Journal of Prevention, Diagnosis and Management of Human Diseases
ISSN: 2799-1202
Vol: 03, No. 04, June-July 2023
http://journal.hmjournals.com/index.php/JPDMHD
DOI: https://doi.org/10.55529/jpdmhd.34.1.8

Lipoproteins Levels in Rheumatoid Arthritis

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Received: 12 February 2023 **Accepted:** 06 May 2023 **Published:** 13 June 2023

Abstract: Introduction: Many studies found that people with rheumatoid arthritis (RA) had higher cardiovascular morbidity and death rates. Accelerated atherosclerosis is the primary cause of cardiovascular mortality. Strong risk factors for atherosclerotic events include increased plasma total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and reduced high-density lipoprotein cholesterol (HDL-C).
The purpose of this study: This is to demonstrate how the serum lipid profile changes in RA patients.
Methods: The lipid profile of 50 RA patients who satisfied the 2010 American College of Rheumatology (ACR) criteria for rheumatoid arthritis (RA) was assessed.
Fifty volunteers who appeared to be in good health were used as the control group in this investigation.
Both the patient and control groups' lipid profiles (TC, LDL-C, HDL-C, TG, VLDL, and atherogenic index) were calculated.
Results: According to the study's findings, RA patients had a substantial increase in total cholesterol (P0.05), a significant decrease in LDL cholesterol (P0.05), and a significant increase in HDL cholesterol (P0.05). As a result, rheumatoid arthritis patients' atherogenic index ratio of TC/HDL-C (P0.0001) was considerably greater compared to control groups.
Conclusion: Compared to the healthy control individual, the lipid profile of RA patients is atherogenic.

Keywords: Rheumatoid Arthritis, Lipid Profile, Iraq Patients.

1. INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune illness that is chronic, debilitating, and has an unclear cause. It affects approximately 1% of the adult population. Accelerated coronary

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artery disease is responsible for almost 50% of mortality in RA patients. (Kaplan *et al*., 2006. Howard *et al.*,2006).

Patients with RA seem to be more susceptible to sudden myocardial infarction mortality. (Anoze and Nassir,2008Systemic inflammation has a variety of potential methods by which it might influence cardiovascular disease (CVD), including direct effects on endothelial function and indirect effects on lipoproteins. (Toms *et al.*, 2011).

RA itself has been considered as an independedt risk factor for accelerated atherosclerosis; both diseases, immune-mediated inflammatory processes, play central roles, and the two diseases share several common pathologenic mechanisms. (Nakkem and Szodory., 2010).

As a result of the interaction of known CVD risk factors (e.g., hypertension, dyslipidemia, diabetes, smoking), genetic susceptibility, and systemic inflammation, CVD in RA is multifactorial, with systemic inflammation being the primary participant (Nurmohamed *et al*., 2001).

The risk of CVD in RA is anticipated to rise as a result of a disproportionate reduction of lipid profile elements, including high-density lipoproteins (HDL), as well as complex alteration of lipoproteins and enzymes involved in lipid metabolism. (Toms *et al*., 2010)

Epidemiology

Rheumatoid arthritis (RA) is rather common, with a frequency of 0.5-1.0% in various populations. But the Pima Indian population has been shown to have a significant frequency of RA (5.3%). (Silman and Pearson, 2002). The prevalence of RA also varies throughout the world. For instance, the incidence appears to be lower in several European nations than in the United Kingdom, ranging from (0.1-0.5%) (D. Symmons *et al*. 2002) In a particular rural Black African community where the illness seems to be rare (0.42%). This shift in RA prevalence raises the possibility that RA is related to the way of life seen in industrialized regions. (Mody GM., 2009). The prevalence of RA increases with age, and sex differences diminish in the older age group. However, the onset is most frequent during the fourth and fifth decades of life. Women are affected approximately three times more often than men, and these differences in races may be due to the interaction between genetic constitution and environment triggers (Fauci *et al*., 2008. Eftekharian *et al.*, 2011). The available studies on lipid profile in patients with RA is contraversy. There have been studies reporting either increment, decrement, or similar levels for TC, LDL-C, and HDL-C in comparison to control subjects (Nurmohamed,2007). Dyslipidaemia in RA is likely to be influenced by a variety of variables, including the presence of inflammatory diseases, limited physical activity due to pain and disability, and medication use. Although it seems that RA patients with both early and severe illness have dyslipidaemia. While early dyslipidaemia might be partially attributed to the inflammatory load (Toms *et al*.,2010). The current study's objectives are to assess the alterations in blood lipoproteins in RA patients, including total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, very low-density lipoprotein, and atherogenic index.

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Patients, Resources, and Methods:
Case-control research is used in this study. Ibn-Sina Teaching Hospital patients with RA were included in the study samples. Mosul. Iraq. People who appeared to be in good health made up the control group.\

Patients Categorization:
The participants in this study were split into two groups.
Group 1:
This group consisted of 50 RA patients from the Ibn-Sina Teaching Hospital who met the American College of Rheumatology (ACR)/European League Against Rheumatism (ELAR) criteria of RA in 2010 (Aletaha et al., 2010). Rheumatology Outpatient Clinic and Inpatient Department. Their ages varied from 30 to 70, with a mean and standard deviation of (49.7010.40) years. Patients with a history of familial dyslipidaemia, diabetes mellitus, hypothyroidism, liver or renal disease, Cushing's syndrome, cancer, or any other ailment that affects the lipid profile were also excluded.
Patients receiving lipid-lowering medications, beta-blockers, oral contraceptives including estrogen, progesterone, and thyroxin, as well as vitamin E, were also excluded from the trial.
Group 2:
There were (50) persons in this control group who appeared to be in good health. The control subjects were chosen among the family members who were accompanying the patients at the rheumatology department. Their ages varied from 30 to 70 years, with a mean and SD of 47.26 and 7.22 years, respectively. These individuals met the identical requirements for the patients' group's exclusion.
The participants in the control group did not have any previous history of coronary heart disease. The control group and the study group were matched for age and sex.

Materials:
Materials used in this study are arranged as follows:
1-Speciments.
2-Instrument.
3-Reagents.

Specimens
Blood samples from both the control group and RA patients who had fasted were taken. The individuals were told to fast for between 12 and 14 hours at night. Using sterile, disposable syringes, five milliliters of venous blood were drawn from the anti-cubital vein. Laboratory investigation included TC, TG, HDL, LDL, VLDL, Atherogenic index, and FBS to exclude DM. Blood urea and serum craetinine were to exclude renal disease, which was done for all patients and controls. ECG (read by cardiologist) and ECHO (which done by cardiologist) to evaluated coronary heart disease in rheumatoid patients and to exclude dcoronary heart disease in the control
group

Instruments
1-Spectrophotometer, Cecil (Germany).

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2-Centrifuge,KOKUSAN (Japan).
3-Incubater-37oc. Memmet (Germany).
4-ECG-MAC-1200 (India).
5-ECHO-LoGiQS6 (USA).

Reagents
The reagents utilized in this investigation were chosen based on their correctness, dependability, and availability, and they were bought from the following worldwide vendors and businesses:
1-Reagent for serum triglycerides and serum HDL-cholesterol measurement were supplied by Bio Labo, France.
2-Reagent for serum total cholesterol measurement were supplied by Bio Merieux. France.

2. METHODS

1- Shimadzu Micro-Flow MeterCL-720 was used to detect serum total cholesterol using an enzymatic colorimetric technique.
2-Serum triglycerides were measured by enzymatic method. (Masahiko O *et al*,2005).
3-Separation of serum HDL and determination of cholesterol bound to this feaction (W Greg M *et al*.,2010).
The 4-Atherogenic index is calculated by following equeation:
AI=Total serum cholesterol/HDL-c (Georgiadis *et al*.,2006).
5- The following equation is used to compute LDL-c: LDL-c=Total cholesterol- (HDL)-TG/5 (mg/dl). (2002) Matthias N. et al.

Statistics analyses
The independent two-sample T-Test of unequal variances was used to evaluate all the data by the software program Minitab version 14.0, with (P0.05) being considered a significant difference.

3. THE RESULTS

One-hundred subjects wre included in the syudy (50). RA patients were 42 women (84%) and eight men (16%) with a mean age of 49.70±10.40 years.
The mean age of the 50 control healthy subjects was 47.26 7.22 years, with 42 women (84%) and eight men (16%). There was no statistically significant difference in age between the normal subjects and the rheumatoid arthritis patients (P=0.176), and there was no statistically significant difference in sex distribution either (P=0.793.)
Comparison of patients with RA with the control group in terms of age and sex is shown in

Table 1.

Parameter	RA patients Mean±SD.	Control group Mean±SD.	P-value *
Sex (male/female)	8/42	8/42	NS
Age (year)	49.70±10.40	47.26±7.22	NS

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p>0.05) as no significant difference.*
p<0.05) as a significant difference. *
Independent Two-Sample T-Test was used.*

Serum Total Cholestrol.
In contrast to the control group, the patient findings revealed a high mean blood level of cholesterol with a significant difference (P 0.05).

Serum LDL-C:
With a significant difference (P0.05), the mean blood level of LDL-C in the patient group was greater than the mean serum level of LDL-C in the control group.

Serum HDL-C:
With a significant difference (P0.05), the mean blood level of HDL-C in RA patients was lower than the mean serum level in the control group.

Serum TG and VLDL:
Although the mean serum TG and VLDL levels in the patient group were greater than those in the control group, there was no statistically significant difference between the two groups' serum levels (P>0.05).

Atherosclerotic ratio
The mean atherogenic ratio of TC/HDL-C was greater in patients with RA than in the control group, with a highly significant difference (P0.0001), as shown in Table (2) below. This finding was a result of the results regarding total cholesterol and HDL-C discussed above.

Parameter	Patients with RA (Mean±SD)	Control group (Mean±SD)	*P- value
TG (mmol / L)	5.01±0.63	4.71±0.78	0.037
LDL (mmol / L)	3.22±0.82	2.82±0.79	0.016
HDL (mmol /L)	2.13±0.23	1.01±0.26	0.013
TG (mmol / L)	1.68±0.86	1.52±0.79	0.329
VLDL(mmol /L)	0.78±0.47	0.68±0.37	0.259
TG/HDL	5.29±1.63	4.20±1.11	0.0001

p>0.05) as no significant difference.*
(p<0.05) as a significant difference.*
(p<0.001) as a highly significant difference. *
P<0.0001) as a very highly significant difference. *
Independent Two-Sample T-Test was used.*

4. DISCUSSION

In this study, there were approximately five times as many females as male patients with rheumatoid arthritis. (Table 1), and this was in agreement with research that found the

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female-to-male ratio to be almost (5/1) (Tore K K et al., 2006). It did not correspond with another study, however, which found that the female-to-male ratio was (2.5/1) (Fauci et al., 2008). The men weren't coming to our clinic, which accounts for the disparity. In several research, the lipid profile of RA patients has been examined. In comparison to the general population, several of these studies have found that patients with active or untreated diseases have lower levels of HDL-C and higher TG/HDL-C ratios. However, some researchers did not find any appreciable differences in lipid levels from the healthy population, while others spoke of an overall decline .The present study showed a significant decrease level of HDL cholesterol along with hypercholestermia in RA patients when compared with the control ($P<0.05$). (Table-2). Our results are in accordance with reports from George S*et al* (2009), who have shown the presence of signifigant dyslipidemia in patients with RA in their study.
This study is consistent with another study published by Toms et al. (2011) that discovered dyslipidaemia can manifest in RA patients with both early and advanced disease. Hypercholesterolemia is an important factor in the development of atherosclerosis, whereas increased HDL cholesterol has an atheroprotective function. In contrast, a study that found low total cholesterol levels and did not notice a statistically significant decline in HDL values contradicts our findings. This may be because of the medication used or the activity of an inflammatory disease, which may have an impact on these various lipoprotein levels (Carmen G-G et al., 2009 .)When compared to the control group, RA patients' atherogenic index revealed a very highly significant rise (P 0.0001). (Table-2) and there is growing evidence that lipid component ratios are more predictive of the first myocardial infraction than individual components of the lipid profile. Our findings are consistent with those of other studies that found that the TC/HDL ratio, rather than cholesterol alone, is a more reliable way to assess the lipid profile by overcoming individual fluctuations in lipids that occur as pa (2010) Peters et al. Little-density lipoprotein has been proven to undergo oxidation, generating oxidized LDL, and is linked to an increased risk of coronary heart disease. Ox-LDL causes the production of phospholipids, which in turn activates endothelial cells and starts an inflammatory process that creates foam cells and subsequent fatty streaks. According to Alessandra B. A. et al. (2008), HDL uses its antiatherogenic properties to prevent LDL from oxidizing under normal circumstances .Another significant observation in RA patients was a significant rise in LDL cholesterol (P 0.05). (Table-2). Because of these changed lipoproteins and the rise in lipid peroxidation products, it is likely that RA patients may eventually develop coronary heart disease. This finding is consistent with studies by Nurmohamed (2007), who found a large rise in LDL levels, which they hypothesized may have been caused by elevated levels of secretory group IIa phospholipase A2, an acute phase protein and separate cardiovascular risk factor. However, this study contradicts another study that reported that there was no change in the levels of the basic lipid components, with the exception of LDL levels, which were lower in the RA group (Toms et al., 2010). This dispute can be explained in large part by Another finding was that when RA patients were compared to the control group, there was no discernible rise in TG or VLDL levels ($P>0.05$). (Table-2) and this finding contrasts with one research that indicated a drop in TG level (Suresh and Manohurun, 2005) and is in agreement with another study (R Vottery et al. 2001.) These inequalities can be the result of research design restrictions, such as a limited sample size, disparities in baseline traits, and insufficient correction for participants.

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The findings showed that patients with RA had an atherogenic lipid profile with a significantly lower level of HDL-C in their serum, which led to an increase in the atherogenic ratio of TC/HDL-C, indicating that these patients may be at an increased risk of atherosclerosis.

5. CONCLUSION

*Different altered patterns of lipid and lipoproteins are pobserved in RA patients ‹this suggests that dyslipidemia ‹especially characterized by low HDL and raised atherogenic indices, may be considered as a secondary impact of RA.
* Our findings suggest that the atherogenic index (TC: HDL-c ratio) should be used in place of TC alone to evaluate cardiovascular risk in RA patients, particularly in those with high inflammatory activity.

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