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Key Essential Indicator Values for Rheumatoid Arthritis Patients in Iraq Vary Seasonally

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ABSTRACT

Rheumatoid arthritis clinical symptoms can range from moderate to severe. It can destroy joints, result in chronic disability, and cause early death. A greater risk of cardiovascular disease is one of the clinically relevant comorbidities that rheumatoid arthritis is linked to. There are few, conflicting data that are currently available on lipid problems in RA. Inflammation seems to cause changes in high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol levels. The purpose of this study is to ascertain how seasonal fluctuations in Iraq impact the concentrations of specific vital components in rheumatoid arthritis patients.

Material and subjects: The study included (97) subjects, (55) confirmed rheumatoid arthritis, and (42) apparently healthy controls whose ages ranging between (30-60) years. The samples were collected and followed up across seasons during the period from January 2020 to February 2021. They were among outpatients who attended the Rheumatology Unit in Medical City/Baghdad. Measurements were made and a questionnaire was applied to each participant in the laboratories of the Medical City.

Results: During the winter season, non-significant variations in urea, creatinine, AST, and HDL levels were seen between RA patients and healthy controls, although significant differences (P<0.05) were seen in ALT. In the moderate season, non-significant variations in urea, creatinine, AST, and HDL levels were observed between patients and controls, while significant differences (P<0.05) in ALT and Triglyceride levels were observed. Creatinine, ALT, and AST levels were not significantly different during the summer season, but urea, Triglyceride, and HDL levels were significantly different (P<0.05). Between the winter, moderate, and summer seasons, there were no significant differences in urea, creatinine, ALT, AST, S. Triglyceride, and HDL.While there was a significant difference (P<0.05) in cholesterol levels which increased in the winter season as compared with the summer season.

Conclusion: The inflammatory condition, rather than the changing of the seasons, has a greater impact on the liver and kidney functioning in rheumatoid arthritis patients.

Key words: Indicator values, Rheumatoid arthritis patients, Iraq

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INTRODUCTION

Rheumatoid arthritis (RA) has a wide range of clinical manifestations, ranging from moderate to serious illness, which can result in joint injury, permanent impairment, and early death, RA is a chronic and persistent inflammatory condition of the small and large joints, with structural damage to the articular and the periarticular besides the other consequences of systemic inflammation [1]. Numerous clinically significant comorbidities, such as an increased risk of cardiovascular disease, are associated with rheumatoid arthritis. The latter is obscured by conventional risk factors (such as hypertension and obesity), indicating that different mechanisms are at work when bad consequences occur. Lipids serve a crucial purpose

in mammalian cells [2]. There are few and conflicting published reports on lipid abnormalities in RA. The inflammation tends to be the cause of increases in cholesterol levels, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) [3]. The pattern of lipid metabolism during inflammation is proatherogenic and thought to play a role in atherosclerosis, especially in chronic inflammatory conditions such as RA. The etiology of kidney disease has been linked to both medications and RA complications [4]. Chronic kidney disease (CKD) affects approximately 9–24% of patients with RA, and the average incidence of renal failure is higher in patients with RA than in those without the disease [5]. Previous research has linked renal dysfunction in RA patients to a variety of factors including age, hypertension, and medications [6]. The previous study has discovered fatty modifications, cellular necrosis, chronic passive congestion, and gross atrophy in the livers of untreated RA patients [7]. As a consequence, RA may cause liver damage on its own. The presence of abnormal liver function tests is an independent indicator of mortality [8]. Because of the high mortality rate associated with both rheumatoid arthritis and irregular LFTs, such a population with RA may be at greater risk. The aim of this study to evaluate some vital parameters of Iraqi rheumatoid arthritis patients.

MATERIAL AND SUBJECTS

The study included (97) subjects, (55) patients with confirmed rheumatoid arthritis, and (42) apparently healthy controls who were selected with ages ranging between (35-60) years. The samples were collected and followed up in winter, moderate, and summer seasons during the period from January 2020 to February 2021. They were among those who attended the outpatients' Clinic in Medical City/Baghdad Teaching hospital/ Rheumatology Unit. Measurements were performed and the questionnaire was applied to all participants. Tests were done in Medical City – Teaching Laboratories. Ethical approval and permission were taken from the committee of the Ministry of Health and assigned consent for each patient was documented before taking the blood for the research study. The healthy control group had no history or clinical evidence of RA or any other chronic disease. Lipid profile, kidney function, and liver function estimations were performed by using kits from Roch Germany.

Statistical analysis

Data procession software package SPSS 20 for windows was used to perform quantitative analysis. Data are expressed as mean ± standard error (M ± SE). Differences between means of two major groups are analyzed by using t-test and the significance is tested at a two-tail value. While differences among subgroups are analyzed by using one-way analysis of variance (ANOVA), then if there are significant differences, they are analyzed by the least significant difference (LSD) test. The p-value of differences <0.05was considered significant.

RESULTS

The results showed that there were non-significant differences during winter season between RA patients and healthy control in urea, creatinine, AST and HDL levels, while significant differences (P<0.05) were recorded in ALT (26.38 ± 1.35 mg/dL) (19.02 ± 1.35 mg/dL), Cholesterol (198.06 ± 8.49 mg/dL) (162.66 ± 6.35mg/dL) and Triglyceride (185.78 ± 13.71 mg/dL) (137.27 ± 6.98 mg/dL) sequentially. The results are detailed in the Table 1.

Same results were recorded in moderate season as there were non-significant differences in urea, creatinine, AST and HDL levels between patients and control while there were significant differences (P<0.05) in ALT (25.14 ± 0.96 mg/dL)(15.00 ± 1.70 mg/dL), Cholesterol (174.70 ± 9.40 mg/dL) (183.86 ± 10.74 mg/dL) and Triglyceride level (164.62 ± 13.24 mg/dL)(137.73 ± 7.82 mg/dL), as shown in Table 2.

In summer season there were non-significant differences in creatinine, ALT, AST levels, but significant differences (P<0.05) were occurred in urea (34.47 ± 1.96 mg/dL) (27.62 ± 1.24 mg/dL), Triglyceride (30.59 ± 1.78 mg/dL) (21.61.71 ± 0.67mg/dL), and HDL (150.15 ± 18.57 mg/dL) (99.28 ± 5.24 mg/dL), and as they illustrated in Table 3.

Results of statistical analysis showed that there were no significant differences in urea, creatinine, ALT, AST, S. Triglyceride, and HDL between winter, moderate, and summer seasons. While there was a significant difference (P<0.05) in cholesterol levels which increased in the winter season (198.06 ± 8.479mg/dl) as compared with the summer season (172.62 ± 7.78 mg/dl) (Table 4).

Table 1: Comparison between RA patients and control in renal, liver, and lipid profile parameters of the winter season.

Parameters (mg/dl)	Control N (42) Mean ± SE	Patients N (55) Mean ± SE
Urea	28.00 ± 2.30	26.00 ± 1.29
Creatinine	0.65 ± 0.04	0.67 ± 0.02
ALT	19.02 ± 1.35	26.38 ± 1.35*
AST	19.78 ± 1.24	22.80 ± 1.21
Cholesterol	162.66 ± 6.35	198.06 ± 8.49*
Triglyceride	137.27 ± 6.98	185.78 ± 13.71*
HDL	23.71 ± 1.58	27.43 ± 2.32
	* P<0.0.5	

Table 2: Comparison between RA patients and control in renal, liver, and lipid profile Parameters of moderate season.

Parameters (mg/dl)	Control N (42) Mean ± SE	Patients N (55) Mean ± SE
Urea	28.13 ± 1.74	27.17 ± 1.72
Creatinine	0.76 ± 0.05	0.89 ± 0.22
ALT	15.00 ± 1.70	25.14 ± 0.96*
AST	18.86 ± 1.12	22.74 ± 1.68
Cholesterol	183.86 ± 10.74	174.70 ± 9.40*
Triglyceride	137.73 ± 7.82	164.62 ± 13.24*
HDL	22.46 ± 1.83	34.23 ± 3.40
	* P<0.0.5	

Table 3: Comparison between RA patients and control in renal, liver, and lipid profile parameters of the summer season.

Parameters (mg/dl)	Control N (42) Mean ± SE	Patients N (55) Mean ± SE
Urea	34.47 ± 1.96	27.62 ± 1.24*
Creatinine	0.78 ± 0.39	0.70 ± 0.27
ALT	19.43 ± 0.88	22.06 ± 1.90
AST	17.80 ± 1.02	20.01 ± 1.52
Cholesterol	166.38 ± 7.28	172.62 ± 7.78
Triglyceride	99.28 ± 5.24	150.15 ± 18.57*
HDL	21.61.71 ± 0.67	30.59 ± 1.78*
	* P<0.0.5	

Table 4: Differences in Renal, liver, and lipid profile parameters of RA patients groups according to seasons.

Parameters(mg/dl)	Winter Mean ± ER	Moderate Mean ± ER	Summer Mean ± ER
Urea	26.0 ± 1.29	27.27 ± 2.72	27.62 ± 1.24
Creatinine	0.67 ± 0.02	0.89 ± 0.22	0.70 ± 0.27
ALT	26.38 ± 2.43	25.14 ± 0.96	22.06 ± 1.90
AST	22.80 ± 1.21	22.74 ± 1.68	20.01 ± 1.52
Cholesterol	198.06 ± 8.479[a]*	174.70 ± 9.40	172.62 ± 7.78
Triglyceride	185.78 ± 13.71	164.62 ± 13.24	150.15 ± 18.57
HDL	27.43 ± 2.32	34.23 ± 3.40	30.59 ± 1.78

DISCUSSION

Environmental factors induce complex post-translational modifications in genetically vulnerable populations, which in turn trigger a pathologic activation of the immune system, ultimately leading to the clinical initiation of the disease [9]. And before the first clinical signs of RA, the immune initiation of the disease can be seen in the development of autoimmunity associated with the disease [10].

The renal function of rheumatoid arthritis patients was assessed by measuring blood urea and creatinine, as the blood urea value was significantly decreased. These results, along with the results of another study that indicated a decrease in blood urea in rheumatoid arthritis patients [11] indicated that the kidneys of such patients were susceptible to seasonal changes.

On the other hand, the finding of increased levels of Creatinine in healthy individuals during the summer season, which causes reduced blood flow toward the kidney during heat stress conditions, was similarly, reported in previous studies done by Srikandakumar, et al., Suhair, and Indu, et al. [11-13]. The significant elevation in ALT during winter and moderate season in patients compared to healthy control, probably because of the use of MTX is in line with Akhlaghi, et al. who showed a trend of increasing liver enzyme concentrations in RA patients. Moreover, other studies have reported that there was a slight increase in the levels of aminotransferase (AST and ALT) in the blood of such patients [14,15]. The elevation of liver enzymes in this study may vary with disease activity, long-term MTX therapy, and different doses of therapy. Inflammation and MTX treatment may disrupt liver enzyme metabolism.

Concerning the high lipid levels in rheumatoid arthritis patients compared to the control group, it may be due, in part, to the limited physical activity of the patients, and in part to the effect of the medications taken by rheumatoid arthritis patients. Among the interesting things in this regard is that patients who underwent methotrexate therapy were more likely to have dyslipidemia than those receiving other DMARDS treatments [16]. A previous study reported elevated cholesterol and HDL cholesterol levels for those taking MTX drugs plus etanercept [17]. Studies reported that rheumatoid arthritis is linked to abnormal lipoprotein patterns. Increased cholesterol levels from baseline associated with increased TG and HDL led to a greater development of the disease activity [18].

In this study, the results of the lipid profile analysis indicate that it may depend on the progression of rheumatoid arthritis disease and response to treatment. Some other attributes this increase to aging, which is a risk factor for lipid profile disorders [19], as well as prolonged inflammation [20]. Therefore it can be assumed that aging and disease duration are potential risk factors for dyslipidemia in patients with RA. Therefore, improvement of the lipoprotein profile of those patients appears to be associated with suppression of inflammation [21].

The observed increase in cholesterol level during the winter season in this study can be explained depending on [22] who suggests that long-term cold exposure can increase the rate of lipolysis to some extent in adipose tissues, especially in Brown adipose tissues (BAT) which plays a major role in TG metabolism and controls TG clearance [23]. The BAT produces heat to maintain body temperature by consuming TGs that are stored in intracellular lipid droplets (LDs) [24]. Besides, monthly mean cholesterol level is negatively correlated with monthly mean temperature. And the seasonal differences in cholesterol levels were independent of body weight and other potential confounding factors [25].

Given the high prevalence of dyslipidemia (i.e., pathologic changes of plasma lipid molecules, including triglycerides, cholesterol, LDL, and HDL and their ratios) in RA patients and the inflammatory nature of RA, The survey of inflammation-induced plasma lipid alteration in RA patients could be the subject of further investigation [26]. On the other hand, intact metabolism is a critical factor that guarantees the proper function of the immune cells, and impairment of metabolic reactions in these cells contributes to RA inflammation [27,28].

CONCLUSION

The inflammatory condition, rather than the changing of the seasons, has a greater impact on the liver and kidney functioning in rheumatoid arthritis patients?

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