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Original Research Article

Case Control Study of Dyslipidemia in Rheumatoid Arthritis in Correlation with Rheumatoid Factor and C-Reactive Protein

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Abstract

Introduction: Rheumatoid arthritis (RA) is a systemic chronic autoimmune disease characterized by symmetric polyarthritis. It is also proved that patients with RA are more prone for premature atherosclerosis resulting in cardiovascular accidents (CVA). Alterations in lipid profile is commonly seen in these patients. We conducted this study to compare lipid profile of patients with RA with Rheumatoid factor (RF) and C-reactive protein (CRP). *Materials and methods:* A prospective case-control study was conducted on 50 patients with rheumatoid arthritis and 50 healthy controls. Blood samples obtained from such patients attending out-patient department were tested for RF, CRP and lipid profile including total cholesterol, high-density lipoproteins (HDL), low-density lipoprotein (LDL) and triglyceride (TGL). *Results:* In our study, we did not find strong positive or negative correlation between RF, CRP and lipid profile. We noted a weak positive correlation between RF and LDL and total cholesterol (TC). We also observed a weak negative correlation between RF and TGL, HDL and very low -density lipoprotein (VLDL). There was a weak positive correlation between CRP and LDL and a weak negative correlation between CRP and TC, HDL, VLDL and TGL. *Conclusion:* In our study we could not find any gross variation in lipid profile in patients with RA but there was a weak correlation between RF, CRP and lipid profile. This could be due to small sample size. Future studies with large sample size may help to give a satistically significant correlation.

Keywords: Rheumatoid arthritis; Lipid profile; Cardiovascular accidents; C-reactive protein.

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Introduction

Rheumatoid arthritis (RA) is a systemic chronic autoimmune disease characterized by symmetric polyarthritis of peripheral joints.[1] It is characterized by varying degrees of damage of joints resulting in deformities, functional limitations and reduction in quality of life and increase in mortality. It has female preponderance with a peak incidence in young age.[2] RA can

progresss to involve extraarticular sites resulting in vasculitis, rheumatoid nodules, respiratory and cardiovascular diseases, anemia of chronic disease and entrapment neuropathies.[3] It is evident from many epidemiological studies that patients with RA have enhanced risk of premature atherosclerosis resulting in increased mortality from cardiovascular accidents (CVA).[4] The chief predictors of CVA are serum concentrations of low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides (TGL). Inflammation is a constant feature in RA which is implicated in accelerated atherosclerosis leading to risk of CVA.[5] We conducted this study to compare lipid profile of patients with RA with Rheumatoid factor (RF) and C-reactive protein (CRP).

Materials and Methods

Setting: Department of Pathology and Orthopedics, Sanjay Gandhi institute of trauma and orthopaedics, Bengaluru.

Type of study: A prospective case—control study was conducted on 50 patients with rheumatoid arthritis and 50 healthy controls.

Sampling method: A prospective study was conducted from October 2017 to October 2018 on fifty patients with Rheumatoid arthritis fulfilling the revised criteria of the American College of Rheumatology with positive RF and fifty age and sex matched healthy controls without history of inflammatory disease.

Sample collection: Blood samples obtained from such patients attending out-patient department at SGITO were tested for RF, CRP and lipid profile including total cholesterol, HDL, LDL and TGL.

RF and CRP were measured by turbidometric immunoassay by Coral Clinical systems (Division of Tulip Diagnostics (P) Ltd). The normal cut off value for RF was <20 mg/dl and CRP was <0.6 mg/dl. Lipid profile was determined using BS 300 on overnight fasting sample. The normal range for total cholesterol, HDL, LDL and TGL are <200 mg/dl, 60 mg/dl, 60–130 mg/dl and <150 mg/dl respectively.

Inclusion criteria

Cases: Subjects fulfilling revised criteria of American College of Rheumatology.

Controls: Healthy individuals without evidence of inflammatory disease.

Exclusion criteria

Cases: Subjects not fulfilling revised criteria of American College of Rheumatology.

Controls: Subjects with clinical and laboratory evidence of inflammation.

Ethical clearance: Obtained

Statistical methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean +/- SD (Min-Max) and results on categorical measurements are presented in numbers and percentages. The 2-tailed Pearson correlation coefficient is used to establish correlation between two parameters. Coefficient values range from +1 to –1, +1 indicates a perfect positive relationship, –1 indicates a perfect negative relationship and 0 indicates that no relationship exists.

Coefficient value between +/– 0.50 and +/– 1: strong correlation

Coefficient value between +/– 0.30 and +/– 0.49: moderate correlation

Coefficient value below 0.29: weak correlation

Results

In the present study, 27 (54%) among cases and 33 (66%) among controls were females showing a slight female preponderance. Among cases, 15 (30%) were in the age group of 31–40 years, followed by 10 (20%) in 41–50 years age range.

In our study, we did not find strong positive or negative correlation between RF, CRP and lipid profile. We noted a weak positive correlation between RF and LDL and TC (Table 1 & 2). We also observed a weak negative correlation between RF and TGL, HDL and VLDL (Table 3, 4 & 5). There was a weak positive correlation between CRP and LDL (Table 6) and a weak negative correlation between CRP and TC, HDL,VLDL and TGL (Table 7, 8, 9 & 10).

Among cases the mean TC value was 181.42 mg/dl, mean HDL was 50.73 mg/dl, mean LDL was 103.27 mg/dl and mean TGL was 140.73 mg/dl. Among controls the mean TC value was 185.11 mg/ dl, mean HDL was 44.57 mg/dl, mean LDL was 102.15 mg/dl and mean TGL was 166.45 mg/dl. There was not much variations noted in lipid profiles of cases and controls in our study.

Table 1: Correlation between RF and TC

Correlations			
		Total Cholesterol	**RF**
Total Cholesterol	Pearson Correlation	1	0.049
	Sig. (2-tailed)		0.738
	N	49	49
RA	Pearson Correlation	0.049	1
	Sig. (2-tailed)	0.738	
	N	49	49

Table 2: Correlation between RA and LDL

Correlations			
		RA	**LDL**
RA	Pearson Correlation	1	0.087
	Sig. (2-tailed)		0.553
	N	49	49
LDL	Pearson Correlation	0.087	1
	Sig. (2-tailed)	0.553	
	N	49	49

Table 3: Correlation between RF and TGL

Correlations			
		RA	**TGL**
RA	Pearson Correlation	1	–0.020
	Sig. (2-tailed)		0.892
	N	49	49
TGL	Pearson Correlation	–0.020	1
	Sig. (2-tailed)	0.892	
	N	49	49

Table 4: Correlation between RF and HDL

Correlations			
		RA	**HDL**
RA	Pearson Correlation	1	–0.051
	Sig. (2-tailed)		0.730
	N	49	49
HDL	Pearson Correlation	–0.051	1
	Sig. (2-tailed)	0.730	
	N	49	49

Table 5: Correlation between RF and VLDL

Correlations			
		RA	**VLDL**
RA	Pearson Correlation	1	–0.049
	Sig. (2-tailed)		0.738
	N	49	49
VLDL	Pearson Correlation	–0.049	1
	Sig. (2-tailed)	0.738	
	N	49	49

Table 6: Correlation between CRP and LDL

Correlations			
		CRP	**LDL**
CRP	Pearson Correlation	1	0.040
	Sig. (2-tailed)		0.782
	N	49	49
LDL	Pearson Correlation	0.040	1
	Sig. (2-tailed)	0.782	
	N	49	49

Table 7: Correlation between CRP and TC

Correlations			
		Total Cholesterol	**CRP**
Total Cholesterol	Pearson Correlation	1	–0.167
	Sig. (2-tailed)		0.250
	N	49	49
CRP	Pearson Correlation	–0.167	1
	Sig. (2-tailed)	0.250	
	N	49	49

Table 8: Correlation between CRP and HDL

Correlations			
		CRP	**HDL**
CRP	Pearson Correlation	1	–0.212
	Sig. (2-tailed)		0.143
	N	49	49
HDL	Pearson Correlation	–0.212	1
	Sig. (2-tailed)	0.143	
	N	49	49

Table 9: Correlation between CRP and VLDL

Correlations			
		CRP	**VLDL**
CRP	Pearson Correlation	1	–0.226
	Sig. (2-tailed)		0.118
	N	49	49
VLDL	Pearson Correlation	–0.226	1
	Sig. (2-tailed)	0.118	
	N	49	49

Table 10: Correlation between CRP and TGL

Correlations			
		CRP	**TGL**
CRP	Pearson Correlation	1	–0.241
	Sig. (2-tailed)		0.095
	N	49	49
TGL	Pearson Correlation	–0.241	1
	Sig. (2-tailed)	0.095	
	N	49	49

Discussion

Rheumatoid arthritis (RA) is a chronic systemic disorder characterized by symmetrical chronic polyarthritis which later progresses to result in joint damage, compromising the quality of life and finally increasing morbidity and mortality.[6] It characteristically affects middle-aged individuals with female preponderance, with increasing incidence with age.[7] It manifests with other extra-articular manifestations like rheumatoid nodules, heart or lung disease, vasculitis, entrapment neuropathies and anaemia of chronic disease.[3]

There are evidences suggesting that patients with RA have increased morbidity and mortality which can be attributed to enhanced incidence of cardiovascular disease (CVD).[8] This increased CVD risk is attributed to premature atherosclerosis which may be primarily related to chronic inflammation and secondarily due to physical inactivity and medications.[9] Atherogenic lipid profile is seen in RA and inflammation is a common factor playing a pivotal role in RA and atherosclerosis. There are many evidences emphasizing the role of inflammatory cytokines macrophage migration inhibitory factor, interleukin-1 (IL-1), IL-6, and tumor necrosis factor (TNF), in the pathogenesis of both RA and atherosclerosis.[11] Thus we conducted this study to analyze the alterations in lipid profile in patients with RA who were positive for RF and CRP in comparison with healthy controls.

In our study, we did not find strong positive or negative correlation between RF, CRP and lipid profile. We noted a weak positive correlation between RF and LDL and TC. We also observed a weak negative correlation between RF and TGL, HDL and VLDL. There was a weak positive correlation between CRP and LDL and a weak negative correlation between CRP and TC, HDL, VLDL and TGL. Though there was no strong correlation observed between RF, CRP and lipid profile, there was a weak correlation suggesting alteration in lipid profile in patients with RA. Including more number in the study groups may be required to obtain a statistically significant association.

A study by Rizzo et al. showed that RA patients had elevated levels of plasma TGL and decreased levels of HDL with normal total cholesterol and LDL levels.[11] It was found that lipid abnormalities are frequent in Indian patients with RA with decreased HDL being the common defect.[12] It was demonstrated by Toms et al. that 2% to 26% of patients with RA without cardiovascular disease were dyslipidemic and required therapy with statins. This altered lipid profile in RA was postulated to be due to systemic inflammation excluding genetic, lifestyle and drug factors.[13]

There are latest evidences which hypothesize a contradictory effect of HDL being cardioprotective. It has been postulated that in chronic inflammatory conditions like RA, there is presence of nonprotective "proinflammatory HDL" which favors accumulation of oxidized phospholipids in LDL cholesterol.[14] It is also been suggested that presence of other inflammation- induced factors like oxidative stress, insulin resistance, prothrombotic state, endothelial dysfunction, increased homocysteine levels and non-inflammatory factors like genetic polymorphism and antirheumatic drugs contribute to CVD in RA.[15]

There are not enough reports to establish the association of lipid levels with disease activity in RA. Only a few studies were successful in establishing this association. Many studies have demonstrated an association of lipid levels with CRP.[16] This was contradictory to a latest US registry study.[17] In our study we could only establish a weak association between lipid levels and CRP.

Conclusion

In our study we could not find any gross variation in lipid profile in patients with RA but there was a weak correlation between RF, CRP and lipid profile. This could be due to small sample size. Future studies with large sample size may help to give a satistically significant correlation.

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