

Correlation between CRP and Atherogenic Index and Assessment of Cardiovascular Disease Risk in Patients with Rheumatic Arthritis

Sabira Dabeer¹, Neha Sharma², Abhay Nagdeote³

^{1,2}Geetanjali Medical College and Hospital, Udaipur, Rajasthan, India.

³ESI-PGIMSAR and Model Hospital, Andheri, Mumbai, Maharashtra, India.

Corresponding Author: Dr Sabira Dabeer

ABSTRACT

Background- Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease, which affects approximately 1-2% of the world's population with an annual incidence rate of between 0.5% and 1%. Most common cause of morbidity and mortality in RA is cardiovascular disease.

Aim & Objective-: To find out atherogenic index (AIP) in patients with RA and study the correlation between CRP(C- reactive protein) and AIP.

Methods:- A prospective cross sectional observational study was done in biochemistry department of ESIPGIMSAR & Model hospital Andheri Mumbai from January 2015 to August 2016. This study involved 100 subjects between the age group of 30-50 years, including age and sex matched control. Parameters included were RA factor, anti-ACCP, CRP, ESR and fasting lipid profile (HDL-C, LDL-C, TG, VLDL-C and total cholesterol).

Results:- Deranged lipid profile with high AIP (0.52 ± 0.14) and a positive Pearson coefficient of correlation ($r = 0.98$) between AIP and CRP was found in patients with rheumatoid arthritis.

Conclusion: - Chronic inflammation in rheumatoid arthritis causes dyslipidemia leading to high risk of cardiovascular diseases in RA patients.

Keywords: Dyslipidemia, atherosclerosis, cardiovascular diseases, inflammation, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease, which affects approximately 1-2% of the world's population with an annual incidence rate of between 0.5% and 1%. [1] RA has female: male ratio of 3:1 and has a peak age of onset between forty and seventy years of age. [2] Most common cause of morbidity and mortality in RA is cardiovascular disease and atherosclerosis is most common cause of cardiovascular disease. There is

lack of literature between risk of cardiac diseases and RA patients. Estimation of serum biochemical parameters such as total cholesterol, triglyceride, VLDL-C, HDL-C and LDL-C and atherogenic index (AIP) may prove beneficial in assessing cardiovascular risk in patients with RA. So, the present study has been carried out to investigate the serum levels of above mentioned parameters in patients with rheumatoid arthritis.

MATERIALS AND METHODS

This cross sectional, observational study was performed at ESI-PGIMSR and Model Hospital, Andheri, Mumbai, from January 2015 to August 2016. A total of 100 subjects between the ages of 30 to 50 years were included. After explaining the study procedure, detailed clinical history and relevant clinical examination was done and written consent was taken from all the subjects. The 100 subjects were divided into two groups.

Group A: - 50 patients with diagnosed RA as per ACR-EULAR guidelines, having score more than 6 and positive for either anti-CCP (Anti-cyclic citrullinated peptide) or RF factor. These patients were selected from patients attending outpatient department of medicine and orthopedic Outpatient Department and ward.

Group B: - 50, age and sex matched healthy normal subjects not suffering from RA (negative for anti-CCP & RF factor) were enrolled as control group.

Inclusion criteria:

Diagnosed cases of RA having ACR-EULAR score more than equal to 6 were included with either positive for anti-CCP or RF factor, abnormal ESR & CRP, involvement of more than one joint and duration of symptoms more than 6 weeks.

Exclusion criteria: Patients with ACR-EULAR score less than 6, negative anti-CCP and RF factor, Diabetes Mellitus, hypothyroidism, liver and renal diseases,

family history of dyslipidemia, metabolic syndrome, smokers and those taking lipid lowering drugs, vitamin E supplements, oral contraceptive pills, thyroxin & β - blockers and having any other systemic illness were excluded from this study.

5 ml blood samples were collected in plain and EDTA tubes for estimation of various parameters. Serum lipid profile, CRP and Anti-CCP were done on Cobas 6000. [3-8] RA factor was done by latex slide test method. [9] AIP was calculated by Log TG/HDL. [10] VLDL was calculated using Friedewald formula.

RESULTS

Microsoft Office Excel 2007 was used for all calculations and SSPS software version 11.5 was used for statistical analysis. Student's unpaired, two tailed t-test was used to analyze all statistical data. P-value less than 0.05 ($P < 0.05$), less than 0.001 ($P < 0.001$) and more than 0.05 ($P > 0.05$) were considered statistically significant (S), highly significant (HS) and non-significant (NS) respectively. Pearson coefficient of correlation was calculated between CRP and AIP.

Table 1: Prevalence of CRP, RF & ACCP (Anti-CCP) in all groups

Parameters	Group A (Case) Positive	Group A (Case) Negative	Group B (Control) Positive	Group B (Control) Negative
RF Factor	37 (74%)	13 (26%)	0	50
ACCP	24 (48%)	26 (52%)	0	50

Table shows prevalence of case and control

Table 2: Comparison of mean ESR and ACCP (Anti-CCP) values in all groups

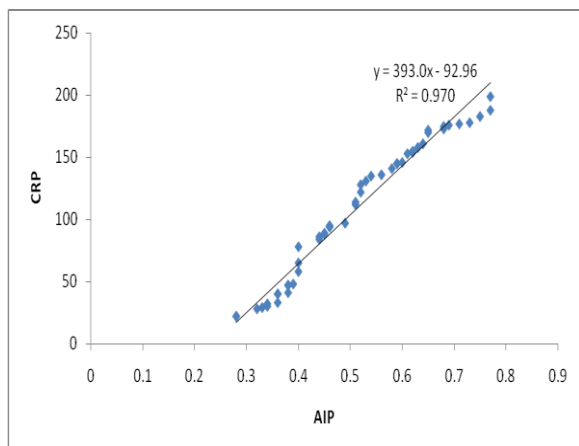
Parameters	Group A(Case)	Group B(Control)	t test	p value
ESR	48.04±21.70	13.10±7.48	10.65	<0.001* HS
ACCP	50±51.78	9.24±0.86	5.50	<0.001*HS
CRP	108.28±55.02	4.82±3.4	13.3	<0.001*HS

* HS; highly significant, comparative analysis of various groups

Table 3: Comparison of mean lipid profile parameters in all groups.

Parameters	Group A(n=50) Mean±SD CASE	Group B(n=50) Mean±SD CONTROL	t test	p value
Total cholesterol(mg/dl)	193.96±23.01	167.08±20.93	6.04	<0.001* HS
LDL-C (mg/dl)	120.61±21.83	96.28±21.12	5.6	<0.001* HS
HDL-C (mg/dl)	30.32±3.30	44.90±8.27	11.45	<0.001* HS
VLDL-C (mg/dl)	46.90±13.94	25.11±5.54	10.16	<0.001* HS
Triglyceride (mg/dl)	234.50±70	125.56±27.70	10.16	<0.001* HS
AIP	0.52±0.14	0.09±0.13	15.10	<0.001* HS

* HS; highly significant, lipid profile values shows in various case and control group.



Graph 1: Pearson coefficient of correlation between CRP and AIP of Group A.

The Pearson coefficient between CRP and AIP in rheumatoid arthritis patient was found to be $r=0.98$.

DISCUSSION

Rheumatoid arthritis (RA) is a chronic inflammatory disease of autoimmune origin. [1,2] Cytotoxic T-cells, plasma cells and pro-inflammatory cytokines (TNF- α , IL-1) are involved in its pathophysiology. These inflammatory markers are not restricted to the articular tissue but are present in systemic circulation as well and are responsible for extra-articular manifestations of RA. Altered lipid profile due to systemic inflammation causes early atherosclerosis resulting in increased incidence of cardiovascular morbidity and mortality in RA. [11]

Atherogenic index of plasma (AIP) is considered a better marker to evaluate atherogenic lipid profile as compared to individual lipid component. [10] All the participants were evaluated for Anti-CCP, RF, CRP & ESR to confirm the diagnoses.

In group A, RA factor positive and negative cases were 74% and 26% respectively. Anti-CCP positive and negative cases were 48% and 52% respectively. 26% were positive for both Anti-CCP & RA factor. All 50 participants of group A were positive for rheumatoid arthritis. Controls were negative for the same. (Table-1).

Table -2 shows mean serum value of Anti-CCP for group A (50 ± 51.78) which is

higher than group B (9.24 ± 0.86) and was statistically significant ($p<0.001$). [12,13,14]

The mean ESR (48.04 ± 21.70) and CRP (108.28 ± 55.02) of group A were higher than group B, ESR (13.10 ± 7.48) and CRP (4.82 ± 3.4) and were statistically significant ($p<0.001$).

Table- 3 shows, mean \pm SD for TC, TG, HDL-C and LDL-C level of group A (193.96 ± 23.01) mg/dl, (234 ± 70)mg/dl, (30.32 ± 3.30), A (120.61 ± 21.83) as compared to group B (167 ± 20.93) mg/dl, (125.56 ± 27.70) mg/dl, (44.90 ± 8.27) mg/dl and (96.28 ± 21.12)mg/dl, respectively. We found statistically significant p – value for the same ($p<0.001$). Similarly, the mean of serum VLDL-C level for group A (46.90 ± 13.94) mg/dl was high as compared to group B (25.11 ± 5.54) mg/dl ($p<0.001$). Our results were consistent with the study of Batún Garrido JA et al and Lakatos J. [15,16] Even though the production of cholesterol decreases in RA but, due to increase inflammation its clearance from body decreases. This along with the lack of physical activity due to pain and stiffness may cause elevated levels of TC. TG is mainly transported in VLDL-C; therefore, hypertriglyceridemia occurs because of either increase production or impaired clearance of VLDL-C. We have not found more studies related to AIP.

Various cytokines released during inflammation like TNF- α disturbs lipoprotein metabolism by reducing the activity of lipoprotein lipase. This causes rise in TG and VLDL-C levels. Inflammation, alter the normal structure and composition of LDL-C thus their normal uptake by hepatocytes decrease and uptake by macrophages increases. Inflammation also decreases enzyme activity of hepatic lipase, LCAT (lecithin-cholesterol acyltransferase), CETP (cholesteryl ester transfer protein), due to which HDL-C can no longer carry out reverse transport of cholesterol. The HDL-C particles are phagocytosed by macrophages, hence reduced HDL-C levels are observed in RA patients. [17]

The mean AIP of group A 0.52 ± 0.14 was significantly higher than group B 0.09 ± 0.13 ($p < 0.001$) which shows that the derangement in lipid profile of group A is more than that of group B. AIP reflects relationship between protective and atherogenic lipoprotein. It has been suggested that an AIP values of, under 0.11, between 0.11 and 0.2 and value more than 0.21 are associated with low, intermediate and high risk of CVD respectively. ^[10]

In present study we found a positive correlation between CRP and AIP, the Pearson coefficient (r) between CRP and AIP was 0.98 in RA patients. This shows that as inflammation increases CRP increases and so is the AIP and hence the risk of cardiovascular diseases in RA patients.

Abnormal lipid profile due to chronic inflammation is a predisposing factor for early atherosclerosis and increased risk of cardiovascular disease in RA patients than in general population. Early diagnosis with lipid profile and atherogenic index will be helpful in predicting cardiovascular risk in RA patients

Thus, in the present study, highly significant alterations in serum total cholesterol, triglyceride, VLDL-C; HDL-C & LDL-C in rheumatoid arthritis patients were observed. RA patients also showed increased atherogenic index, all these disturbances in lipoprotein may actively participate in initiation and progression of atherosclerotic vascular disease in RA patients.

CONCLUSION

From the present study, it can be concluded that chronic inflammation in RA patients leads to elevated serum levels of total cholesterol, triglyceride, LDL-C, VLDL-C & atherogenic index as well as depleted levels of protective cholesterol HDL-C indicate increased cardiovascular risk in rheumatoid arthritis.

Abbreviations:-

Anti- CCP- anti cyclic citrullinated peptide
RA- rheumatoid arthritis
ESR- Erythrocyte sedimentation rate
TNF- α - Tumour necrosis factor- α
IL1- Interleukin-1

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