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A STUDY OF RHEUMATOID FACTOR AND ITS RELATION TO ISCHEMIC HEART DISEASE

Author: JOSHUA PRASAD K S^{1*}, PEERSAB M PINJAR²

¹Junior Resident, Dept of General Medicine, S S Institute of Medical Sciences and Research Centre, Davangere.

e-mail ID : drjoshua.prasad@gmail.com ,

Contact No : +919535142934

² Professor, Dept of General Medicine, S S Institute of Medical Sciences and Research Centre, Davangere.

e-mail ID: drpeersab@gmail.com ,

Contact No: +919886725133

***Corresponding Author and reprint request to:**

DR JOSHUA PRASAD K S, Junior Resident, Dept of General Medicine, S S Institute of Medical Sciences and Research Centre, Davangere.

e-mail ID: drjoshua.prasad@gmail.com,

Contact No : +919535142934

ABSTRACT

Introduction: Subjects with autoantibody rheumatoid factor (RF) have strong association with Rheumatoid Arthritis (RA) and have an increased prevalence of Ischemic Heart Disease (IHD). Presence of RF in general population may also share an increased likelihood of developing IHD and that RF may have a special role in the pathogenesis of IHD.

Objective: To analyse RF as an independent and additional risk factor for IHD in general population.

Methods: A cross sectional observational study was conducted on fifty patients with rheumatoid arthritis with RF positive status, attending S.S Hospital, Davangere during the study period and evaluated for IHD by ECG. All subjects included in the study had been explained about the procedure and valid informed written consent was taken. Those who are included in the study were also evaluated for traditional risk factors like h/o Diabetes, smoking (in the past / present), family h/o IHD and were clinically examined for Hypertension ,BMI for Obesity and features of RA.

Results: Among 50 patients with RF positivity, 18 (36%) were males and 32 (64%) were females. 8 patients had ischemic changes in ECG, out of which, 6 (75%) were males and 2 (25%) were females. Among 8 patients with ischemic changes, 6 patients had traditional risk factors, 4 were males (75%) and 2 were females (25%). In addition, 2 patients without traditional risk factors had ischemic changes and both of them were males.

Conclusion: RF per se can be considered as an independent risk factor for IHD in men and if associated with traditional risk factors, it increases the prevalence of IHD. However, more female patients have RF positivity, they are not vulnerable to IHD.

Keywords: Rheumatoid factor, Ischemic Heart disease, Traditional risk factors

INTRODUCTION

Ischemic heart disease (IHD) is a leading cause of death in the western world and has increased incidence in our country (India) also. Most of the subjects with IHD have one or more traditional risk factors including diabetes, smoking history, hypertension, obesity, a family history of IHD and hyperlipidemia.¹ In recent years, new risk factors for IHD have been identified, including the presence of inflammation as demonstrated by a raised highly sensitive C reactive protein (hs-CRP).² Subjects with chronic inflammatory diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus also have greatly increased risk of developing IHD.³

The autoantibody rheumatoid factor (RF) is strongly associated with Rheumatoid Arthritis (RA), may be present in subjects many years before they develop RA⁴ and its presence confers a risk of developing RA that increases with increasing titre.⁵ However RF is associated with other autoimmune rheumatic disease, viral or bacterial infections and is present in as many as 15% of normal adults.⁶ Recently, RF has been associated with an increased likelihood of developing IHD in patients with inflammatory polyarthritis.⁷

We hypothesized that the presence of RF in general population may identify the subjects with a similar immune pathology to patients with RA ,who may also share an increased likelihood of developing IHD and that RF may have special role in the pathogenesis of IHD. To explore this, we investigated whether the presence of RF was associated with an increased risk of IHD among a population of fifty patients (both males and females) with Rheumatoid Arthritis.

AIMS AND OBJECTIVES

1. To analyse RF as an independent and additional risk factor for IHD in general population.
2. To compare Rheumatoid factor between males and females in the effect of IHD (Ischemic heart disease) with or without traditional risk factors.

MATERIALS

Subjects: Patients with Rheumatoid Arthritis who were all positive to Rheumatoid factor attending S.S Institute of Medical Sciences and Research Centre, Davangere between March 2023 to July 2023.

Period of Study: March 2023 to July 2023

Sample Size: 50

Design of Study: Cross sectional observational study

Inclusion Criteria:

1. Hypertension
2. Obesity
3. Diabetes mellitus
4. History of smoking
5. History of Ischemic Heart Disease
6. Family history of Premature Coronary Artery Disease (CAD)
7. Dyslipidemia

Exclusion Criteria:

1. Chronic infection
2. Age <18 y
3. Elderly patients (>60 years)
4. Patients with thyroid abnormality
5. Patients not willing to participate in the study

Table 1. Criteria Considered in the study

S. No	PARAMETERS	VALUES
1.	Obesity	BMI >23 Kg/m ²
2.	Hypertension	BP >140/90 mmHg or on anti-hypertensive medication
3.	Diabetes Mellitus	FBS > 110 mg/dl
4.	Dyslipidemia VLDL LDL HDL TGL	>100 mg/dl >100 mg/dl < 40mg/dl >160mg/dl
5.	Family history of CAD First degree relative - Male First degree relative - Female	<55 y <65 y

METHODOLOGY

Fifty patients with rheumatoid arthritis and who were positive for RF (by ELISA method) attending S.S Hospital, Davangere during the study period evaluated for IHD by ECG.

All subjects included in the study has been explained the procedure and valid informed written consent was taken. Those who are included in the study were evaluated for traditional risk factors like h/o Diabetes, smoking (in the past / present), family h/o IHD and they were clinically examined for hypertension ,body mass index for Obesity and features of RA.

Patients with BP >140/90 mmhg were considered as hypertensives in this study. Complete Blood Count, Chest Xray, Fasting blood for sugar, lipid profile were measured.

A resting 12 lead ECG was carried out for features of IHD. The following changes in the ECG were taken as marker of ischemia

- The combination of ST elevation in a set of leads and reciprocal ST depression in a set of leads.
- Inversion of T with ST still being elevated.
- Presence of pathological Q waves

Statistical Analysis:

Patients were categorized on their Rheumatoid factor positive with or without traditional risk factors and Ischemic changes.

The significance of Association between the factors was collected using PEARSON CHI-SQUARE TEST.

$p < 0.05$ was taken as significant.

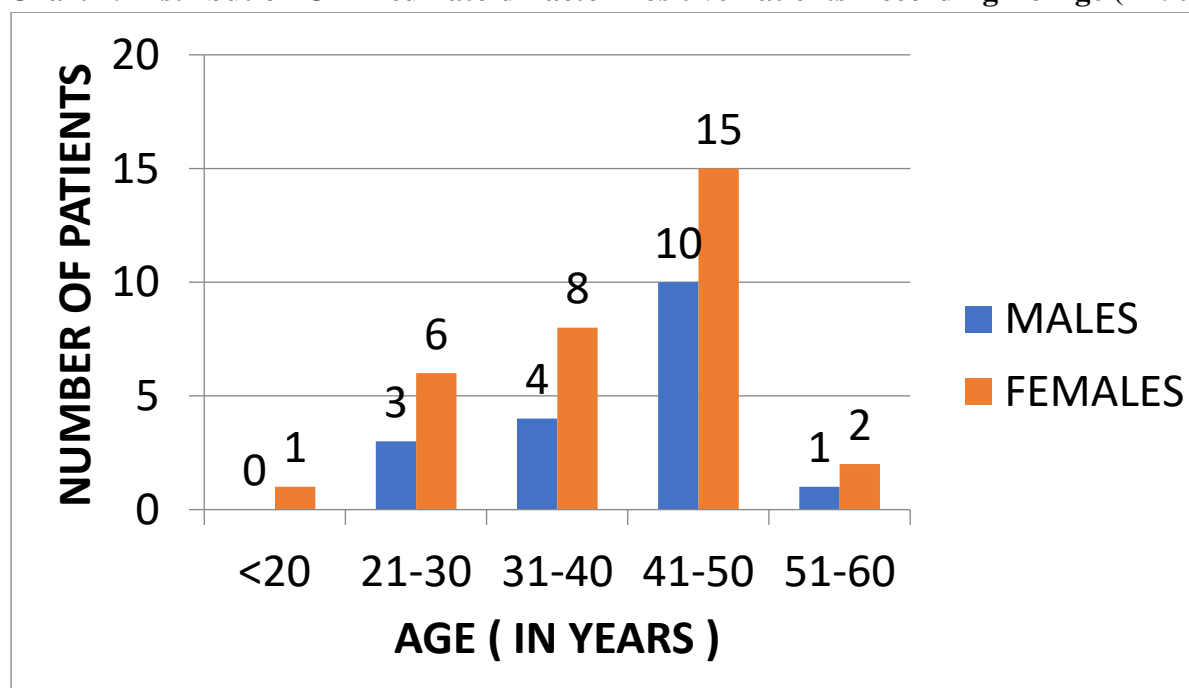
RESULTS

Table 2. Distribution of Rheumatoid Factor Positive Patients According To Age (n=50)

AGE (y)	Males	Females	Total
<20	0	1	1
21-30	3	6	9
31-40	4	8	12
41-50	10	15	25
51-60	1	2	3
Total	18	32	50

In this study, maximum number of patients, $n = 25$ (males-10 and females-15) were in the age group of 41-50 years.

Chart 1. Distribution Of Rheumatoid Factor Positive Patients According To Age (n=50)



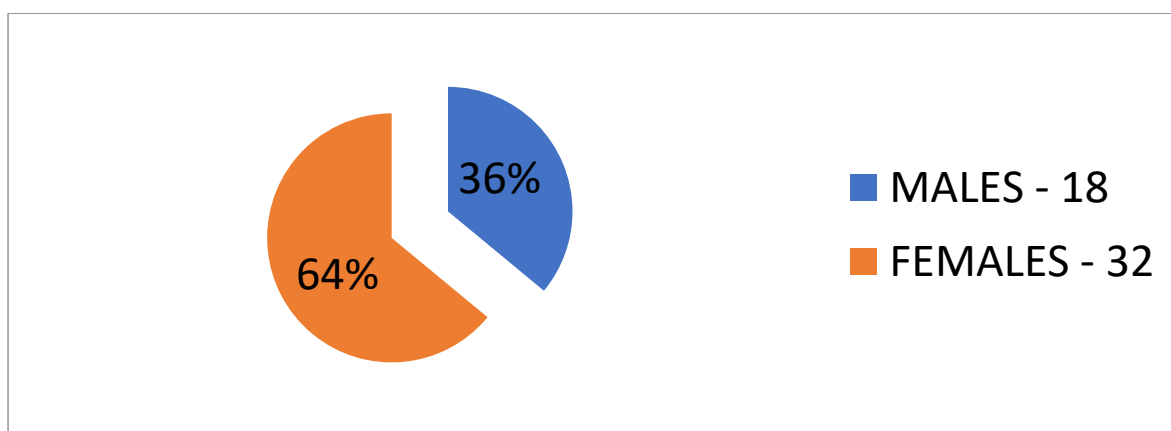
In this study, maximum number of patients, $n = 25$ (males-10 and females-15) were in the age group of 41-50 years.

Table 3. Distribution of Rheumatoid Factor Positive Patients According To Gender (n=50)

Gender	Number	Percentage (%)
Male	18	36
Female	32	64
Total	50	100

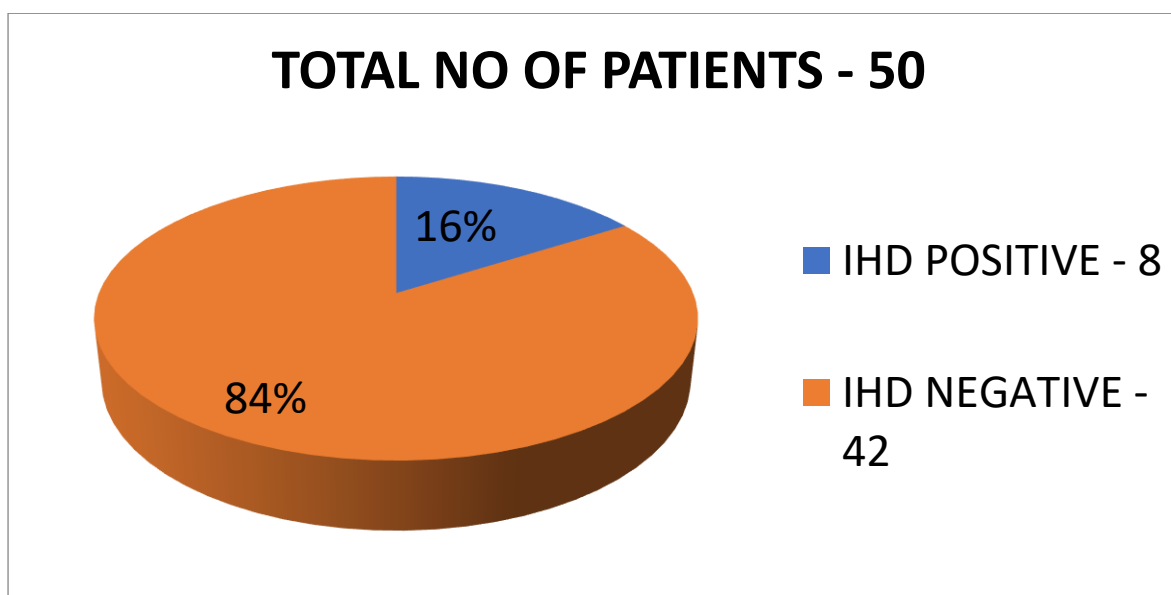
In this study, 36 % patients were males and 64 % patients were females.

Chart 2. Distribution of Rheumatoid Factor Positive Patients According To Gender (n=50)



In this study, 36 % patients were males and 64 % patients were females.

Chart 3. Ischemic Changes in RF Positive Patients



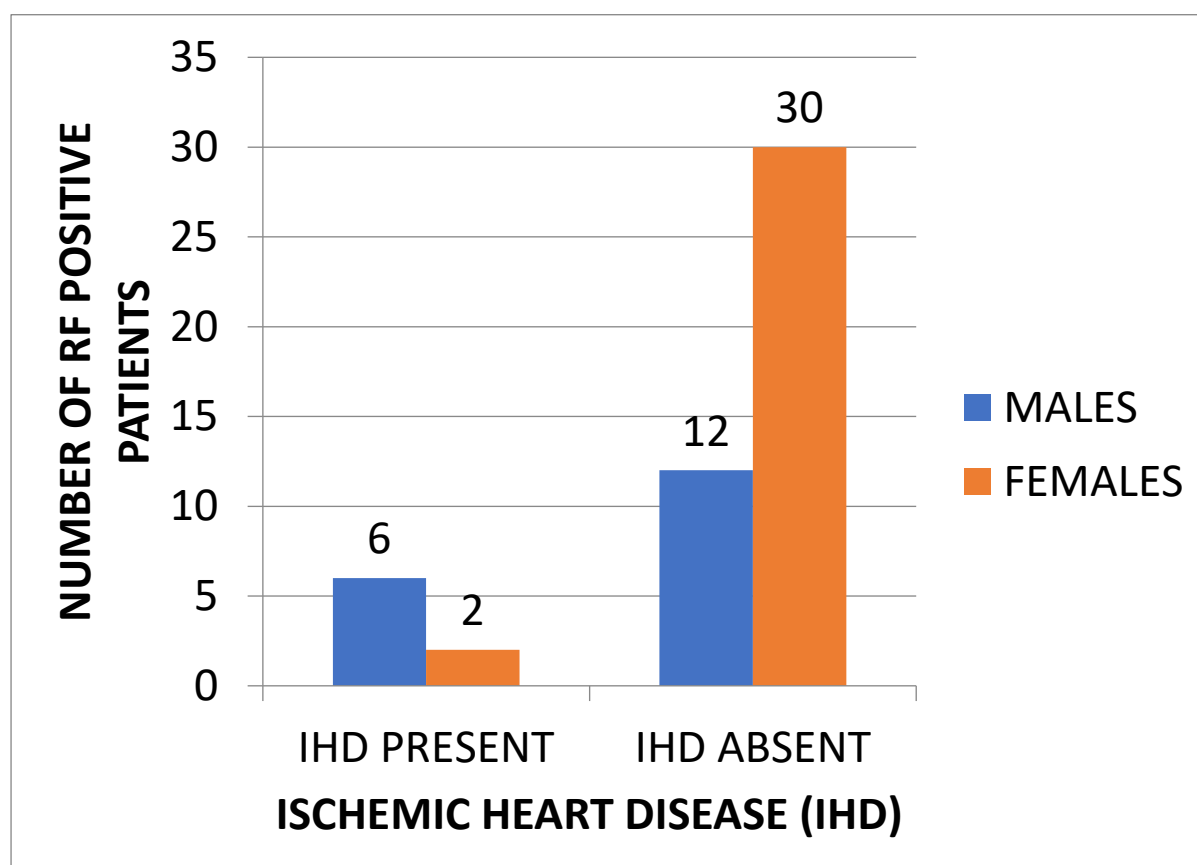
Out of 50 patients, 8 patients had IHD and 42 patients had no IHD.

Table 4. Distribution of Rheumatoid Factor Positive Patients According To Gender with respect to Ischemic Heart Disease (n=50)

Gender	IHD Present		IHD Absent		Total	
	Number	%	Number	%	Number	%
Male	6	75	12	28.57	18	36
Female	2	25	30	71.42	32	64
Total	8	16	42	84	50	100

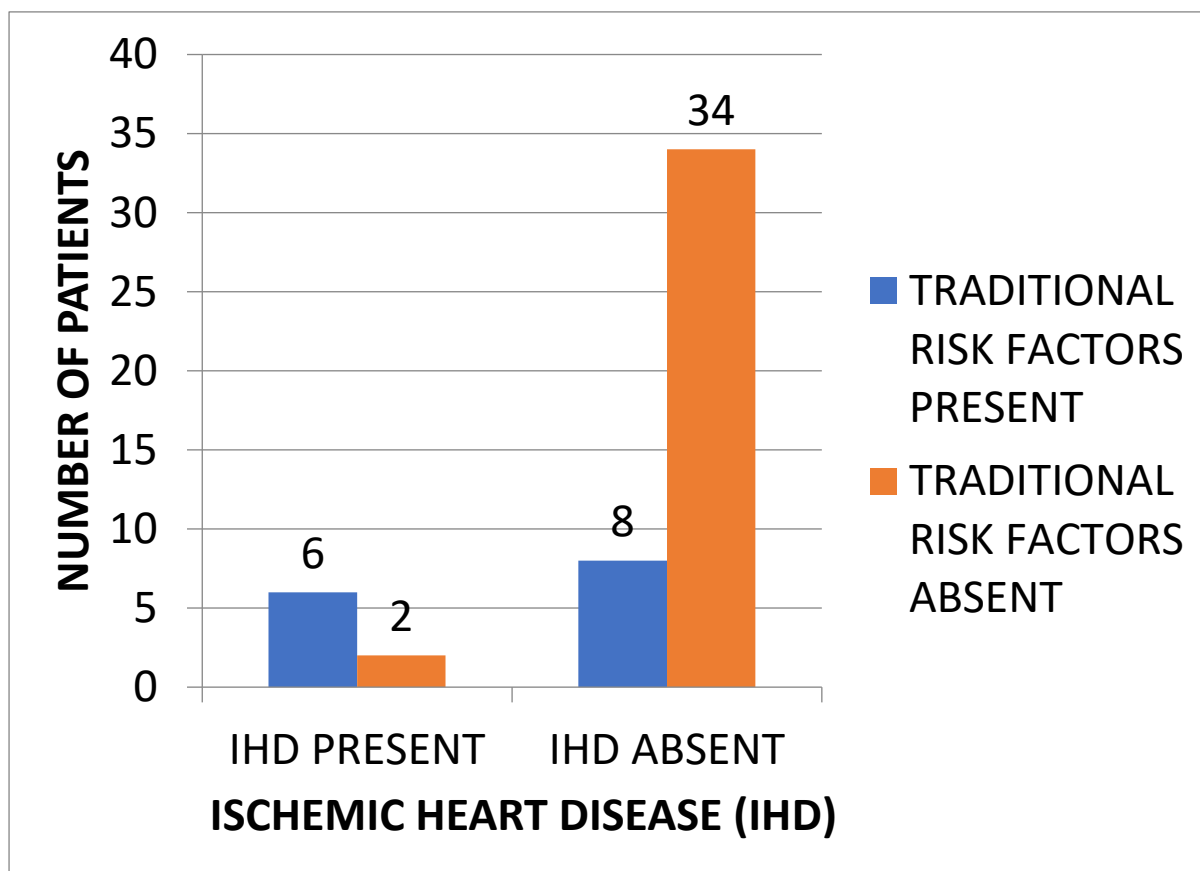
Out of 50 RF Positive patients, 8 patients have Ischemic heart disease (IHD) . Out of them, only 2 patients are females and 6 are males.

Chart 4. Distribution of Rheumatoid Factor Positive Patients According To Gender with respect to Ischemic Heart Disease (n=50)



Out of 50 RF Positive patients, 8 patients have Ischemic heart disease (IHD). Out of them, only 2 patients are females and 6 are males.

Chart 5. Distribution of Rheumatoid Factor Positive Patients with respect to Ischemic Heart Disease and Traditional Risk Factors (n=50)



- Out of 8 RF patients who had IHD, 6 had traditional risk factors present and 2 had NO traditional risk factors.
- This indicates that patients with RF positive and traditional risk factors present, they had a greater risk of developing IHD.

Table 5. Distribution of Rheumatoid Factor Positive Patients According To Gender with respect to Ischemic Heart Disease and Traditional Risk Factors (n=50)

Gender	IHD Present		IHD Absent		Total
	Traditional Risk Factors		Traditional Risk Factors		
	Present	Absent	Present	Absent	
Male	4	2	5	7	18

Female	2	0	3	27	32
Total	6	2	8	34	50

- 4 male and 2 females with RF positive with traditional risk factors had ischemic changes and 2 Male RF Positive patients without traditional risk factors had IHD.
- This indicating that males with RF and traditional risk factors have greater risk of IHD compared to females.

DISCUSSION

In the study, a total of 50 patients (who had Rheumatoid Arthritis and RF positive) of age group more than 18 years and less than 60 years were included. Most of these RF positive patients clustered between 30-50 years and maximum number of patients were within 41-50 years age group which had 25 patients (50% of the study population).

In this study 36% were males and 64% were females. The M:F ratio was 1:1.77. This is concordant with Edwards C J et al⁸ where the M:F ratio was 1 : 1.02 . In our study, females were more common in present study population. This is because the patients selected were suffering RA which is more common in females. Considering the ischemic changes, 8 patients had ischemic changes in ECG constituting 6 males (75 %) and 2 females (25 %). Males were affected more than females even though the majority of the study population were females. This is also similar to Edwards C J et al.⁸

Evaluating the 16% (n=8) who were RF positive with Ischemic changes, 6 patients had traditional risk factors (75%). The other 2 patients had only RF positivity without any traditional risk factor (25%). This indicates that patients who had RF positivity and traditional risk factors present, they had a greater risk of developing IHD.

Among the 6 RF positive patients who had traditional risk factors with ischemic changes, 4 were males (66.67 %) and 2 were females (33.33%). This is concordant with Edwards C J et al⁸ and Kenneth J Warrington et al.⁹

In this study, only 2 patients had RF positivity without any traditional risk factors along with ischemic changes and all of them were males. This is 25% of the total RF positive status with Ischemic changes and 11.11% of the total male population in the study. No female RF positive patients had IHD without traditional risk factor. This is concordant with Edwards C J et al.⁸

The long term Herfordshire Cohort study reported by Sydall H E et al¹⁰ had similar results. RF positive male patients without traditional risk factors are vulnerable to IHD. Females with traditional risk factors did not have IHD which is discordant with this study.

By these data, we can conclude that males with RF positive status and traditional risk factors have a greater risk of developing IHD when compared to females.

In this study, Autoantibody RF as per se (without any traditional risk factor) which can be stated as a risk factor for IHD in about 11.11% (2 out of 18) of men and 4% (2 out of 50) of the study population. This goes with many other similar studies from various parts of the world.

Most of the studies state the prevalence to be around 4-28%; Edwards C J et al⁸ - 11.6% (in men), Kenneth J Warrington¹ et al⁹ - 1.97% (in general population). From the observation and analysis of our study, we assumed that there is an association between RF and IHD. This association was significantly more in male patients.

However, this study has a number of potential limitations. The most important one is the type of study i.e., cross-sectional study. Accordingly, this study needs a confirmation by a longitudinal cohort study.

CONCLUSION

. This study suggests that RF is an independent risk factor for IHD in men and if associated with traditional risk factors, it increases the prevalence of IHD. However, more female patients have RF positivity, they are not vulnerable to IHD.

It also enlightens the importance of inflammation in atherosclerosis and suggests that autoimmune processes may play a part. In addition, it raises the intriguing possibility that RF may have a direct role in the pathogenesis of some subjects with IHD.

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ABBREVIATIONS

RF	: RHEUMATOID FACTOR
RA	: RHEUMATOID ARTHRITIS
IHD	: ISCHEMIC HEART DISEASE
Hs-CRP	: HIGHLY SENSITIVE C-REACTIVE PROTEIN
CAD	: CORONARY ARTERY DISEASE
VLDL	: VERY LOW DENSITY LIPOPROTEIN
LDL	: LOW DENSITY LIPOPROTEIN
HDL	: HIGH DENSITY LIPOPROTEIN
TGL	: TRIGLYCERIDE
BMI	: BODY MASS INDEX
BP	: BLOOD PRESSURE
ECG	: ELECTROCARDIOGRAM