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Evaluation of the level of omentin, irisin and apelin with some biochemical indicators in the blood serum of patients with rheumatoid arthritis in the city of Kirkuk

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Abstract
The study was conducted on 80 samples, 45 samples were for patients with rheumatoid arthritis and 35 samples were a control group (healthy) without any disease and their ages ranged between (35-60) years. The samples were collected from Kirkuk Teaching Hospital and outpatient clinics. The results of the current research showed that there was a significant decrease in each of the levels (omentin, apelin, irisin, and IL-6) in the blood serums of patients with rheumatoid arthritis compared to healthy subjects, at a probability level of $P \leq 0.001$. The results of the current research showed a significant increase in each of the levels (CRP, AST, ALP, ALT) in the serum of patients with rheumatoid arthritis compared to healthy people.

Keywords: Rheumatoid arthritis, Omentin, Irisin, Apelin, IL-6

Introduction
Rheumatoid arthritis (RA) is a chronic disease affecting up to 1% of populations in developed countries. Certain genetic and environmental factors appear to promote the development of RA, but patients can present with heterogeneous signs and symptoms [1]. Rheumatoid arthritis occurs in about 5 per 1000 people and can lead to severe joint damage and disability. Significant progress has been made over the past 2 decades regarding understanding of disease pathophysiology, optimal outcome measures, and effective treatment strategies, including the recognition of the importance of diagnosing and treating RA early [2].
Omentin-1 is one of the important adipokines, and it is a glycoprotein, which is a glycoprotein in the year of 295, oligosaccharides [3], a discovery made in 2003 by Yang and has names including Intelectin [4] Intelectin-1 and endothelial lectin [5] and also stimulate the intestinal lactoferrin receptor [6]. It includes two forms, Omentione-1 and Omentine-2 (4). There are two types of omentin genes located next to each other in the chromosomal region Iq22-Iq23, which produce omentin-1 and omentin-2 [7]. Both forms show a different pattern of tissue expression in humans, as omentin-1 is the dominant form in plasma and adipose tissue [8] Omentin-1 is synthesized in visceral adipose tissue but is found in lower concentrations in the heart, lung, and placenta [3]. It was also found that its concentration is low in the fatty tissues under the skin [9] The physiological concentrations of omentin-1 in humans range between 100-800 ng /ml [8], as it is known to be expressed or produced in many physiological and pathological conditions, including obesity, insulin resistance, and inflammatory conditions [10].
Irisin It is a hormone consisting of 112 amino acids, and it was discovered for the first time in 2012 by Bostrom. Adipomyokine is secreted primarily by skeletal muscle as well as subcutaneous adipose tissue and visceral, and immunohistochemical studies showed that smaller amounts of irisin are also produced by the testes. liver D, pancreas, brain, spleen, heart B, and stomach [11].
In 1993, the gene for the receptor G-protein coupled with 380 amino acids was discovered. This receptor was named APJ, which is very similar to the angiotensin II receptor type1 (AngII-AT-1) found in humans. The isolation of 36 amino acids, the APJ receptor, and the propellant of apelin, which is an alternative factor denoted by the symbol (APLN), was isolated for the first time from the stomach of cows [12], and is linked to cells by the G protein receptor [13], and is found on the surfaces of some types of cells [14].
Interleukin-6 is a type of interleukin, as it is a glycoprotein with a molecular weight of 21-26 kDa and contains 28 amino acids (15). IL-6 is a pro-inflammatory cytokine and is produced by

various types of cells, including B lymphocytes, T lymphocytes, macrophages, monocytes, mast cells, and other non-lymphoid cells such as fibroblasts, endothelial cells, and T cells. Keratinocytes, and cancer cells [16]. IL-6 plays a major role in many inflammatory and autoimmune disorders [17] and its overexpression during inflammation and tissue injury is responsible for cytokine release syndrome [18].

Material and Methods

Collection of specimens

Estimation of CRP level in blood serum

Rheumatoid arthritis was diagnosed by using the VEDA.LAB device for the purpose of measuring C-reactive protein based on the method [19].

Estimation of interleukin-6 and hormone levels in serum.

The levels of each of (IL-6, Omentin, Irisin, Apelin) in the blood serum were estimated by the method of immunosorbent assay (ELISA) using the measurement kit for each hormone and the ELISA system according to the manufacturer, Mybiosource, USA.

Estimation of (AST), (ALT, and (ALP) enzyme activity in blood serum

The activity of the enzyme aspartate amino transferase (AST) and the activity of the enzyme alanine transferase (ALT) in blood serum were estimated using the ready-made analysis kit prepared from the French company Randox [20], as well as the activity of the alkaline phosphatase enzyme in blood serum depending on the colorimetric method and according to the prepared analysis kit Made by the French company Biolabo according to the ready-made measuring kit from the linear company [21].

Statistical Analysis

The SPSS statistical program was used to analyze the obtained results, if the arithmetic mean and the standard deviation ± SD were used for the data under study. The T-test was also used to compare the immunological and biochemical variables between the two groups of patients and the control at a probability level ($p \leq 0.001$).

Result and Desiccation

Measuring the levels of immunological and biochemical variables for the samples under study:

Table 1: shows the mean ± standard deviation of immunological and biochemical variables for the samples under study.

Parameters	Mean ±S.D		P
	Control n =40	Rheumatoid arthritis n =40	
CRP (mol/L)	8.13±1.34	25.11±6.21	≤0.001
IL6 (pg/ml)	63.13±160.45	37.76±112.56	≤0.001
Omentin (pg/ml)	265.76±21.11	195.87±10.27	≤0.001
Irisin (ng/ml)	40.77±4.13	21.98±2.13	≤0.001
Apelin (pg/ml)	210.32±14.13	98.74±11.12	≤0.001
AST (U/L)	7.12±46.21	36.19±60.23	≤0.001
ALT (U/L)	8.25±20.74	32.38±48.32	≤0.001
ALP (U/L)	6.14±25.10	13.15±35.32	≤0.001

The results showed that there was a significant increase at the level of probability $p \leq 0.001$ in the level of C-reactive protein, the activity of liver enzymes and the level of (ALT, AST, ALP) in the blood serum of a group of patients with rheumatoid arthritis compared to healthy people as in Figures (1, 2, 3, 4). The results also showed a significant decrease in the level of each of (interleukin-6, omentin, irisin, apelin) in the serum of patients with rheumatoid arthritis compared to healthy people, as shown in Figures (8, 7, 6, 5) respectively.

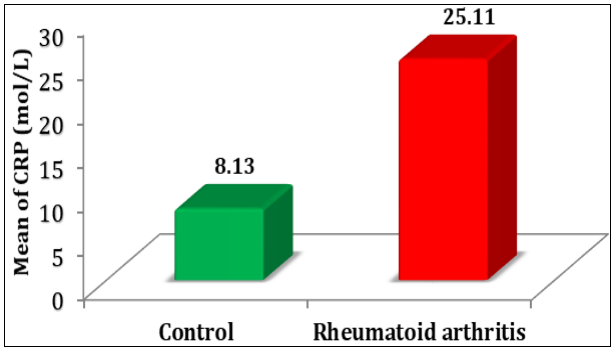

Fig 1: CRP level in the blood serum of the samples under study

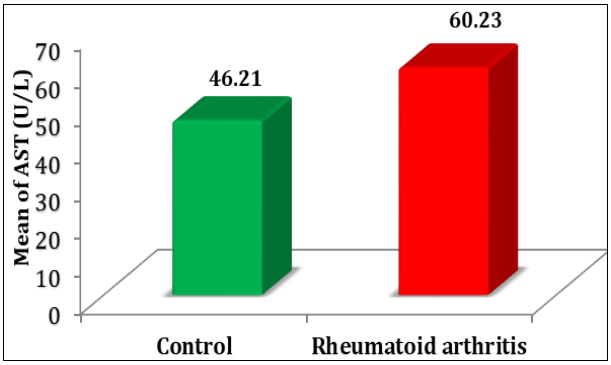

Fig 2: The activity level of AST enzyme in the blood serum of the samples under study

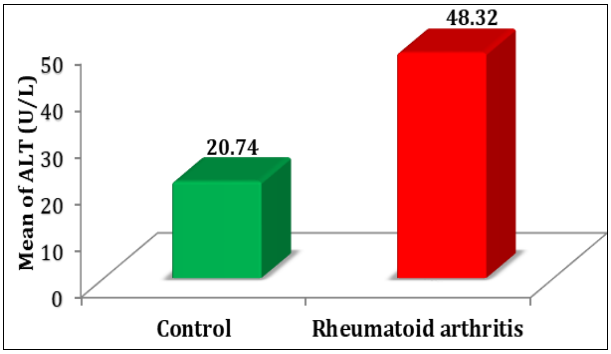

Fig 3: The activity level of ALT enzyme in the blood serum of the samples under stud

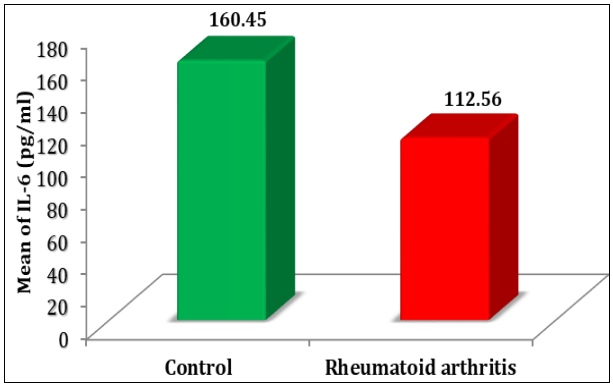

Fig 4: IL-6 level in the blood serum of the samples under stud

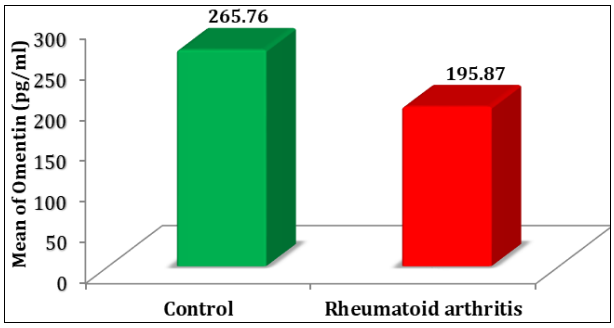

Fig 5: Omentin level in the blood serum of the samples under stud

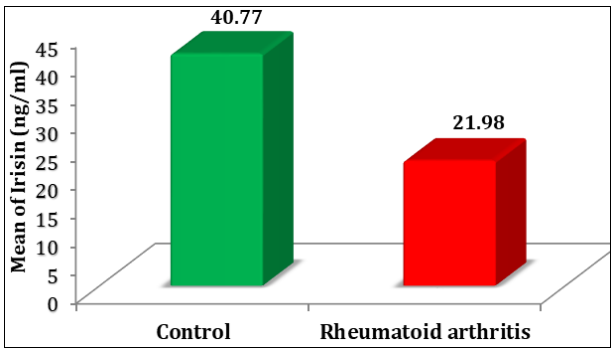

Fig 6: Irisin level in the blood serum of the samples under stud

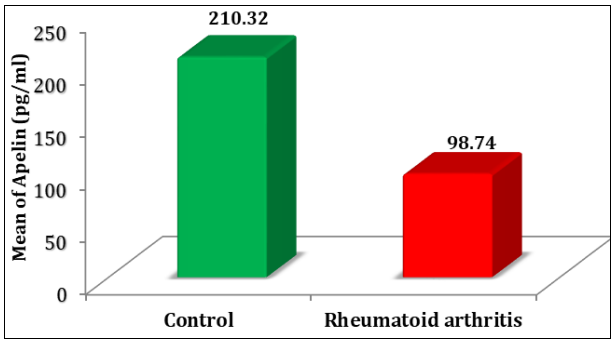

Fig 7: Apelin level in the blood serum of the samples under stud

C-reactive protein is a diagnostic indicator for the diagnosis of rheumatoid arthritis, and its high level in the group of patients confirms this, as the results of our current study agree with the results of both (Firas) [22] and (Anwar F) [23]. Active protein C is one of the acute inflammatory proteins, which occur when infection or inflammation occurs, as it is synthesized or produced in hepatic cells, in addition to many cells, including lymphocytes, endothelial cells, macrophages, smooth muscle cells, and cells. It is an acute phase protein, and can be used to diagnose rheumatoid arthritis, monitor the effect of treatment, and early detection of the disease [24-25].

In addition, other studies have shown a variation in the percentage of C-reactive protein, and the reason for this discrepancy may be due to the fact that patients are in different stages of the disease as well as the stages of treatment in the majority of rheumatoid arthritis patients who are treated with methotrexate, which works to inhibit the first interleukin, IL-1. Which stimulates the synthesis of acute phase proteins [26].

On the other hand, liver function showed a significant increase in each of (AST, ALT, ALP), as the results of the current study agree with the results of (Hassan) [27], (Ibrahim) [28], and ((Tawfeeq [29] and (Jasim) [30], as the reason for the rise in liver enzymes is due to a significant increase in the weight of the liver in patients with rheumatoid arthritis, in addition to the occurrence of necrosis and vacuolization of the liver cells, leading to an increase in the concentration of liver enzymes in the blood [31] Another study showed a high level of liver enzymes in patients with rheumatoid arthritis, and the reason for this rise is due to an expansion of the hepatic bile duct under the influence of the disease, which leads to damage to the liver, in addition to general liver disorders, which are present at a high rate in patients with rheumatoid arthritis. Rheumatoid arthritis [32-33].

Elevated liver enzymes may occur as a result of the build-up of glycogen in liver cells, which may lead to cirrhosis of the liver, which occurs as a result of the accumulation of fat inside the liver cells and its toxicity [34]. In addition to the abnormal structural changes that occur to the hepatocytes, such changes can lead to increased necrosis of the hepatocytes, which releases enzymes into the bloodstream [35]. Or the reason for the rise may be due to patients suffering from obesity, viral hepatitis, alcohol consumption, as well as coronary heart disease, which leads to an elevated level of liver enzymes in patients with rheumatoid arthritis (36). Or the reason for the rise in liver enzymes may be due to the hormonal state and the occurrence of a rise in body mass in addition to osteoporosis in females, as liver enzymes are present in the plasma membrane of osteoblasts and have a fundamental role in bone formation [37-38].

In addition, interleukin-6 showed a significant decrease in the serum of patients with rheumatoid arthritis compared with the control group. To the role of interleukin-6 in stimulating and activating B lymphocytes to differentiate and then produce antibodies, including rheumatoid factor [39]. In addition, interleukins are a soluble protein substance secreted from white blood cells, and its function is to activate the immune system by activating helper lymphocytes. It also mediates immune and inflammatory processes, including rheumatoid arthritis [40].

Interleukin-6 is a multifunctional cellular kinetic. It plays a major role as a mediator of several acute-phase inflammatory responses. These include inflammatory cells, activation of lymphocytes, and stimulation of hepatocytes to manufacture acute-phase proteins. Interleukin-6 is low in normal conditions and its levels in serum. It cannot be detected in the case of weak inflammation, and its increase contributes to many diseases, especially in people of advanced age, such as lymphoma, rheumatoid arthritis, and Alzheimer's [41]. And interleukin-6 is one of the acute phase proteins, as its concentration rises in the serum within a few hours after infection with bacterial infections and in turn stimulates the synthesis of C-reactive protein. Therefore, interleukin-6 is an indicator of the presence of acute infection [42]. It also mediates chronic inflammatory processes and autoimmune disorders such as type 1 diabetes, Digital Marketing Institute-DM1, thyroiditis, endothelial function disorders, and thrombus formation. In addition, interleukin-6 affects the B-cell that produces immunoglobulins, its activity, and efficacy. T-cell toxicity and contributes to host protection from acute environmental stress [43].

In addition, irisin showed a significant decrease in the serum of rheumatoid arthritis patients compared with the control group, as the results of the current study agree with (Roomi) [44], and (Samar A), as the reason for the decrease in the level of the hormone irisin It leads to a decrease in physical activity in athletes, which in turn leads to a decrease in the level of irisin and a gradual loss of bone [45]), which leads to making bone tissue more sensitive to the action of irisin than adipose tissue, and the effect of irisin depends on the dose given [46].

In addition, apelin showed a significant decrease in the serum

of rheumatoid arthritis patients compared with the control group, as the results of the current study agree with (Gunter S) [47], and (Di Franco M) [48].

Apelin reduces inflammation and improves diabetic nephropathy through decreased monocyte infiltration and activation of NF-κB [49]. Another study showed that mRNA and protein levels are decreased in patients with rheumatoid arthritis and inversely related to indicators of severity of rheumatoid arthritis. The decrease in apelin expression may be attributed to downregulation of IL-6-mediated bone-forming protein receptor expression, which leads to inactivation of the PPARγ/β- complex. catenin, thereby impairing transcription of the APLN target gene, which encodes apelin [50-51].

In addition, omentin showed a significant decrease in the serum of rheumatoid arthritis patients compared with the control group, as the results of the current study agree with (Šenolt L) [52], and (Zhong X) [53], as the reason for Decrease in the level of the hormone omentin to metabolism (insulin resistance, diabetes mellitus, CV disease, rheumatoid arthritis and obesity) [54-55]. Omentin plays a major role in bone homeostasis, inhibiting the anti-osteal and pro-osteogenic effect of macrophages, In addition, omentin can be used as a biomarker for bone metabolism, inflammatory diseases, cancers, and rheumatoid arthritis [56-57].

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