



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

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ABSTRACT To analyse the rheumatic factor is an independent and additional risk factor for ischemic heart disease and comparing in male / female, and correlation between high titre and low titre of rheumatoid factor in the effect of ischemic heart disease with or without traditional risk factor. Patients who are all positive to Rheumatoid factor attended, Osmania General Hospital, Hyderabad, from May 2017 to October 2019. 100 patients with RF positivity. There were 70 females and 30 males, age distribution of those included in the study. The study is conducted with the maximum available resources in the hospital. The most important is the fact that this is a cross-sectional study and will need confirmation by a longitudinal cohort study

KEYWORDS : Rheumatoid Factor, Ischemic Heart Disease

INTRODUCTION

Ischemic heart disease is a leading cause of death worldwide¹.

Most of the subjects with Ischemic heart disease have one or more traditional risk factors including diabetes, smoking history, hypertension, obesity, a family history of IHD and hyperlipidemia².

In recent years new risk factors for IHD have been identified, inflammation is widely considered to be an important contributing factor of the pathophysiology of ischemic heart disease³.

In consideration of the important role that inflammatory processes play in IHD, recent work has been focused on biomarkers of inflammations demonstrated by raised highly sensitive C-reactive protein (hs-CRP)⁴.

Subjects with chronic inflammatory diseases such as rheumatoid arthritis (RA) and systemic lupus erythematosus exhibit an increased prevalence of pro-atherogenic risk factors, which may very well contribute to the burden of IHD, Cardio Vascular Disease events and atherosclerotic disease⁵.

Rheumatoid factors are antibodies directed against the Fc region of immunoglobulin G. Infections and chronic diseases may be characterised by the presence of serum rheumatoid factors, but unlike those detected in rheumatoid arthritis patients, the rheumatoid factors produced during infections are usually transient and not detrimental⁶.

The autoantibody rheumatoid factor is strongly associated with Rheumatoid Arthritis, may be present in subjects many years before they develop rheumatoid arthritis and its presence confers a risk of developing rheumatoid arthritis that increases with increasing titre. Rheumatoid factor is present in as many as 15% of normal adults⁷.

To explore this, the study was conducted to find out whether the presence of rheumatoid factor was associated with increased risk of ischemic heart disease among general population.

AIMS AND OBJECTIVES

- To analyse the rheumatic factor is an independent and additional risk factor for ischemic heart disease in general population.
- And comparing in male/female, and correlation between high titre and low titre of rheumatoid factor in the effect of ischemic heart disease with or without traditional risk factor.

MATERIALS & METHODS

Patients who are all positive to Rheumatoid factor attending Osmania General Hospital, Hyderabad, Telangana from May 2017 to October 2019.

INCLUSION CRITERIA

Hypertension, Obesity, Diabetes mellitus, History of smoking, History of IHD, Family history of IHD

EXCLUSION CRITERIA

Chronic infection, Elderly patients (>60 years), Patients with thyroid abnormality.

RESULTS

Of the hundred patients with RF positivity, there were 70 females and 30 males, age distribution of those included in the study.

Table:1

1	Total Numbers of Patients (n)	100
	Female	70
	Male	30
2	Age	
	<40 years	44
	40-60 years	56
3	ECG-Ischemic Changes	
	Total	20
	A. With Traditional Factors	14
	Male	10
	Female	4
	B. Only RF positive	6
	Male	5
	Female	1
	High Titre- RF	4
	Low Titre-RF	2

TABLE-2: Sex Distribution of Ischemic Changes in Relation to RF Positivity with varying titres:

Ischemic changes in ECG (N=20)			
Male (15)		Female (5)	
RF-High Titre 10 (50%)	RF-Low Titre 5 (25%)	RF-High Titre 2 (10%)	RF-Low Titre 3 (15%)

In the present study there were 20 patients who had RF positivity with Ischemic changes in ECG. 15 were males and 5 were females. Of these 10 males and 2 females had high titre of RF with ischemic changes.

Thus the majority of patients with high titre of RF along with ischemic changes are males.

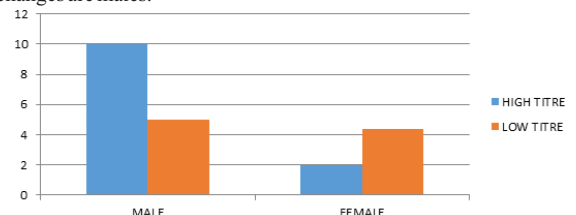


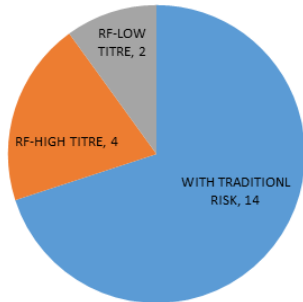
TABLE- 3: Sex Distribution in Relation to Ischemic Changes in Lone RF Positive and Titres

Sex	Rheumatoid Factor	ECG Ischemic Changes			
		Present		Absent	
		Number	Percent	Number	Percent
Male	High Titre	4	100%	-	-
	Low Titre	1	7.14%	13	92.86%
Female	High Titre	0	-	18	100%
	Low Titre	1	3%	33	97%

Subjects with ischemic changes with RF positivity alone without the presence of traditional risk factors were tabulated above with sexual differentiation and also with respect to varying titres of RF.

Table: 4 Sex Distribution in relation to Ischemic Changes in lone RF Positive and Titres:

Ischemic Changes in ECG (N=6)			
Male (5)		Female(1)	
RF-High Titre	RF-Low Titre	RF-High Titre	RF-Low Titre
4 (80%)	1 (20%)	0	1

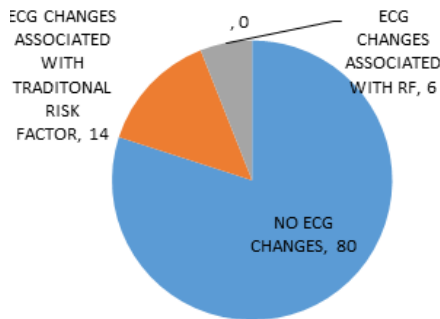


In the present study Lone RF without traditional risk factors was seen in only 5 male patients, with only one female patient .Of the 5 male patients 4 had high titre RF (>320). Considering the association of traditional risk factors and additional risk factor with RF positivity, 14 had ischemic changes.

Table: 5 Ischemic changes in relation to RF with and without traditional risk factors in percentage

RF with Traditional risk factors	ECG Ischemic Changes			
	Positive		Negative	
	Number	Percentage	Number	Percentage
Present	14	50%	14	50%
Absent	6	8.33%	66	91.66%

Subjects with ischemic changes in RF positive with traditional risk factors are 50% without traditional risk factors are 8.33 %.



DISCUSSION

In the study population, most of the RF positive patients clustered between 30-50 years. Dividing the study population with ischemic changes by ECG, by age, 25% were below 40 years and 75% were above 40 years. All of the above patients had RF positivity along with traditional risk factors and ischemic changes in the ECG.

In this study 30% were males and 70% were females. The M:F ratio was 1:2.33. 20 patients had ischemic changes in ECG constituting 15 males (50%) and 5 females (7.14%) patients of the total study population. This is concordant with Edwards C J et al⁸

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Most of the of the studies state the prevalence to be between 4-28%. Edwards C J et al. 11.6% (in men), Kenneth J Warrington1 et al 4-1.97% (in general population).

Among these 5 patients were males and there was only one female. This indicates an association of RF and IHD a strong possibility especially in males.

Of these 5 male patients, 4 patients had high titre of RF positivity which is 80% and one patient had low titre of RF which is 20%. This concurs with the earlier study by Edwards C J et al and del Puente A et al⁹.

In this study, Autoantibody RF which is risk factor for IHD in men is 16.66% (5 out of 30); confidence interval(CI) is 5-28 and 5% (5 out of 100) study population.

A study done on Effect of rheumatoid factor on mortality and coronary heart Disease by Gunnar Tomasson, Thor Aspelund et al showed that of 11,872 subjects, 140 had positive RF. A total of 2385 subjects (20.4%) died from cardiovascular disease and this rate was higher among RF-positive subjects than Rf¹⁰.

This non-cardiovascular mortality was also associated with positive RF status (Hazard ratio 1.40, 95% Confidence interval 1.06 to 1.85) adjusted for age and sex (RF-positive subjects had increased all-cause mortality (Hazard ratio 1.47, 95% Confidence interval 1.19 to 1.80) and cardiovascular mortality (Hazard ratio 1.57, 95% Confidence interval 1.15 to 2.14) after adjusting for age and sex.

In a general population cohort, RF was associated with increased all-cause mortality and cardiovascular mortality after adjustment for cardiovascular risk factors, even in subjects without joint symptoms.

A study done on RF do not predict cardiovascular disease and mortality in the general population in the Busselton Health Survey by Johannes Nossent, Warren Raymond et al¹¹ done on 2,323 participants (46% male, mean age 50 years) free of CVD at baseline in 1972.

The predictive value of RF for coronary heart disease, all cardiovascular disease and all-cause mortality was estimated by adjusted hazard ratios (HR) from Cox regression models. After adjustment for standard risk factors, RF positivity was not predictive of future CHD (HR 1.05), CVD (HR 1.04) or mortality (HR 1.03) in the full CVD-free cohort.

This study showed that RF detected by Latex agglutination do not independently predict future CHD, CVD or death in the general population. However, the presence of RF in is associated with a moderate, borderline significant increase in the long term adjusted risk for all-cause mortality.

A study by Susanna Sihvonen, MarkkuKorpela et al on The predictive value of rheumatoid factor isotypes, anti-cyclic citrullinated peptide antibodies, and antineutrophil cytoplasmic antibodies for mortality in patients with rheumatoid arthritis done on 604 patients with RA participating in a cross-sectional study in 1987.

Results of that study were the 604 patients with RA, 55% were positive for RF, 66% for anti-CCP, and 14.5% for perinuclear ANCA. Twelve patients (19%) with RF were anti-CCP-negative and 34 (40%) without RF were anti-CCP-positive. Of the total 604 patients, 160 had died by 1999. Positive RF and high IgA and IgM RF levels predicted increased mortality, while positive anti-CCP or ANCA did not. However, high anti-CCP levels were related to an increased mortality risk. The study shows that the Patients with positive RF, especially IgA and IgM isotypes, carry a risk of dying earlier than patients without these serological findings.

From the observation and analysis of study, it is assumed that there is an association between high titre of RF and IHD. This association was significantly more in male patients.

This study has a number of potential limitations. The study is conducted with the maximum available resources in the hospital. The most important is the fact that this is a cross-sectional study and will need confirmation by a longitudinal cohort study.

CONCLUSIONS

1. RF per se can be considered as one of the risk factor for Ischemic Heart disease in males.

2. High titre RF alone can further increase the Incidence of IHD.
3. RF associated with traditional risk factors increase the prevalence of IHD.
4. Though more female patients have positive RF, they are not vulnerable to IHD.

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