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Evaluation of the Lipid Profile and its Correlation to Inflammatory Markers in a Sample of Rheumatoid Arthritis Patients in Iraq

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ABSTRACT

Rheumatoid arthritis (RA) is one of the most prevalent chronic, autoimmune diseases of the joints. Although the disease itself is rarely deadly, complications such as disorders of pulmonary and cardiovascular can increase mortality. RA patients can suffer from significant dyslipidemia at various stages of the disease, where the lipid profile may be altered because of the inflammatory activity of the disease. Therefore, the present study aimed to estimate the correlation between lipid profile and markers of inflammation including rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) in a sample of Iraqi RA patients. In this study a total of 60 samples were obtained from RA patients and 30 samples from healthy individuals as a control group then samples were tested to measure the levels of lipid and inflammatory markers. The Correlation between lipid profile and inflammatory markers was studied by using Pearson's correlation (r=−1 to 1). Out of 60 RA patients, 50 were females (83%) and 10 were males (17%) with a mean of age 46.15±10.74 years and a mean disease period of 9.17±6.73 years. The mean of total cholesterol in patients was 194 ± 45.39 mg/dl and the mean of triglycerides was 118 ± 46.78 mg/dl while the mean of HDL, LDL, and VLDL were (46.13±11.14, 125.7±38.63, and 23.59±9.35 mg/dl) respectively in the patients. The mean of RF was (92.04±71.21 IU/ml) while CRP was (5.877±5.92 mg/l) and ESR was (34.17±17.85 mm/h). In conclusion, there was no correlation between inflammatory biomarkers and parameters of lipid profile.

Introduction

Rheumatoid arthritis (RA) is a disease categorized as one of the popular inflammatory, chronic, autoimmune diseases of the connective tissues. In RA patients, the flexibility of performing daily tasks and the life quality related to health are greatly impacted[1]. RA affected starts with small joints then proceeds to large ones, and ultimately the heart, skin, lungs, and kidneys. Joint bone and cartilage are usually damaged, and ligaments and tendons become weak, however, all these damages lead to distortions and erosion of bone[2,3]. Although RA itself is not a fatal disease, its complications like cardiovascular and pulmonary disorders may increase mortality[4].

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Clinically, the most important biomarkers or inflammatory markers that are currently used to determine RA in the first discovery or monitoring of the activity of the disease in advanced stages include rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)[5]. Furthermore, the high levels of these inflammatory markers can be related to rising risks of other damage or disorders in the patient's body such as an increase in cardiovascular (CV), atherosclerosis, anemia, etc.[6,7]. Some changes in lipid profile can be noticed in RA patients where the levels of total cholesterol can be reduced in active RA, as have levels of high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL). Conversely, the variables of lipid profile have increased after treatment with anti-inflammatory medications[8]. Most possibly the lipid increase is not linked to an increase in the number of cardiovascular risks in patients

because of anti-inflammatory action, traditional disease-modifying anti-rheumatic medications, such as TNF have shown a lowering in the death rate of Cardiovascular in patients of RA [9]. Finally, the present study aimed to investigate the lipid profile in a sample of Iraqi rheumatoid arthritis patients and assess the correlation with inflammatory markers of RA disease (RF, ESR, and CRP).

Materials and Methods

Study design and Subjects

This study was performed at the laboratories department in Fallujah Teaching Hospital, Ramadi Teaching Hospital, and the Biology Department in Science College at Anbar University between November 2021 and November 2022. A total of 90 persons participated in this study and were classified into two groups patients and control where they included 60 RA patients and 30 healthy persons. The subjects were obtained from patients who visited the Rheumatology Unit of AL-Fallujah Teaching Hospital while the samples of healthy people from Anbar University.

Selection criteria of study participants

All participants in this study with the age ranged from 20-60 years old. Samples and information were taken after the agreement of participants before adding them to the current study. All patients had previously been diagnosed with RA according to the American College of Rheumatology which was based on clinical examinations, X-ray findings, and laboratory tests and they were under treatment by taking suitable drugs that were suggested by the rheumatologist. None of the participants were a smoker or alcoholics or had other diseases such as diabetes mellitus, hypertension, kidney diseases, hyperthyroidism, and liver diseases. Moreover, individuals taking medicines including lipid-lowering drugs, thyroxin, beta-blockers, estrogen, vitamin E, and progestin, and also individuals with obesity (body mass index >30) were excluded.

Samples collection

Blood samples were collected in the morning after 10 hours of overnight fasting; 5 ml were obtained from venipuncture with a disposable syringe. After that, the blood was separated into two aliquots: a total of 3 mL was transferred into the Gel tube to complete the tests of lipid profile, RF, and CRP by separating the serum with centrifuged for 10 minutes. Additionally, 2 mL was deposited into the ESR tube to finish the ESR test. ESR tubes were lightly shaken to mix the blood with the anticoagulant to avoid clotting before the test was completed. The collected serum was stored at - 20^{o}C until the time of use.

Laboratory tests

Serum concentrations of rheumatoid factor (RF), C- reactive protein (CRP), and lipid profile (total cholesterol, triglycerides, LDL, HDL, and VLDL) were measured by using an automated analyzer (Cobas C311, NO.1339-10, Hitachi High-Technologies Corporation, Tokyo, Japan) with its reagents that were provided from the same company. Erythrocyte sedimentation rate (ESR) was measured by using the Westergren method where RF, CRP, and ESR were measured to estimate the inflammatory status.

Statistical analysis

A statistical analysis of data was conducted using "SPSS version 22". The statistical significance criterion was defined at a p-value less than 0.05, with a p-value < 0.05 considered significant and a p-value < 0.01 considered highly significant with a 95% confidence interval. The descriptive statistics include the mean and standard deviation (SD) for all parameters. The Independent-Samples T-Test was used to calculate the comparisons between controls and cases. "Pearson's correlation" (r=1 to 1) was utilized to study the correlation between lipid profile and inflammatory markers[10]. In addition, the application of Excel 2010 has been used to create standard curves and shapes that describe every parameter.

Results and discussion

A total of 90 individuals were included in this study consisting of 60 patients with Rheumatoid Arthritis disease and 30 individuals were healthy people. The mean of the patient's age was 46.15±10.74 and the range of disease period from 1-20 years with a mean of 9.17±6.73. The percentage of females was 83% (n=50)

which is higher than the percentage of males, which amounted to 17% (n=10).

The results of the lipid profile in the group of the patients and control of the current study are enumerated in Table 1 which shows there is no significant difference comparison between the patients group and the control group at p-value >0.05. The mean of total cholesterol (TC) was 194 ± 45.39 mg/dl in the patients' group and 183.2±31.05 mg/dl in the control group, while the mean of Triglycerides (TG) was118±46.78 mg/dl in the patients group and 106.9±26.74 mg/dl in the control group. Moreover, the mean of HDL, LDL, and VLDL were (46.13±11.14, 125.7±38.63, and 23.59±9.35 mg/dl) respectively in the patient's group while in the control group were 48.63±9.04, 113.2±26.72, and 21.38± 5.34 mg/dl also.

Furthermore, the results of inflammatory markers in the patients group and the control group as listed in Table 1 show a highly significant rise in the patients group of the present study compared with the control group at p-value < 0.001. The mean of rheumatoid factor (RF) in the patients group was 92.04±71.21 IU/ml and 4.73±1.92 IU/ml in the control group. The mean of C-reactive protein (CRP) was 5.877±5.92 mg/L in the patients group and the control group was 0.820±0.317 mg/L while the ESR mean was 34.17±17.85 mm/h and 15.47±9.85 mm/h in the patients and control group respectively.

Table 1: Results of the parameters mean ±SD of study groups

Parameter	Mean ±SD		P- value
	Patients	Controls	
TC (mg/dl)	194±45.39	183.2±31.05	0.189
TG (mg/dl)	118±46.78	106.9±26.74	0.158
HDL (mg/dl)	46.13±11.14	48.63±9.04	0.291
LDL (mg/dl)	125.7±38.63	113.2±26.72	0.077
VLDL (mg/dl)	23.59±9.35	21.38± 5.34	0.158
RF (IU/ml)	92.04±71.21	4.73±1.92	< 0.001
CRP (mg/L)	5.877±5.922	0.820±0.317	< 0.001
ESR (mm/h)	34.17±17.85	15.47±9.85	< 0.001

The results of the correlation between lipid profile and inflammatory markers showed there was no positive or negative significant relationship discovered between RF, CRP, or ESR and the parameters of lipid profile where the results listed in Table 2.

Table 2: Results of the correlation between parameters of study groups

	ESR	RF	CRP	TC	TG	HDL	LDL	VLDL
ESR	1	-.055-	.156	.094	.105	.139	.074	.104
RF		1	-.189-	-.035-	-.158-	-.031-	-.001-	-.158-
CRP			1	.132	.142	.114	.107	.142
TC				1	.607**	.121	.952**	.607**
TG					1	-.308-*	.539**	1.000**
HDL						1	-.066-	-.308-*
LDL							1	.539**
VLDL								1

However, the level of body lipids is within a specific range and is regulated by several mechanisms, which can be affected by different disorders or diseases[11]. In addition, rheumatoid arthritis patients can develop severe metabolic problems such as dyslipidemia as a result of their poor dietary status and use of non-steroidal medicines [12,13]. Therefore our study was established, and it aims to examine the correlation between lipid components and inflammatory markers in RA disease. However, the mean of total cholesterol in our study is (194 mg/dl) in conformity with previous studies[14,15,16] which recorded a mean of total cholesterol of about 200 mg/dl in ineffective patients with RA while the mean of triglycerides was 118 mg/dl which were conformity with the former studies[17, 18]. Moreover, slightly lower in our study participants than in prior studies by Curtis et al. [17] and Chen et al.[19],The mean of HDL (46.13 mg/dl) was still in line with other studies[20]. HDL levels in

participants of this study may have been low due to genetic or environmental causes or bad nutritional habits, as HDL levels are generally low in this region of the world's population. The mean of LDL in our study was 125.7 mg/dl and VLDL 23.59 mg/dl which are similar to what has been documented in other research[17,20]. The relative stability of lipid levels in the present study population is a representation of dyslipidemia that occurs in RA patients who are using anti-inflammatory medications such as the use of non-steroidal or biological drugs. Furthermore, lipid levels are dependent on other factors in RA patients like age, BMI, and nutritional habitat such as intake of carbohydrates and fats.

Finally, there was no significant statistical between RF and lipid profile which coincides with the findings performed by Yoo[21]. The present study also found there is no correlation between CRP, ESR, and lipid profile which is in line with the results of previous studies[22,18]. On the other hand, some studies found a correlation between CRP, ESR and some parameters of lipid profile like total cholesterol such as a study completed by Mahdi et al.that found ESR and CRP have a significant positive connection with rising serum levels of total cholesterol respectively, furthermore, high ESR and CRP are shown to have a statistically significant correlation with high LDL respectively. Raised ESR and CRP were, respectively, related to decreased HDL values[23]. The association between inflammatory markers and lipid profiles in RA can be shown in different patterns and it varies based on the sex and menopause state. It is unclear why there is a connection between inflammation levels and lipid profiles or whether inflammation itself is a cause of the aberrant lipid metabolism seen in RA patients. Acute phase response, insulin resistance, and abnormal lipid metabolism have recently been identified as potential cardiovascular risk factors in RA[21].

Conclusion

The current study supports the observation of the different patterns of dyslipidemia found in patients with rheumatoid arthritis which could explain the increase of cardiovascular risk in RA patients. Furthermore, there is no correlation between inflammatory markers of RA and lipid profile and inflammation can only account for a tiny portion of the observed lipid variations between individuals who go on to develop rheumatoid arthritis and controls. It is still unclear if lipids affect how susceptible people are to developing inflammatory disorders like rheumatoid arthritis.

Abbreviations

RA, Rheumatoid arthritis; RF, rheumatoid factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; TC, total cholesterol; TG, Triglycerides; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol; VLDL, very low-density lipoprotein cholesterol.

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تقييم صورة الدهون وارتباطها بالمؤشرات الالتهابية في عينة من مرضى التهاب المفاصل الرثوي في العراق

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الخلاصة:

التهاب المفاصل الرثوي أحد أمراض المناعة الذاتية المزمنة التي تصيب المفاصل وهو نادرا ما يكون مميتًا ، إلا أن مضاعفاته مثل اضطرابات الرئة والأوعية الدموية يمكنها زيادة معدل الوفيات. و صورة الدهون للمرضى يمكن ان تتغير نتيجة النشاط الالتهابي للمرض لذلك فان هذه الدراسة بحثت العلاقة بين صورة الدهون والمؤشرات الحيوية الالتهابية متضمنة العامل الرثوي ، ومعدل ترسيب كريات الدم الحمر ، والبروتين التفاعلي– C في عينة من المرضى العراقيين.حيث اخذت 60 عينة من المرضى و 30 عينة من الأفراد الأصحاء. دراسة الارتباط بين صورة الدهون ومؤشرات الالتهاب تمت باستخدام مقياس ارتباط بيرسون (1الى1– = r) . اظهرت النتائج ان من بين 60 مريضًا بالتهاب المفاصل الرثوي ، كان 50 منهم من الإناث (83٪) و 10 من الذكور (17٪) وبمتوسط عمر 46.15 ± 10.74 سنة وبمتوسط فترة للمرض 9.17 ± 6.73 سنة. حيث كان متوسط الكوليسترول الكلي 194 ± 45.39 مغم / ديسيلتر وكان متوسط الدهون الثلاثية 118 ± 46.78 مغم / ديسيلتر في المرضى بينما كان متوسط HDL و LDL و VLDLهو 46.13 ± 11.14 و 125.7 ± 38.63 و 23.59 ± 9.35 مغم / ديسيلترعلى التوالى في المرضى ايضا. و كان متوسط العامل الرثوي RF هو 92.04 ± 71.21 وحدة / مل بينما كان البروتين التفاعلي– C هو 5.877 ± 5.92مغم / لتر و معدل ترسيب كريات الدم الحمر كان 34.17 ± 17.85 مم / ساعة. وكملخص لم يظهر ارتباط معنوي بين المؤشرات الحيوية الالتهابية للمرض ومتغيرات صورة الدهون في المرضى.

الكلمات المفتاحية: التهاب المفاصل الرثوي ، العامل الرثوي (RF) ، معدل ترسيب كريات الدم الحمر (ESR) ، صورة الدهون ، الكولسترول .