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# Comparing The Levels of Some Biochemical Markers in Rheumatoid Arthritis Patients With and Without Depression

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RESEARCH ARTICLE

# Comparing The Levels of Some Biochemical Markers in Rheumatoid Arthritis Patients With and Without Depression

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## ABSTRACT

One of the most common comorbidities of rheumatoid arthritis is depression, which is an independent mood disorder. This study aims to examine the blood levels of some biochemical markers in rheumatoid arthritis patients with and without depression compared to healthy group. This study included three groups: rheumatoid arthritis patients with depression, rheumatoid arthritis patients without depression, and a healthy group. The results showed that patients groups had significantly ($P \leq 0.05$) higher activity of acetylcholine esterase and ceruloplasmine, carbonyl, ischemic modified albumin (IMA), interleukin 6 (IL-6), tumor necrosis factor $\alpha$ (TNF-$\alpha$), Haptoglobin, and Cupper, and significantly ($P \leq 0.05$) lower levels of total protein, albumin, globulin, thiol, iron, and zinc than control group. Free amino was significantly ($P \leq 0.05$) lower in patients with depression group compared to the control and significantly ($P \leq 0.05$) increases in patients with Rheumatoid arthritis without depression compared to control. Serotonin was significantly ($P \leq 0.05$) lower in patients with depression group compared to the control and significantly ($P \leq 0.05$) increases in patients with Rheumatoid arthritis, the study suggests that the presence of depression in Rheumatoid arthritis patients is associated with additional biochemical changes that may reflect more severe or complex pathophysiological interactions. The lower levels of serotonin and free amino in Rheumatoid arthritis patients with depression indicate a potential link between mood disturbances and biochemical imbalances.

**Keywords:** Acetyl cholinesterase, Depression, Rheumatoid arthritis, Serotonin, Tumor necrosis factor -$\alpha$

## Introduction

The severe inflammation of joints known as rheumatoid arthritis (RA) mostly affects the joints.[1] Although RA is characteristically marked by symmetric arthritis in the small joints of the hands and feet, any synovial joint can be involved as the disease progresses. Joint swelling results from synovial invasion into the nearby articular structures, which destroys the bone and cartilage.[2] Joint swelling is the main symptom in inflammatory arthritis, typified by symmetric, poly articular pain and swelling, usually in the hands and feet's tiny joints.[3] Although the exact origin of RA is still unclear, experts generally agree that a combination of hereditary and environmental factors have a role.[4] The main environmental risk factors are food, using tobacco, being a woman, and becoming older. The serological test is represented by Cyclic Citrullinated Peptides (CCP) antibodies.[5] The presence of these autoantibodies is characteristic of the disease.[6] Depression is one of the common mental health conditions. The etiology of depression remains incompletely understood, but significant contributions from immune system dysfunctions involving the central nervous system and inflammatory responses have been proposed.[7] Depression is one of the most frequent comorbidities in RA; it takes an important toll on the quality of life of these patients

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and leads to a decrease in life expectancy. Depression in patients with RA is associated with poor long-term outcomes. Multiple studies showed that depression in RA is associated with increased pain, fatigue, and physical disability.[8] Patients with RA may experience depression for a variety of reasons; they consist of discomfort brought on by physical symptoms, functional restrictions, the production of cytokines that promote inflammation, the advancement of illness, and disability.[9] Higher depression is predicted by increases in pain, disease activity, and the Health Assessment Questionnaire Disability Index.[10] At present, many studies have attempted to use biological agents for the efficacy of RA-associated depression, but there is no consensus.[11] Excessive production of reactive oxygen species (ROS) is involved in RA pathogenesis, leading to oxidative stress and tissue damage. It has been suggested that prooxidant/antioxidant imbalance in RA may be due to the acceleration of certain cellular responses or insufficient antioxidant defense systems.[12] Excessive ROS in RA patients will impair the function of the enzyme defense system against free radicals, leading to a rapid increase in free radical levels, increasing the debilitating effect on the hippocampus, amygdala, and cortical connections, and ultimately accelerating the onset of depression.[13] Acetylcholinesterase (AChE) is one of the hydrolase enzymes (E.C 3.1.1.7) that hydrolyzes acetylcholine into choline and acetic acid.[14] Acetylcholinesterase is present in the central and peripheral nervous systems, and the activity of AChE is also crucial for cellular oxidative stress.[15] Increasing evidence shows that the non-neuronal cholinergic system plays an important role in the pathology of RA.[16] Cytokines are key signaling molecules of the immune system, like Tumor necrosis factor alpha (TNF-$\alpha$) and interleukin 6 (IL-6), which are pro-inflammatory cytokines IL-6, one of the major pro-inflammatory cytokines responsible for immune response activation. TNF-$\alpha$ is secreted mainly by macrophages and lymphocytes in response to cell damage caused by infection or malignant transformation.[17] TNF and IL–6–induced osteoclasts may contribute to the pathology of inflammatory arthritis associated with joint destruction. TNF-$\alpha$ inhibitors are used in clinical settings to counteract the high TNF-$\alpha$ levels that cause joint inflammation, hence avoiding TNF-$\alpha$ tissue damage in RA17. Zinc, Cu, and Fe are trace elements playing critical roles in many essential body processes and mineral balance maintenance.[18] The relevance of trace elements in RA was highly concentrated since many of them were co-factors in metabolic processes influencing collagen with bone formation or immune system goals. Serotonin has been considered a peripheral hormone with immunomodulatory properties.[18] Most peripheral (i.e., outside the nervous system) serotonin is produced by intestinal enterochromaffin cells, and interestingly, mucosal sites have been shown to trigger the development of RA after release from enterochromaffin cells, serotonin enters the bloodstream, is absorbed by platelets, and is stored in dense granules until activated.[19] Measuring oxidative stress by protein markers like free amino, thiol, and carbonyl groups, protein peroxidation can occur by various mechanisms: an increase in the production of ROS, a decrease in the rate of scavenging of ROS, an increased susceptibility of the protein to oxidation and a decrease in the rate of removal of oxidized species.[20] Acute phase proteins such as Haptoglobin, Ceruloplasmin, proteins, and albumin are produced in the liver in response to inflammatory cytokines. This study aims to compare the levels of some biochemical markers in RA patients with and without depression compared to control.

## Materials and methods

Estimations of some biochemical markers in 180 blood samples with an age range between 30-70 years were selected in this study and divided into three groups: Group I (50) individuals who appear to be healthy subjects as control, Group II (65) individuals suffer from rheumatoid arthritis, and Group III (65) individuals suffer from rheumatoid arthritis and depression. The study was conducted in the biochemistry lab of the Kirkuk Teaching Hospital in Kirkuk. Specialized doctors diagnosed the cases of patients from (February to October) 2023. All patients were subjected to a personal interview using a specially designed questionnaire format of full history with detailed information.

### *Methods*

The activity of acetylcholine esterase was assayed by modified Ellman method.[21] Ceruloplasmin (CP) according to the method of Menden et al.[22] Total protein (TP) is determined by using Lowry et al[23] method using bovine serum albumin as standard. Bromocresol green (BCG) is used to assess albumin.[24] Estimating free amino groups was performed according to the Zaia et al. method.[25] Thiol groups were assayed according to the method of Ellman.[26]

The carbonyl group of the protein was estimated using the method of Levine et al.[27] Ischemia-modified albumin level was determined by Bar-Or et al.[28] IL-6, TNF, Haptoglobin determined by using ELIZA kit (Bioassay Technology Laboratory), and Serotonin

**Table 1.** The serum Acetylcholine esterase and Cp activity and the specific activity in all studied groups.

| | Healthy group | | RA group | | RA with depression | |
|---|---|---|---|---|---|---|
| Enzyme | Activity U/L | Specific activity U/mg | Activity U/L | Specific activity U/mg | Activity U/L | Specific activity U/mg |
| AchE U/ml | 5.961± 1.30 | 0.009±0.003 | 8.53 ± 1.17* | 0.016±0.003* | 9.22 ±1.84*a | 0.02±0.005*a |
| CP mg/l | 205.4±16 | 0.45±0.07 | 317.3±31.24* | 0.62±0.13* | 314.3 ±40.3*a | 0.51±0.15*a |

Data expressed as mean ± SD (*) Significant variations (P ≤0.05) between both patients' groups and control group. Small letters are considered significant variations (P ≤0.05) between both patient's groups of RA.

**Table 2.** Levels of some biochemical markers in all studied groups.

| Parameters | Healthy group | RA group | RA with depression |
|---|---|---|---|
| TP g/dl | 6.48 ±1.32 | 5.37±0.88* | 4.76±0.76 *a |
| Albumin g/dl | 4.17 ±0.91 | 3.071±0.33* | 2.179±0.82 *a |
| Globulin g/dl | 2.64±1.20 | 2.067±0.93* | 1.970±0.13 * |
| AGR | 2.61±0.58 | 2.14±0.28* | 1.55±0.16* |
| IMA(Abs) unit | 0.36 ±0.073 | 0.40 ±0.059 * | 0.53±0.069 *a |
| Free amino mmol/L | 0.038 ± 0.004 | 0.039±0.003* | 0.034± 0.004*a |
| Free amino/TP | 0.006 ± 0.002 | 0.0076±0. | 0.0073±0.002 |
| Carbonyl nmol/ml | 5.48±1.4 | 13.72±2.25* | 15.72±3.28*a |
| Carbonyl /TP | 0.88 ±0.32 | 2.62 ±0.7 * | 3.37 ±0.9*a |
| Thiol $\mu$mol/L | 18.3±02.1 | 12.90±0.93* | 11.28±0.85*a |
| Thiol/TP | 2.90 ±09 | 2.46±0.41* | 2.44±0.45 * |

Data were expressed as mean ± SD. (*) Significant variations (P ≤0.05) between both patient's groups with RA compared to the control. Small letters mean significant variations (P ≤0.05) between both patient's groups of RA.

determined by using ELIZA kit (SunLong Biotech Co., LTD).

### *Statistical analysis*

Results and discussion statistical analysis was done using GraphPad Prism Version 8 (GraphPad Software, San Diego, CA, USA). Values were expressed as (mean ± Standard Deviation [SD]). The comparison of (mean ± SD) was performed using the ANOVA test. Statistical significance was defined as (P ≤ 0.05) and the correlation between the parameters.

## Results and discussion

The results in Table 1. indicated that there was a significant (P ≤0.05) increase in (AchE and CP) activity and specific activity in the patients' groups compared to the control and between patients' groups.

The results in Table 2. indicated that there was a significant (P ≤0.05) increase in the levels of IMA, free amino, carbonyl and carbonyl /TP, an important (P ≤0.05) decrease in TP, albumin, thiol in patients' compared to control and between patients' groups, a significant (P ≤0.05) decrease in the globulin, albumin globulin ratio (AGR) and thiol/ TP in patients compared to the control.

Table 3. clarifies the levels of some cytokines and trace elements as (mean± SD) in all studied groups. The results in Table 3. indicated that there was a significant (P ≤0.05) increase in IL-6 and TNF-$\alpha$ and an important (P ≤0.05) decrease in Zn levels in patients compared to control. Haptoglobin and Cu increased significantly (P ≤0.05) increase, while Fe levels significantly (P ≤0.05) decreased in the patient groups compared to the control and between patients' groups. Serotonin was significantly (P ≤ 0.05) higher in patients with RA compared to the control and significantly (P ≤ 0.05) lower in RA patients with depression compared to the control.

The results in Table 4, of the correlation coefficient analysis showed that there were very good positive and or/negative liner relationships between (TP-globulin) and (TP- thiol/TP, TP- free amino /TP and thiol/TP– free amino/TP) in RA patents respectively. The result in RA patients with depression indicated that there were moderate positive liner relationships between (TP – free amino /TP, carbonyl–carbonyl /TP, and thiol/TP – free amino/TP) and very good negative liner relationships between (TP-thiol/TP). The absence of correlation between the other measured biochemical markers indicated that all these markers contributed independently to the disease process.

Several important functions of AChE, i.e., the role in apoptosis, role in adhesion of pathological proteins, and participation in oxidative stress and inflammatory response that are common to different disorders, so a disturbance in the activity of

**Table 3.** Levels of some cytokines and trace elements in all studied groups.

| Parameters | Healthy group | RA group | RA with depression |
|---|---|---|---|
| IL-6 ng/L | 1.38±0.03 | 2.694±0.74* | 2.80±0.63* |
| TNF-$\alpha$ ng/L | 6.98 ±3.14 | 107.7±45.39* | 113.9±101.3* |
| Haptoglobin ng/ml | 0.65 ±0.61 | 1.82 ±0.08*. | 2.1 ±0.2*a |
| Serotonin g/L | 3.44±0.46 | 3.80±0.23* | 2.56±0.31*a |
| Fe $\mu$g/dl | 130.6±19.81 | 78.68±59.28* | 39.59±13.83*a |
| Cu $\mu$g/dl | 109.7±14.46 | 230.6±33.47* | 201.3±36.46*a |
| Zn $\mu$g/dl | 100.2 ±19.4 | 63.9±12.9* | 61.43±12.2* |

Data were expressed as mean± SD (*) Significant variations (P ≤0.05) between both patient's groups with RA compared to the control. Small letters mean significant variations (P ≤0.05) between both patients' group of RA.

**Table 4.** Analysis of correlation coefficients between biochemical parameters studied in the group of patients with rheumatoid arthritis.

| | RA group | | RA with depression | |
|---|---|---|---|---|
| Parameters | P | *R* | P | *r* |
| AchE – Hp | 0.00061 | 0.46** | NS | — |
| CP – AGR | 0.0081 | 0.34** | NS | — |
| CP - albumin | 0.0162 | 0.37** | NS | — |
| CP – Carbonyl | NS | — | 0.011 | 0.37** |
| TP – AGR | <0.05 | –0.52 | 0.026 | –0.28* |
| TP – globulin | <0.05 | 0.75 | 0.0005 | 0.42** |
| TP – carbonyl/TP | <0.05 | 0.66 | <0.05 | –0.52 |
| TP – thiol /TP | <0.05 | –0.89 | <0.05 | –0.907 |
| TP – Free amino/TP | <0.05 | –0.906 | <0.05 | 0.73 |
| Albumin–free amino | 0.042 | –0.23* | NS | — |
| Albumin – globulin | NS | –0.22 | 0.049 | –0.25* |
| Albumin – AGR | 0.0002 | 0.45 | <0.05 | 0.68 |
| Globulin – AGR | <0.05 | 0.67 | <0.05 | –0.69 |
| Globulin- Carbonyl/TP | <0.05 | –0.48 | NS | — |
| Globulin –thiol /TP | <0.05 | –0.72 | 0.0018 | –0.39** |
| AGR - Carbonyl/TP | 0.014 | 0.30** | NS | — |
| AGR - Thiol /TP | <0.05 | 0.56 | NS | — |
| HP–free amino | NS | — | 0.025 | –0.38* |
| HP – Cu | NS | — | 0.016 | 0.40** |
| Serotonin – globulin | NS | — | 0.048 | 0.35* |
| Carbonyl-Carbonyl/TP | 0.0047 | 0.39** | <0.05 | 0.74 |
| Carbonyl – thiol | NS | — | 0.008 | –0.33 |
| Carbonyl /TP – thiol/TP | <0.05 | 0.61 | 0.0009 | 0.41 |
| Thiol – thiol/TP | NS | — | 0.0001 | 0.47 |
| Thiol /TP – free amino/TP | <0.05 | –0.89 | <0.05 | 0.72 |
| Free amino – free amino/TP | 0.0002 | 0.46 | <0.05 | 0.62 |

(*) mean significant at 0.05.
(**) mean significant at 0.01.
1. $0 < r \leq 0.19$ are very low correlation.
2. $0.2 \leq r \leq 0.39$ and $0.4 \leq r \leq 0.59$ are low correlation.
3. $0.6 \leq r \leq 0.79$ and $0.8 \leq r \leq 1$ are very high correlation. [29]

AChE, may reflect depressive disorders, the role of AChE is crucial for maintaining proper neurotransmission and preventing overstimulation of nerve cells. [29] Its activity is essential for normal physiological function and is implicated in various neurological conditions and toxicological contexts. [30] While apoptosis and adhesive proteins are markers of cellular changes, their impact on neurobiology and neurochemistry can contribute to the development or exacerbation of depression through various pathways involving neuroinflammation, neuroplasticity, and neurotransmitter function. [31,32] The increase in AChE is a compensatory mechanism to decrease the high acetylcholine levels. [33] Acute-phase reactant CP is activated in the central nervous system because of oxidative injury. [34] The two groups of patients in the current study have higher blood CP activity, which may indicate a significant role in the development of depression. Increased CP activity binds to large amounts of Cu, participating in mental disease. [35]

Ceruloplasmin activity was elevated in patients with RA, possibly because of the greater degree of inflammation in this group.[36] The results of AChE and CP-specific activity between patients' groups may indicate the power effect of AChE in RA patients with depression. Both patients ' groups ' total protein and albumin levels decreased significantly compared to the control. According to Ben-Hadj-Mohamed et al.[37] albumin decreased in RA patients because albumin targets inflamed joints; hence, hypoalbuminemia is a common occurrence in active RA patients or participation in the onset of depression. There is evidence to suggest that the pathophysiology of depression is associated with an excess of free radicals.[38] This excess of free radicals results in oxidative stress, which is the source of oxidative damage linked to neurodegeneration and other mental illnesses, including depression.[39] Oxidative stress activates inflammatory pathways, whereas inflammation increases oxidative stress (e.g., an increase in the levels of cytokines IL-1 leads to decreased levels of albumin).[40] The higher level of IMA in two patent groups of RA compared to control may be due to tissue hypoxia and injury. Also, the high level of IMA might be related to pro-inflammatory cytokines, which are produced in response to chronic inflammation. In depressive disorders, one study reported a positive correlation between the severity of depression and IMA levels.[41]

Significant elevations in pro-inflammatory cytokines IL-6 and TNF-$\alpha$ were observed between two patient groups of RA compared to control. This is consistent with several studies.[42] The development and progression of RA are associated with certain inflammatory cytokines; the activation of inflammation also plays a crucial role in immune deregulation and joint inflammation.[43] Increased levels of pro-inflammatory cytokines, such as IL-6 and TNF-$\alpha$, have been linked to changes in neurogenesis and brain plasticity.[41] Other studies support the suggested role of IL-6 in depression.[44] Serotonin levels are significantly increased in RA patients and significantly lower in RA with depression patients as compared to control. In recent years, serotonin is a peripheral hormone shown to have immunomodulatory properties.[45] Intriguingly, mucosal areas have emerged as a trigger site for developing RA intestinal cells that generate most peripheral serotonin (i.e., outside the nervous system).[46] Increased IL-6 level is associated with reduced serotonin metabolites that cause depression, inflammatory markers including C-reactive protein, and erythrocyte sedimentation rate increase the levels of pro-inflammatory cytokines TNF-a, IL-6 so increase levels of inflammation Biological scarring that increases the risk of Depression.[47] Haptoglobin significantly increases in RA patients with and without depression compared to the control. Since HP is an acute phase protein, tissue damage or localized or systemic inflammation may cause serum HP concentration to rise multiple times. Pro-inflammatory cytokines such as IL-6 and (TNF)-$\alpha$ have the potential to increase HP secretion[48] dramatically. In the depression group, higher levels of pro-inflammatory cytokines and positive acute-phase proteins have been linked to immune system activation in depression.[49] Evaluating the relationship between oxidative stress and RA has garnered significant attention. Still, there is a shortage of information on introducing an oxidative biomarker consistent with an anti-CCP antibody to validate the diagnosis.[50] Protein carbonyl has been identified as one of the most promising indicators of oxidative stress among many biomarkers.[51] In the current study, there were significant increases in carbonyl levels in both groups of RA patients compared to control. Carbonyls develop quickly and stay in the bloodstream over extended periods. The results of thiol cleared that there was a significant reduction in thiol levels in RA patients with and without depression compared to the control. Thiol is an antioxidant defense compounds that serve as ROS scavenger—and oxidizes as free thiol group proteins, leading to a significant decrease in detectable plasma protein thiol groups.[52]

This study also showed a significant increase in free amino levels in RA patient groups compared to control; these results are supported by Sandell,[53] who found the same results in RA patients. When proteins are exposed to oxidants, original amino acid residues are lost, unstable intermediates are formed, and stable products are formed. Each of these events can be used to quantify protein damage. Analysis of total free amino groups can provide information on oxidative reactions occurring in poorly understood systems.[54] The results also showed that free amino significantly decreased in RA with depression. Depression is thought to be linked to the lack of neurotransmitters such as serotonin and norepinephrine.[55] For example, serotonin is synthesized from tryptophan, and norepinephrine is synthesized from tyrosine. Low levels of serotonin and norepinephrine are directly involved in the pathogenesis of depression. The decreased concentration of serum-free amino is due to the chronic catabolic status in the depression caused by the poor appetite, which is a common symptom of this disorder.[56]

Comparing the amounts of trace elements between two patient groups of RA indicated a reduction in the level of Zn and an increase in Cu levels when compared to the control. The antagonistic interaction between Cu and Zn may be due to these alterations.[57] Serum Cu levels were greater in depressed groups

because it binds to serotonin.[58] At the same time, Fe levels in two patient groups of RA were lower than control. Anemia in RA may be produced by hepcidin overexpression, which causes localized Fe deposition. Iron might directly contribute to the inflammatory response by encouraging T cells to produce pro-inflammatory cytokines.[59] Iron deposition has been noted in the synovial fluid of RA patients as well as in the central nervous systems of people suffering from inflammatory disorders such as multiple sclerosis, Alzheimer's, and Parkinson.[60] Dietary Fe deficiency raises the risk of depression, according to several studies.[61] Individuals with a history of Fe deficiency and anemia are more likely to experience sadness.[62]

## Conclusion

According to the current study results may indicate that the pro-inflammatory agents have been considered as pathogenic factor associated with the mechanism of developing depression with the important role of inflammatory processes in depression pathogenesis, increased levels of IL-6 and TNF-$\alpha$ in blood serum are associated with decreased serotonin metabolites, leading to depression and increased inflammation therefore, the results showed that patients with depression had lower levels of serotonin. In contrast, patients with RA without depression had high levels. Cytokines patterns will offer rich biomarker opportunities and will play a part in introducing personalized medicine strategies. The results also showed changes in some oxidation protein markers, so it is important to evaluate the relationship between oxidative stress and RA and the need for oxidative biomarkers consistent with anti-CCP antibodies to validate the diagnosis. Finally, the correlation results may suggest that these interrelated parameters mentioned above may be beneficial in evaluating these RA patients. Further studies are needed to confirm the impact of various biochemical parameters in RA patients with or without depression.

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## Authors' declaration

- Conflicts of Interest: None.
- We hereby confirm that all tables in the manuscript are ours
- No animal studies are present in the manuscript.
- Authors sign on ethical consideration's approval.
- Ethical Clearance: The project was approved by the local ethical committee at University of Kirkuk.

## Authors' contribution statement

S.I. performed the experiment, verified the data acquisition and analysis, and wrote the manuscript with support from I.G., S.I. contributed to sample preparation and interpretation of the results. I.G. conceived the original idea and supervised the project, including drafting and proofreading the manuscript.

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# مقارنة مستويات بعض العلامات الكيميائية الحيوية في مرضى التهاب المفاصل الروماتويدي مع وبدون الاكتئاب

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## الملخص

أن أحد أكثر الأمراض الشائعة المصاحبة للالتهاب المفاصل الروماتويدي هو الاكتئاب، وهو اضطراب مزاجي مستقل، لذا تهدف هذه الدراسة إلى فحص مستويات بعض المتغيرات البيوكيميائية لدى مرضى التهاب المفاصل الروماتويدي المصابين بالاكتئاب وبدونه مقارنة مع المجموعة (الضابطة) الاصحاء. حيث شملت هذه الدراسة ثلاث مجموعات: مرضى التهاب المفاصل الروماتويدي الذين يعانون من الاكتئاب، ومرضى التهاب المفاصل الروماتويدي غير المصابين بالاكتئاب، والمجموعة الضابطة. أظهرت النتائج أن مجاميع المرضى لديهم نشاط أعلى معنويا ($P \geq 0.05$) لإنزيم الاستيل كولين استريز، السيرولوبلازمين، الكاربونيل، الإنترلوكين 6 (IL-6)، عامل نخر الورم α (TNF –α )، هابتوغلوبين، والنحاس. واظهرت الدراسة انخفاض ملحوظ ($P \geq 0.05$) في مستويات البروتين الكلي، الألبومين، الجلوبيولين، الثايول، الحديد، والزنك مقارنة مع المجموعة الضابطة. بينما اظهر الأمينو الحرة انخفاضا معنويا ( $P \geq 0.05$) في المرضى الذين يعانون من الاكتئاب مقارنة مع المجموعة الضابطة وارتفاعا معنوية ($P \geq 0.05$) في المرضى الذين يعانون من التهاب المفاصل الروماتويدي بدون اكتئاب مقارنة مع مجموعة الضابطة. وأظهرت الدراسة انخفاض ملحوظ ($P \geq 0.05$) في مستويات السيروتونين لدى المرضى الذين يعانون من الاكتئاب، وارتفع ملحوظ ($P \geq 0.05$) في المرضى الذين يعانون من التهاب المفاصل الروماتويدي مقارنة مع المجموعة الضابطة، وتشير الدراسة إلى أن وجود الاكتئاب لدى مرضى التهاب المفاصل الروماتويدي يرتبط بالمزيد من التغييرات التي قد تعكس تفاعلات فسيولوجية مرضية أكثر تعقيدًا. تشير المستويات المنخفضة من السيروتونين والأحماض الأمينية الحرة لدى مرضى التهاب المفاصل الروماتويدي المصابين بالاكتئاب إلى وجود صلة محتملة بين اضطرابات المزاج والاختلالات الكيميائية الحيوية.

**الكلمات المفتاحية:** أسيتايل كولين أستراز، الاكتئاب، التهاب المفاصل الروماتويدي، السيروتونين، عامل النخر الفا TNF-α.