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Analysis of Hematological and Biochemical Parameters in Patients with Rheumatoid Arthritis in Sulaymaniyah

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic immune-mediated systemic inflammatory disease characterized by chronic synovial inflammation and hyperplasia, which drive joint erosion and damage, and a variety of systemic manifestations, which contribute to the overall burden of the disease, certain environmental and genetic risk factors can lead to the awakening of systemic autoimmunity. For this reason, this current research is designed to investigate some hematological and biochemical parameters in patients with rheumatoid disease in the Kurdistan region.

Methods The investigation included healthy groups of 50 healthy people (21 men and 29 women) and 162 patients with rheumatoid disease (43 men and 119 women). The disease was diagnosed at Shahid Dr Hemn Hospital and Smart Health Tower from October 2022 to December 2022. SPSS statistical software (Version 20) (social science statistical package) was used to analyze the data. Differences in mean values between 2 groups were analyzed by two samples' t-tests (independent student's t-test).

Results The results highlighted that rheumatoid disease was significantly correlated with age, sex, and daily exercise. Hematological markers (WBC, HGB) changed significantly, and inflammatory markers (ESR, CRP) also increased significantly in the rheumatoid disease groups in both genders.

Conclusion: This study found that rheumatoid disease induces alterations in most physiological and hematological markers within the body. Elevated levels of inflammation markers, particularly in individuals with rheumatoid disease, were associated with noticeable manifestations such as joint swelling, stiffness, or redness.

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INTRODUCTION

Rheumatoid arthritis is a persistent inflammatory disease that affects a patient's quality of life by destroying joints and causing functional impairment (Ishida et al., 2018). The most common chronic autoimmune inflammatory arthritis worldwide is defined by joint inflammation that causes pain, fatigue, and functional deterioration. These symptoms harm a patient's quality of life and capacity to work (Michaud et al., 2021). Rheumatoid arthritis affects one in every 200 people worldwide, and women experience the condition two to three times more frequently than men. Although anyone can be affected, the most excellent onset occurs between 50 and 59 (Smith & Berman, 2022). The change from an at-risk host to an overtly autoimmune host is the first step in the RA disease process. The loss of self-tolerance is shown by identifying altered

protein antigens and developing autoantibodies (Checkpoint 1). Although this tolerance deficit's exact timing and location are unknown, autoantibodies appear years or even decades before the joint illness. Clinically, the host with obvious autoimmunity does not show symptoms. DNA instability and an inherent alteration in metabolic networks within the cell cause T cells to differentiate into tissue-invasive, transient effector T cells. In the sixth decade of life, failure to tolerate tissue results in early synovitis (Checkpoint 2), quickly developing into chronic synovitis (Checkpoint 3). T-cell pyroptosis, tissue-protective macrophage populations, and autoaggressive dedifferentiated synoviocytes cause joint injury. In most situations, tissue tolerance is irreversible (Weyand & Goronzy, 2021).

Over the past few decades, numerous studies have been published on the incidence and prevalence of rheumatoid arthritis (RA), indicating a significant variance in the occurrence among various groups. Most research in North America and Northern Europe estimates a mean annual incidence of 0.02–0.05% and a prevalence of 0.5–1%. The projected survival period for RA patients is likely to drop by three to ten years, and the disease is associated with a higher death rate. Epidemiological data suggest that a higher incidence of RA is associated with genetic variables (Prasad et al., 2023). However, RA is considered a multifactorial disease resulting from the interaction of genetic and environmental factors, which contribute to its occurrence and expression. The main risk factors for the disease include genetic susceptibility, sex and age, smoking, infectious agents, hormones, diet, and socioeconomic and ethnic factors. Most of these factors are likely associated with both the onset and severity.{Zuo, 2022 #232}{Miller, 2022 #233}.

Estimates of the prevalence of RA range from 0.5% to 1.0%, and in some populations, they can exceed 50%. A definitive RA was found in % of Iraqi population samples (Abdul-Qaharr & Al-Osami, 2013).

Kurdistan is a region with a high prevalence of rheumatoid arthritis disease, with wide variations in the causes and treatments of rheumatoid disease. The objectives of this study are to determine the prevalence of rheumatoid disease, to demonstrate the different aspects related to a rheumatoid disease such as epidemiology, pathogenesis, or the types of rheumatoid disease, determine the associated risk factors of rheumatoid disease and analysis of hematological and biochemical parameters in Rheumatoid Arthritis in with rheumatoid disease in Sulaimani City.

METHOD

This study involved 1,260 participants (43 men and 119 women) and 50 control (21 men and 29 women) who participated in this study. Along with blood sampling, a questionnaire was also collected, composed of several questions, including information about the participant's history and lifestyle; all Samples were obtained from Shahid Dr Hemn Hospital and Smart Health Tower from October 2022 to December 2022.

Blood samples (10 ml) were collected from the 162 patients and 50 control participants. The first part of the blood was collected for evaluation of hematopathological markers in tubes with EDTA as anticoagulant at a concentration of 50 microns, the second part of the blood was collected to estimate the 50 microns, the second part of the blood was collected for estimation of erythrocyte sedimentation rate of the erythrocytes in tubes containing 0.5 ml of sodium citrate. In contrast, the remaining blood was in plain tubes, centrifuged at 15000 rpm for 15 minutes. The serum was separated for biochemical analysis that included markers for liver injury, including ALT, AST, and ALP; kidney function markers, including Creatinine and Urea; and inflammatory markers, including ESR and CRP.

According to the manufacturer's protocol, these blood samples were analyzed for blood parameters using a fully automated Complete Blood count analyzer (Beckman Colter) (United States). The hemodynamic parameters (WBC et al.) were analyzed when the blood samples were collected. The cassette of the biochemical reagent kit (Roche et al. 400 plus Reagent) (Germany) was used to measure serum ALP, AST, ALT, urea, creatinine, and CRP analyzed using a fully automated chemical analyzer (Integra 400 plus) (Roche Cobas) (Germany).

Statistical analysis

The results of this study are represented as mean ± standard error (M±S.E.), and statistical analysis was performed using statistically available software SPSS for comparison parameters between groups; a two-sample T-

test was performed to evaluate the correlation between parameters; the person correlation method was used, p <0.05 considered statistically significant.

RESULTS

Demographic Characteristics

In this study, the age range for the distribution of rheumatoid disease ranged from 1 to 80 years, with a peak level in adults between 21-40 years, represented by 41.96 % of patients and more in the female groups (73.46%) with a negative correlation between rheumatoid disease and family history. Furthermore, the results revealed that rheumatoid disease is associated with many demographic factors in different ratios. It showed a higher ratio of education level to primary school (33.33%), occupation to unemployed (66.05%), resident to urban population (70.37 %), and not associated with smoking (88.27%), alcohol consumption (97.53%) and a positive correlation between RD and daily exercise (72.84%). (Table 1). Rheumatoid disease is associated with many demographic factors in different ratios. It showed a higher ratio of education level to primary school (33.33%), occupation to unemployed (66.05%), resident to urban population (70.37 %), and not associated with smoking (88.27%), alcohol consumption (97.53%) and a positive correlation between RD and daily exercise (72.84%). (Table 1).

Hematological markers

In the male group, the results showed a significant increase (P< 0.05) in WBC and a significant decrease (P< 0.05) in HBG in the rheumatoid disease group compared to those of the control group. At the same time, there are no significant differences (P< 0.05) in RBC and PLT count. However, in the female group, there is a significant elevation (P< 0.05) in WBC and a significant reduction (P< 0.05) in the groups in rheumatoid disease compared to those of the control group (Table 2).

Markers of the hepatorenal function

The results of the current study showed a nonsignificant elevation (P> 0.05) in all hepatorenal markers (ALP et al., urea and creatinine) in patients with rheumatoid disease compared to concentrations in the control group of both sex groups (Table 3).

Inflammation markers

Table 4 shows a significant increase in the C-reactive protein and ESR levels in the rheumatoid disease group in both the male and female groups compared to the control groups, respectively.

Table 1. Rheumatoid disease in association with demographic characteristics.

Characteristics	Items	No.	%
Age group	Less than 20	11	6.79
	21-40	**68**	**42**
	41-60	53	32.73
	61-80	30	18.52
Sex	Male	43	26.54
	Female	**119**	**73.5**
Family history	Yes	57	35.19
	No	**105**	**64.8**

Continue: Table 1—rheumatoid disease in association with demographic characteristics.

	Items	No.	%
Characteristics	Primary school	**54**	**33.3**
	Secondary school	42	25.93
	Diploma Degree	14	8.64
	BSc Degree	20	12.35
Occupation	Unemployed	**107**	**66.1**
	Employed	55	33.95
Resident	Rural	35	21.61
	Suburban	13	8.02
	Urban	**114**	**70.4**
Smoking	Yes	19	11.73
	No	**143**	**88.3**
Alcohol	Yes	4	2.47
	No	**158**	**97.5**
Daily exercise	Yes	44	27.16
	No	**118**	**72.8**

Table 2. Comparison of hematologic parameters in control and rheumatoid disease groups according to sex.

Gender		Male			Female		
BMI		Control	RD	Statistical evaluate	Control	RD	Statistical evaluate
Statistics		**Mean± S.E**	**Mean± S.E**		**Mean± S.E**	**Mean± S.E**	
hematological parameters	RBC	4.95±0.43	5.1±0.61	0.164	4.38±0.46	4.51±0.35	0.091
	WBC	6.93±1.69	7.8±1.98*	P< 0.05	7.02±2.31	8.64±1.17*	P< 0.05
	HGB (g/dl)	14.21±1.16	12.79±1.5*	P< 0.05	12.38±1.19	11.87±1.34*	P< 0.05
	PLT	223.65±63.58	228.06±51.92	0.709	271.84±94.29	263.8±62.9	0.61

Table 3. Parameters of the hepatorenal function test in patients with rheumatoid disease.

Gender		Male		Statistical evaluate	Female		Statistical evaluate
BMI		Control	RD		Control	RD	
Statistics		**Mean± S.E**	**Mean± S.E**		**Mean± S.E**	**Mean± S.E**	
Liver parameters	ALP (U/l)	134.43 ± 9.968	156.85 ± 7.354	Nil	132.25 ± 8.833	145.46 ± 8.978	Nil
	ALT (U/l)	18.64 ± 0.959	20.25 ± 2.249	Nil	18.25 ± 2.336	19.72 ± 1.78	Nil
	AST (U/l)	20.07 ± 1.361	21.52 ±0.978	Nil	16.88 ± 1.608	18.0 ±1.201	Nil
Renal parameters	Urea (mg/dl)	21.21 ± 1.419	25.08 ± 1.415	Nil	20.5 ± 2.121	24.41 ±1.881	Nil
	Creatinine (mg/dl)	0.67 ± 0.055	0.764 ± 0.056	Nil	0.555 ±0.055	0.762 ± 0.102	Nil

Table 4. Inflammatory markers in groups of rheumatoid diseases concerning sex

Gender		Male		Statistical evaluate	Female		Statistical evaluate
BMI		Control	RD		Control	RD	
Statistics		**Mean± S.E**	**Mean± S.E**		**Mean± S.E**	**Mean± S.E**	
Inflammatory parameters	CRP (mg/L)	3.48±2.9	5.77±1.44*	P< 0.05	4.23±1.66	6.47±1.37*	P< 0.05
	ESR	2.88 ± 0.639	15.0 ± 3.138*	P< 0.05	7.0 ± 1.732	16.24 ± 1.555*	P< 0.05

DISCUSSION

Demographic Characteristics

This result suggested that rheumatoid disease depends on age. However, RA can occur in individuals of any age, and its incidence continues to increase with age, at least into the seventh decade of life (Boots et al., 2013). The estimated levels of sex hormones justified the division of the age group at the beginning of the disease. Around the age of menopause, women experience an increased incidence of RA, while men experience an increase in incidence after the age of 40. It is believed to play a role in the pathogenesis of RA (Nilsson et al., 2021).

A risk factor for rheumatoid arthritis is family history, which implies that environmental or genetic factors can influence the condition. Numerous environmental and genetic factors have been associated with a higher or lower risk of developing RA. Numerous indications have indicated that heredity plays a vital role in the onset of RA (Deane, Demoruelle et al. 2017). According to a previous study, there is a combined genetic risk factor and smoking component that increases the risk of developing rheumatoid arthritis (RA). It is not clear how much RA is caused by smoking and how smoking affects RA regarding genetic variability (Källberg et al., 2011). Additionally, RA has been associated with several dietary, lifestyle, and environmental factors. Some environmental factors have relatively consistent associations with RA, though many of these associations are only seen in single studies or inconsistent results across multiple studies. Tobacco exposure is the strongest of

these associations (Deane et al., 2017). In addition, both the general public and people with chronic diseases can benefit from regular exercise and physical activity in many ways. Reduced physical activity is a significant and reversible feature of RA. RA patients have been shown to exercise less than their healthy counterparts. In some countries, more than 80% of RA patients are physically inactive, while in the UK, the figure is thought to be around 68% (Sokka & Hakkinen, 2008).

Hematological markers

The results showed a significant increase in WBC and a significant decrease in HBG in the rheumatoid disease group. At the same time, there are no significant differences in the RBC and PLT count in rheumatoid disease groups compared to concentrations in the healthy group of both sex groups, and these results agreed with the results of other studies(Masson 2011, Tekeolu, Gürol et al. 2016). However, anemia in RA patients can have various causes based on the stage and the therapies they are receiving. The most common is iron deficiency anemia, caused by malabsorption or, more frequently, iron loss. Patients with RA may experience hemolytic anemia, anemia linked to myelodysplastic syndrome, folate deficiency anemia (which is typically counteracted in patients taking the antifolate agent methotrexate), vitamin B12 deficiency anemia (though concurrent Biermer anemia is uncommon), or anemia caused by medications such as leflunomide, salazopyrine, or methotrexate through a variety of mechanisms (Tekeolu, Gürol et al. 2016).

Hepatorenal Function Markers

This study did not show a significant increase in the concentration of the ALP enzyme in patients compared to healthy subjects, and these results agreed with the results of other studies (Selmi, De Santis et al., 2011; Olago-Rakuomi, 2017). Indeed, the increase in liver enzymes may be due to liver disorders caused by taking disease-modifying and antirheumatic drugs. The study by (Amital, Arnson, et al. 2009) found that 45% of rheumatic patients receiving methotrexate MTX and other treatments caused an increase in the concentration of ALP enzyme and albumin.

The kidney results obtained from the functional tests showed no significant differences in creatinine concentrations in the patients compared to the healthy subjects. The results of the present study are not in agreement with another study (Isaacs, Zuckerman, et al. 2014) that reported that the study explained the increase in creatinine concentration in tofacitinib-treated rheumatoid arthritis as a result of the impact of the medication on the inflammatory condition. One possible explanation for the elevated serum urea level is that inflammation triggers the body's monocytes to produce inflammatory cytokines like TNF-α, IL-6, and IL-1β. This is because urea stimulates the production of cytokines, suggesting that it plays a role in systemic inflammations such as rheumatism. Furthermore, urea was previously thought to play a significant role as an antioxidant (Lyngdoh, Marques-Vidal et al. 2011).

Inflammation Markers

Chronic inflammation in patients with RA can lead to vascular dysfunction and endothelial cell activation, forming an atheroma. Putative mediators of atherogenic mechanisms include cytokines and acute phase reactants such as reactive protein (Badsha, 2018). These results agree with the results of other studies (Badsha 2018, Mititelu, Pădureanu et al. 2020) reporting that RA progression advances with the aging process, mainly due to systemic inflammation. Overproducing reactive oxygen species (ROS) can enhance cell destruction and decrease antioxidant defense (Mititelu, Pădureanu et al., 2020).

CONCLUSIONS

This research concluded that rheumatoid disease caused a change in most physiological and hematological markers in the body. Especially the inflammation markers that increased in patients with rheumatoid disease

caused visible signs of swelling, stiffness, or redness in your joints.

DECLARATION SECTION

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Ethical Considerations

This research study has received ethical approval from the Ethics Committee of the Sulaimani Polytechnic University.

Conflict of interest

The authors report that there is no conflict of interest.

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None to be declared.

Data availability

Data are available by contacting the corresponding author by email.

Authors contribution

All authors contributed equally to the conception and design of the study, data collection, and analysis and drafted the initial manuscript. All authors critically reviewed and edited the manuscript. All authors approved the submission of the final version of the manuscript.

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