibly through inflammatory mechanisms.

The positive correlation between RF levels and the number of vessels involved (r-value=0.412, p-value=0.001) aligns with the research by Giles JT et al., who found that RF positivity was associated with more extensive coronary artery disease on angiography [11]. Present study findings of 29% triple vessel involvement in the study population further support this association. The relationship between RF and inflammatory markers, particularly the strong correlation with CRP (r-value=0.526, p-value <0.001), corresponds with the findings of Orr CK et al., who demonstrated a significant correlation between serum CRP levels and tissue inflammation scores from knee synovium biopsy samples in patients with RA (n=197; p-value <0.0001) [12]. This reinforces the hypothesis that RF might contribute to cardiovascular pathology through inflammatory pathways.

The demographic profile of this study population showed a slight male preponderance (52%), which was lower than that reported in most cardiovascular studies. Solomon DH et al., reported a male predominance of 65% in their large-scale study of IHD patients [8]. This difference might reflect changing demographics in cardiovascular disease or regional variations in present study population. The high prevalence of traditional risk factors in this study population (diabetes mellitus 52%, hypertension 40%, dyslipidaemia 50%) was comparable to the findings of Qiu L et al., who reported similar distributions in their multicentre study [13]. However, this study uniquely demonstrates that these risk factors may have an additive effect when combined with RF positivity. The mean laboratory values, particularly the elevated lipid profiles and inflammatory markers, are consistent with the findings of Pamies A et al., who demonstrated similar patterns in their cohort of RF-positive cardiovascular patients [14]. This suggests a possible interaction between traditional cardiovascular risk factors and autoimmune mechanisms.

Catastrophic events such as aortic rupture and dissection have been identified as critical causes of sudden death, highlighting the importance of early identification and preventive strategies [15]. The findings from this study, particularly the high prevalence of RF positivity and its correlation with severe cardiac manifestations, can help identify vulnerable populations at risk for adverse cardiovascular outcomes. By integrating RF testing and addressing traditional risk factors such as obesity, hypertension and dyslipidaemia, healthcare providers can develop more effective preventive strategies to reduce the burden of IHD and its complications.

Recent studies have identified obesity as a significant risk factor in cerebrovascular diseases, including spontaneous intracranial haemorrhage [16,17]. The study also found obesity to be highly prevalent in this population, with 70% of patients being overweight or obese (BMI >25 kg/m^2). This aligns with the growing body of evidence suggesting that obesity contributes to systemic inflammation and endothelial dysfunction, which may exacerbate cardiovascular and cerebrovascular pathologies [18,19]. The high prevalence of obesity in this cohort further underscores the need for targeted interventions to address this modifiable risk factor in patients with IHD.

Limitation(s)

The study's limitations include its cross-sectional nature, which prevents the establishment of temporal relationships between RF positivity and the development of IHD. Additionally, the single-centre design might limit the generalisability of the findings to other populations.

CONCLUSION(S)

This study demonstrated a significant correlation between RF and the severity of IHD. The high prevalence of RF positivity (70%) among IHD patients, coupled with its strong correlations with reduced ejection fraction, an increased number of vessels involved, and elevated inflammatory markers, suggests its potential role both as a marker of disease severity and as a possible contributor to disease progression. The findings indicate that RF testing could be a valuable addition to the risk stratification process in IHD patients. Furthermore, the co-existence of traditional cardiovascular risk factors with RF positivity highlights the complex multifactorial nature of IHD pathogenesis. This study provides evidence supporting the consideration of RF status in the comprehensive evaluation and management planning of patients with IHD.

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