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LIPID PROFILE ALTERATION IN RHEUMATOID ARTHRITIS PATIENTS

Biochemistry

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ABSTRACT

INTRODUCTION: It has been proved that rheumatoid arthritis (RA) is linked to dyslipidemia and the risk of cardiovascular complications is higher in these patients. The aim of this study was to evaluate dyslipidemia in RA patients.

MATERIAL AND METHODS: In this study, RA patients were enrolled regarding the inclusion and exclusion criteria. Their demographic information and medication profiles were evaluated. Clinical assessments were performed by evaluation of disease activity score (DAS28) and visual analogue scale. Moreover, laboratory investigations of lipid profile including triglycerides (TG), total cholesterol (Chol), low-density lipoprotein (LDL), and high- density lipoprotein (HDL) were performed.

RESULT: Total of 150 patients with the mean age of 53.8±15.7 years, 64.4% were diagnosed with dyslipidemia. Females in menopausal ages had a higher prevalence of dyslipidemia as well as patients with longer disease duration. Considering DAS28, 100% of the patients with high disease activity were diagnosed with dyslipidemia.

CONCLUSION: According to the results, patients under treatment with prednisolone and methotrexate were more affected by dyslipidemia than those with prednisolone, methotrexate, and hydroxychloroquine. In the patients under prednisolone, methotrexate, and leflunomide treatment, the prevalence of dyslipidemia was significantly lower than those used only prednisolone and methotrexate. Altogether, it is necessary to have more clinical suspicion towards dyslipidemia and its complications in the patients with a greater number of affecting factors.

KEYWORDS

Rheumatoid arthritis, Dyslipidemia, Lipid profile, Cardiovascular diseases

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic disease diagnosed mostly by presenting articular manifestations. This pathology with a prevalence of 0.5- 1% in general population is more common in females [1]. So far, the main pathogenesis of RA is unknown, but it seems that both genetic and environmental factors are involved [2]. Similar to other chronic diseases, RA is accompanied by inflammation which has made the main target for therapeutic agents [3]. Although RA is mostly known for its particular presentations, skin, ocular, and cardiac manifestations are also expectable [4].

Nowadays, cardiovascular diseases (CVD) are known as the leading cause of death worldwide[5]. The most common type of CVD is atherosclerosis which is a chronic inflammatory condition. Interestingly, it has been showed that both CVD and RA have similar pathways of inflammation [6]. Furthermore, mortality caused by CVD is more common (up to 50% higher) in RA patients compared to a normal population which makes it the most common cause of death among these patients. This increase in mortality rate is caused by the higher risk of myocardial infarction (MI) and stroke in RA population which is attributed to CVD and mainly atherosclerosis[7] . Furthermore, it has been shown that MI risk due to CVD in RA patients is 200% (2 folds) higher compared to age and sex-matched controls [8]. Taken together, it seems that CVD is a serious issue in patients diagnosed with RA since it increases the risk factors involved [6-8]. Remarkable risk factors for atherosclerosis are male gender, high serum total cholesterol (Chol), low-density lipoprotein (LDL), low serum high-density lipoprotein (HDL), aging, diabetes, high blood pressure, and smoking.

MATERIALS AND METHODS

Clinical assessments

Patients' demographic information, disease duration, drug history, and disease activity score (DAS28) were evaluated. For calculation of DAS28 score, we considered swollen and tender joints, erythrocytes sedimentation rate (ESR) and visual analogue score. In this evaluation any score ≤2.6, 2.6 < score ≤3.2, 3.2 < score ≤5.1, and <5.1 were considered as remission, low disease activity (DA), moderate DA and high DA, respectively.

Para-clinical assessments

Laboratory makers such as serum total Chol, triglyceride (TG), LDL and HDL were evaluated after 12- hour fasting. Normal values considered as follows: LDL <100 mg/dl, TG <150 mg/dl, total cholesterol <200 mg/dl, and HDL >50 mg/dl. Also, both ESR and C-reactive protein (CRP) serum levels were evaluated. All the laboratory tests were done by the same laboratory expert using the same kits and methods for each parameter. All the kits were provided from Merck Chemi Co™.

RESULTS AND DISCUSSION

According to the literature, patients with RA are more susceptible to dyslipidemia and atherosclerosis (and its complications such as CVD) due to the impaired lipid profile in comparison to the normal population [9]. Thus, it is very important to investigate any possible mechanism that may affect lipid profile in them. In this study, we intended to assess dyslipidemia in RA patients by categorizing them into the different groups according to the different variables such as age, sex, disease duration, and types of medications consumed. It is important to consider all the variables such as age in this study since it has been proved to significantly increase CVD[10]. As the results showed, the patients' mean age in the current study was 54.9±16.8 which was the same as the other studies [11,12]. Also, 87.33% and 12.66% of patients were female and male, respectively. This clearly affirms that RA is more common in women than men as expected. Moreover, according to the epidemiological investigations, females, especially those in menopausal status, are more susceptible to impaired lipid profile which strongly increases the risk of atherosclerotic events . In this study, it was shown that 92% and 100% of females with the age ranges of 56-65 and 66-75, respectively (menopausal ages) were diagnosed with dyslipidemia. In a general aspect, the prevalence of dyslipidemia in our patients was 65.3% which was similar to Nisar *et al.*,'s study [13]. Also, the serum levels of HDL, LDL, TG, and total cholesterol almost were similar to another study by Vijaykumar *et al.,* [14]. The cause of changes in lipid profile is still unclear, but there are some hypotheses proposed to describe this phenomenon. It seems that different polymorphisms such as REL (c-Rel) polymorphism have been shown to affect LDL levels. Also, interleukin 6 (IL-6) which is an inflammatory cytokine is able to induce lipoproteins abnormalities. This interleukin has been shown higher in RA patients with lower HDL levels.

In older age groups, the prevalence of dyslipidemia has been increased.

As our results demonstrate, this increase may be caused by aging which is considered a risk factor for lipid profile disorders as well as prolonged disease duration (prolonged inflammation) [15]. Thus, it could be hypothesized that both aging and disease duration are possible risk factors of dyslipidemia in RA patients. However, due to the decrease in the age range of 76-85 years, this hypothesis may be confounded, although this age group only consisted of only three patients.

In the current study, the prevalence of dyslipidemia was evaluated in different disease activities measured by DAS 28. As mentioned in the results, patients with higher disease activity score had more lipid abnormalities. A higher ratio of dyslipidemia in RA patients with higher disease activity is proved by other studies as well [16,17]. It seems that in patients with higher disease activity, inflammation is more bolded than other cases and exposure to higher amounts of inflammatory cytokines in this situation is responsible for the higher prevalence of dyslipidemia in RA cases.

Also as mentioned in the results, patients consuming hydroxy chloroquine had less prevalence of dyslipidemia in comparison to others. Thus, it could be concluded that hydroxychloroquine is a protective agent in these patients which is also proved by Morris *et al.,*'s study [18].

In their study, it was showed that hydroxychloroquine is able to reduce LDL, TC, TG and it also increases HDL levels [18]. Generally, disease-modifying antirheumatic drugs (DMARDs) are introduced to improve the lipid profile, or at least, not to affect lipid profile.

It has been demonstrated in patients with systemic lupus erythematosus that women consuming prednisolone had impaired lipid profile in comparison to the same patients who did not receive this medication [19]. Moreover, methotrexate alone has been determined to impair lipid profile of patients with RA. On the other hand, hydroxychloroquine is affirmed to improve lipid profile in different metabolic and inflammatory diseases [20].

CONCLUSION

We found that the prevalence of dyslipidemia is notably higher in RA patients. Impairment of lipid profile in this survey was shown by decreased HDL and increased LDL, TG and total cholesterol levels. Taken together these findings, authors strongly recommend controlling lipid profile in RA patients. Also, according to the results, in RA patients with higher disease activity index, lipid profile impairment was more frequent. Therefore, it seems only reasonable to treat RA patients to decrease the risk of hyperlipidemia as a cardiovascular risk factor. Somehow, more case-control studies with a higher number of patients should be done to confirm our results. Also, we found out that the patients using hydroxychloroquine or leflunomide had lower rates of dyslipidemia compared to others. Accordingly, we suggest using or adding these medications to control both lipid profile and disease activity as a "one stone two birds" method for the treatment of RA patients. All suggested treatment opinions in this paper, of course, need clinical trials which authors strongly recommend.

Table 1. Mean of lipid profile according to the gender

	Female	Male	Both gender
HDL	53.77±13.95	46.68±13.72	53.68±12.6
LDL	96.97±22.63	93.98±22.63	97.63±22.8
TG	127.13±34.83	126.21±32.86	126.12±34.1
Total Cholesterol	176.98±37.98	178.24±38.86	176.35±39.2

Table 2. Prevalence of dyslipidemia in different ages and disease duration

Age (year)	Prevalence of dyslipidemia	Duration of disease (years)	Prevalence of dyslipidemia
25-35 (N=23, 15%)	33.7=68% (N=8)	1-5 (N=70, 47%)	56.73% (N=39)
36-45 (N=39, 26%)	74.79% (N=28)	6-10 (N=46, 30%)	65.21% (N=30)
46-55 (N=49, 33%)	52.07% (N=26)	11-15 (N=21, 14%)	86.72% (N=18)
56-65 (N=25, 17%)	94% (N=23)	16-20 (N=13,9%)	85.62% (N=11)
66-75 (N=11, 7%)	100% (N=11)	--	--
76-85 (N=3, 2%)	67% (N=2)	--	--

Table 3. Prevalence of dyslipidemia in different groups of medications

Medication(s)	Number of patients	Prevalence of dyslipidemia
Prednisolone, methotrexate, and hydroxyl-chloroquine	97	64.55% (N=61)
Prednisolone and methotrexate	30	74.19% (N=23)
Prednisolone, methotrexate, and leflunomide	8	55.55% (N=5)
Prednisolone and hydroxyl-chloroquine	3	0%
Prednisolone and sulfasalazine	1	100% (N=1)
Prednisolone, methotrexate, and sulfasalazine	5	50% (N= 2)
Prednisolone, hydroxyl-chloroquine, and sulfasalazine	1	50% (N=1)
Prednisolone, methotrexate, hydroxyl chloroquine, and Sulfasalazine	1	100% (N=1)
Prednisolone	1	100% (N=1)
No medication	3	100% (N=3)

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