

The Effect of Etanercept Treatment on the levels of Albumin and C-reactive Protein and their Ratio in Iraqi Psoriatic Patients

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Abstract

Background: Psoriasis, a common chronic autoimmune dermatological disease, is identified by scaling and inflammation seen in the skin. Both environmental and genetic factors contribute to its pathogenesis.

Objectives: To examine changes in albumin and C-reactive protein levels and their ratios, and the effect of Etanercept treatment on these indicators in the serum of Iraqi Psoriasis patients compared to healthy individuals.

Methods: A total of 100 Psoriatic patients were enrolled in the study and matched with healthy individuals (n=93) attending the Department of Venereology and Dermatology at Baghdad Teaching Hospital from November 2024 to April 2025. The levels of C-reactive protein and albumin, as well as their ratio in these patients, were compared with those of the control group. Furthermore, the effects of the biologic treatment were followed up for these parameters using 30 patients, before receiving any treatment, and after three months of Etanercept treatment.

Results: The serum level of albumin showed a highly significant decrease, with a highly significant increase in the concentrations of both serum C-reactive protein and the CRP/albumin ratio in the patient group compared to the control group, respectively. Furthermore, the three-month treatment with Etanercept induced a substantial difference in the albumin levels, and a very notable decrease in both C-reactive protein concentration and CRP/albumin ratio.

Conclusion: Psoriasis is a disease that affects the albumin and C-reactive protein levels, as well as their ratio. In the interim, using Etanercept for three months as biotherapy revealed alterations in the measured levels, achieving concentrations nearly similar to those of normal healthy individuals.

Keywords: Albumin; Biomarkers; C-reactive protein to albumin ratio; Etanercept treatment; Psoriasis.

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Introduction

Psoriasis is a chronic inflammatory skin disease characterized by rapid keratinocyte proliferation, leading to erythematous plaques covered with silvery scales, often symmetrically distributed. The exact cause is unknown; however, genetic, environmental, and immunological factors are implicated. Psoriasis may also involve other organs, including joints, nails, and the liver (1). Psoriatic skin patches are mainly erythematous and flaky, and are the cause of the aberrant expression in patients with psoriatic skin (1, 2). Although the exact cause of the disease remains unknown, other researchers worldwide have recently focused their attention on oxidative stress as a crucial factor in the pathogenesis of this disease (3).

Total protein is considered the most abundant compound in serum samples, with albumin being the principal constituent. Human serum albumin has a distinctive structure with an amino acid sequence

regulation, nutrient transport, antioxidant activity, and waste removal (4). Ehlting *et al.* (2021) reported that an abnormal albumin level is a clear indicator of liver malfunction (5). The belief that plasma proteins are crucial for assessing a variety of diseases has increased markedly in the past decade, as they provide pathophysiological information. On the other hand, inflammation is more closely related to a variety of clinical conditions associated with characteristic alterations in the sera acute phase proteins (APPs) (6). The C-reactive protein (CRP) and albumin are now recognized as acute-phase reactants and have been used as vital biological markers of inflammation to predict disease incidence and mortality in many ailments. During inflammation, the CRP levels increase (positive acute-phase reactants), whereas the albumin levels decrease (negative acute-phase reactants) (7).

Although a non-specific marker, CRP is the most sensitive indicator of inflammation, with elevated levels directly correlated with the degree and severity of tissue damage. Its relatively short half-life of 6–8

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specific to humans at its amino terminus. This is synthesized by the liver and enables osmotic pressure

hours ensures that it is a very effective tool for monitoring disease progression, including skin diseases (7, 8). Elevated C-reactive protein (CRP) levels have been observed in patients with Psoriasis, where it plays a significant part as a biomarker as well as in assessing the severity and stage of the disease (9). More recently, the CRP-to-albumin ratio has been identified as an indicator of increased inflammation and is credited with greater importance than the CRP levels in plaque Psoriasis (9, 10).

Psoriasis is a chronic inflammatory condition that can be treated with an array of approaches, including biologic therapies, phototherapy, topical medications, and systemic medications (11, 12). Enbrel (Etanercept, ETN), a tumor necrosis factor- α (TNF- α) inhibitor, is licensed to treat this disease and is one of the biologic drugs in use now (12).

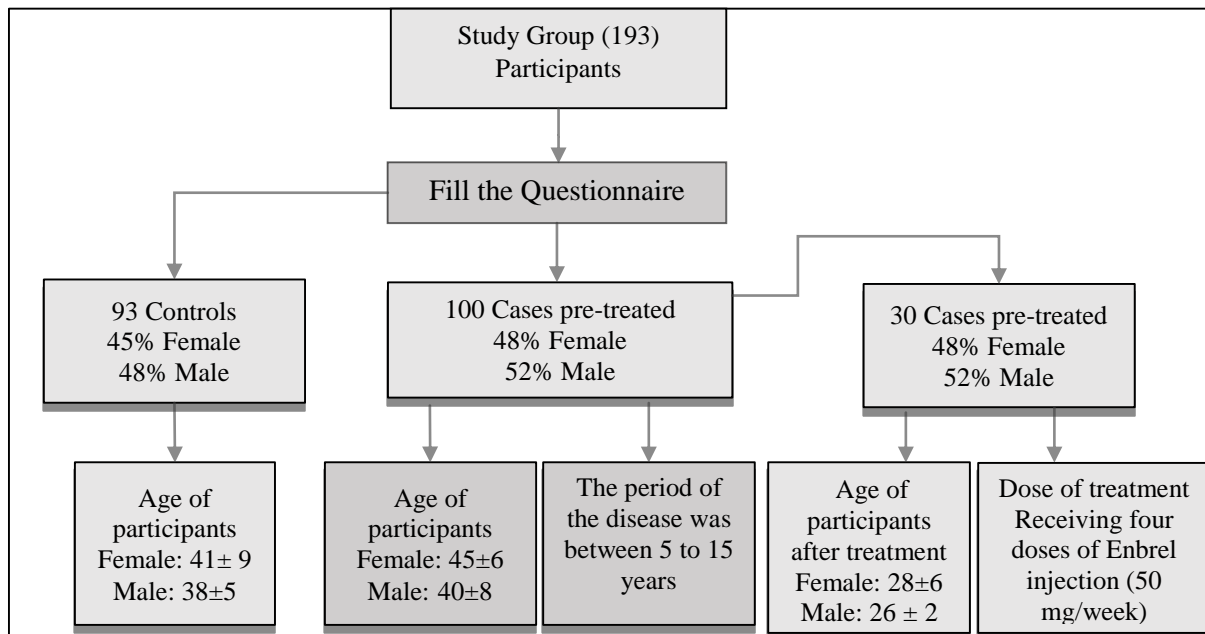
The current study aimed to measure the levels of albumin [Alb] and C-reactive protein [CRP] and the [CRP]/[Alb] ratio as vital parameters in this inflammatory disease, as well as to investigate the

effect of the ETN treatment on these parameters in Iraqi psoriatic patients.

Patients and Methods

The study participants were divided into two main groups: the patient group and the healthy control group for comparison. A total of 193 Iraqi participants (male and female), aged 9 to 65 years, were included in the study. The study groups comprised 100 patients and 93 healthy control individuals.

To study the effect of the Etanercept (Enbrel®) treatment, serum samples were collected from a subgroup of the patients (n= 30) twice: before receiving any type of treatment, including the biological one, and after three months of initiating treatment with Etanercept administered as 50 mg/week, 4 doses. The healthy control participants had not received any medication for at least three months before sample collection. Detailed information in Flowchart 1 illustrates the study design, participant enrollment, and group allocation



Flowchart 1: Study design and participant grouping.

The patients were attending the Department of Venereology and Dermatology at the Baghdad Teaching Hospital, Medical City Complex, Baghdad, Iraq, during the period from November 2024 to April 2025. The diagnosis of those patients was performed under the supervision of a dermatologist after physical examination. The study was approved by the ethical committee of the College of Science, University of Baghdad, under the code (CSEC/0126/0009). All participants gave formal informed consent after a full explanation was given to them on the aim of the study.

Sample Handling, Anthropometric, and Laboratory Test: venous blood (5–10 mL) was collected from each participant into serum tubes, centrifuged at 3000 × g for 10 minutes, and the separated serum was stored at -20 °C until analysis.

Samples were obtained twice from the same patients before and after biologic therapy. Serum albumin was measured using the dye-binding method (Linear, Spain) (13), and CRP was determined using a Biosystems kit (Spain) (14). The CRP/albumin ratio was calculated as CRP (g/dl) divided by albumin (g/dl) (4).

Inclusion criteria: Patients with clinically diagnosed Psoriasis who were candidates for biologic therapy and evaluated before and after treatment were included in the study.

Exclusion criteria: Patients and control group members with vitiligo, chronic inflammatory diseases, active inflammatory state, chronic pancreatitis, chronic renal failure, or other chronic or acute inflammatory diseases were excluded. Patients and control individuals were taking medications,

particularly immunosuppressants, and those with a history of smoking, lipid-lowering therapy, or alcohol consumption.

Statistical analysis

A statistical analysis was conducted using GraphPad Prism software version 10 for drawing charts and SPSS version 27. Means ± standard deviations were used to report the variables. The significance of differences between mean values was estimated using

Student's t-test and a paired-samples t-test; *P*-values < 0.05 were considered significant, and *P*-values < 0.001 were considered highly significant.

Results

The concentration of each of Albumin and CRP in serum was determined in the Psoriasis patients and control groups, and the results were presented in **Table 1**.

Table 1: Mean value ± SD of Albumin and CRP levels in the sera of patients as compared with those of controls

Sample	[Alb.] (g/dl) Mean ± SD	Sig. (2-tailed) <i>P</i> -value	[CRP] (mg/L) Mean ± SD	Sig. (2-tailed) <i>P</i> -value
Control N = 93	3.937 ± 0.47	0.000**	19.35 ± 1.4	0.000**
Patients N = 100	3.159 ± 0.44		63.72 ± 13.3	

**Correlation is highly significant (*P*<0.001).

It was clear that in the sera samples of the patients, a highly significant decrease (*P* < 0.001) in [Albumin] with a highly significant increase in [CRP] were measured compared with that of the control group. In a previous work, the presence of oxidative stress in Iraqi patients with Psoriasis was confirmed (3). And

since no report has been found in the literature that investigates [CRP]/ [Alb] in Iraqi patients with this type of inflammatory disease. Therefore, this ratio was calculated in the serum samples of the patients and control groups, and the results were illustrated in Figure 1.

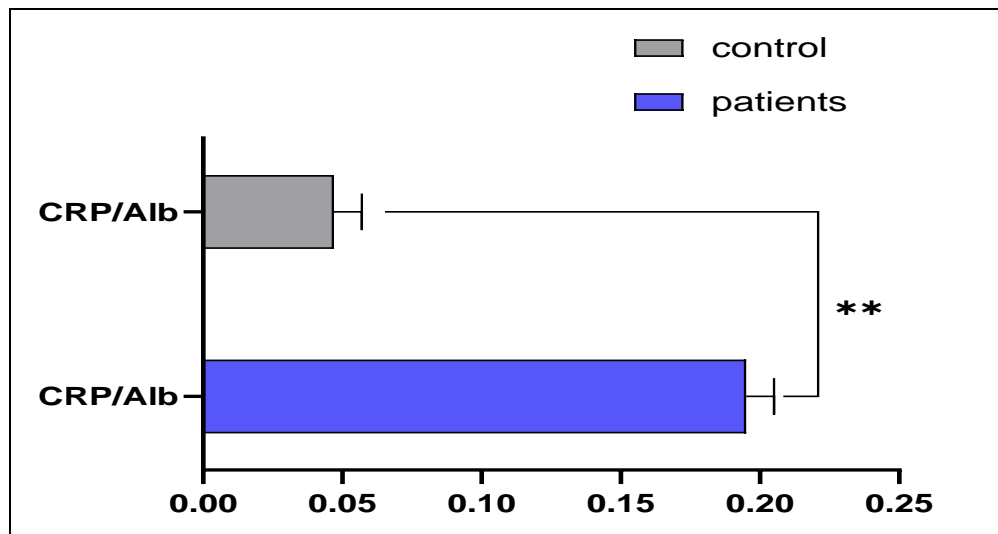


Figure 1: Comparison of [CRP]/ [Albumin] between the patients (n=100) and the control group (n=93). **The results represented the mean value ± SD in serum samples (*P*<0.001).

The above results illustrated the presence of a highly significant increase (*P* < 0.001) in this ratio in sera samples of the Iraqi psoriatic patients compared with that of the control group.

As far as the effect of biological treatment is concerned, no previous work has been found in the literature about the impact of Enbrel (ETN) treatment

on the current study's parameters in psoriatic patients. Therefore, in order to study this impact, these measurements were followed in the sera of 30 patients before and after treatment for three months with Etanercept, and the results are illustrated in **Table 2**.

Table 2: Mean value ± SD of CRP, Albumin and CRP/Alb ratio in the sera of the psoriatic patients before and after three months of Etanercept.

Parameter	Number	Mean ± SD	<i>P</i> -value paired T-test
CRP pretreated & post-treated (mg/L)	30	51.266 ± 24.36	0.000**
Alb. pretreated & post-treated (g/dl)	30	2.687 ± 0.493	0.000**
CRP/Alb ratio pretreated & post-treated	30	0.190 ± 0.067	0.000**

**Correlation is highly significant (*P*<0.001).

As it is obvious from the above results, a highly significant decrease ($P < 0.001$) was observed in the serum albumin level of pretreated patients in comparison to that of both the control and the post-treated patients. In the post-treated patients, the [Alb] increased to approach that of the control group. Meantime, it was obvious that there was a highly significant decrease ($P < 0.001$) in CRP level in the post-treated patients to approach its level in the healthy control group, compared to the same patients' group before receiving the treatment. The result of [CRP]/ [Albumin] ratio was calculated in the pretreated patients' group ($n=30$) as well as,

after three months receiving treatment with Etanercept, and the results showed the presence of a highly significant decrease ($P < 0.001$) in [CRP]/ [Alb] ratio in serum sample of post treated patients with ETN for three months compared with the ratio in pretreated patients. Receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic performance of inflammatory biomarkers in Psoriasis patients compared to healthy controls. As shown in Figure 2, serum CRP exhibited a high diagnostic accuracy with an AUC of 0.919 (95% CI: 0.883–0.956; $P < 0.001$). At a cutoff value of 45.00 mg/L, CRP demonstrated a sensitivity of 99% and a Specificity of 75%.

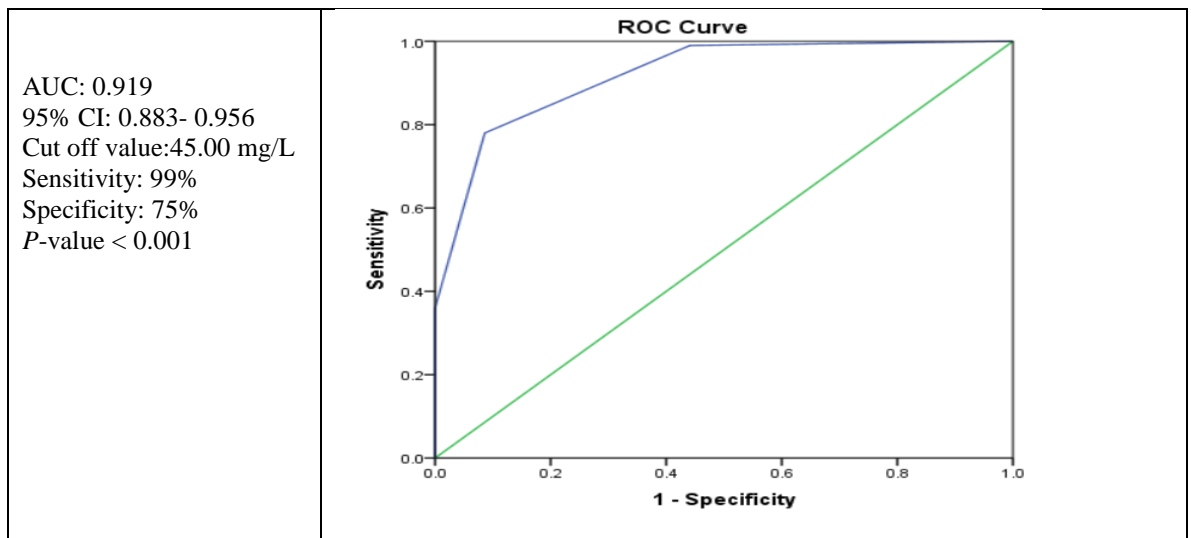


Figure 2: The curve of [CRP] level between the Psoriasis patient group and the control group.

Serum [albumin] exhibited significant diagnostic value with an AUC of 0.847 and a 95% CI between 0.79–0.90 ($P < 0.001$). As well as 6.04 g/dl, a cutoff

value yielded a sensitivity of 76% and a Specificity of 90% (Figure 3).

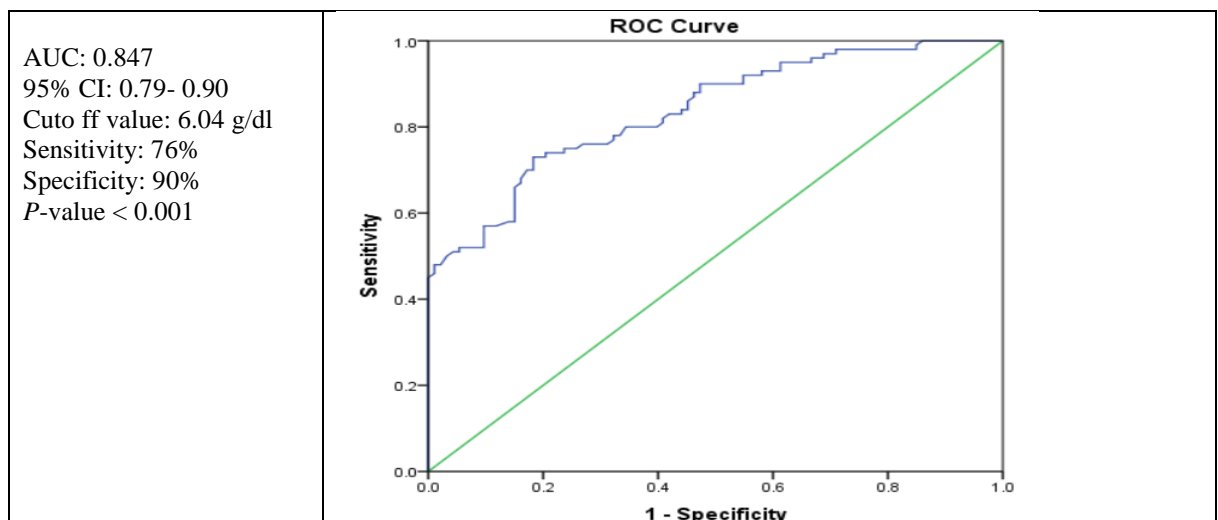


Figure 3: The curve of [Albumin] level between the patient group and the control group.

From Figure 4, the evaluated [CRP]/[albumin] ratio showed the diagnostic performance in the ROC analysis. The ROC curve analysis revealed an AUC

of 0.966, with a 95% CI between 0.945–0.987 ($P < 0.001$). At a 48.1 cutoff value, this ratio has 92% sensitivity and a 91.4% Specificity.

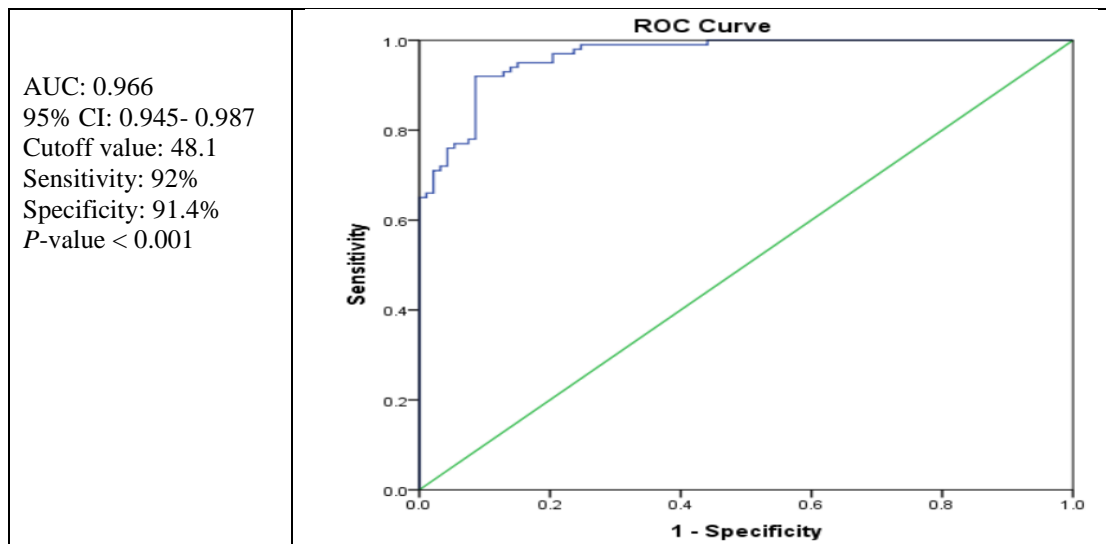


Figure 4: Curve of the CRP/Alb ratio in the Psoriasis group and the control group.

Discussion

This study provides novel data by evaluating serum CRP and albumin levels and their ratio before and after Etanercept treatment, with a follow-up analysis in the same patients. In addition, it represents the first Iraqi study to investigate these biomarkers in relation to treatment response.

The results of the measurement of serum [albumin] agreed with the results of Wang *et al.* (2025) in China, who studied the inflammatory effect on keratinocytes and Psoriasis development in sera of the patients compared with that in the healthy control (15). And agreed with Sahoo *et al.* (2024), who studied serum albumin levels in Psoriasis and its association with disease severity in Indian patients compared with that of healthy controls (16).

Sari *et al.* (2022) demonstrated a correlation between elevated serum CRP levels and neutrophil activation (8). Abdel Rasul and Hasan; reported the connection between Psoriasis and inflammation, recognizing that CRP is among the top markers of this disease (3). Several studies have investigated the role of CRP in Psoriasis, such as Mawada *et al.* (2025) on C-reactive protein and leucocyte activation in Psoriasis, which revealed that psoriatic patients have significantly high CRP baseline levels compared to healthy controls (7). The obtained result of serum [CRP] in the current study agreed with the result of a survey by Shakh *et al.*, who studied the C-reactive protein as a marker of disease severity and cardiovascular risk in Indian patients with Psoriasis vulgaris (17). And also agreed with Solak *et al.*, who in his review concerning CRP in serum sample of psoriatic patients compared with healthy control who were matched in age and gender with the patient group reported that this parameter level elevated in some stages of the disease severity, including the moderate & severe forms only while no enough evidence for such similar association was reported for the mild form of this disease (18).

Albumin is the protein most abundantly present in blood plasma (4), and a reduction in its level was detected in the sera of Psoriasis patients (Table 1). Such a drop was reported to occur during the

inflammatory process and in chronic inflammatory diseases (19). The decrease in plasma [Alb] may be explained as follows: the albumin level drops when either impairment of albumin formation or its excessive loss occurs (20). In psoriatic patients, the hypoalbuminemia observed is caused by an increase in albumin consumption by the psoriatic skin due to a rise in lymphatic return, which can serve as a compensatory mechanism, thus increasing the catabolism of endogenous albumin (21). On the other hand, the inflammation process, including the reaction of the acute phase and the chronic inflammatory response, is the commonest cause of decreased [Alb]. The main factor responsible for this is the loss of the extravascular space, induced by the increase in the vascular permeability at the site of inflammation (21, 22). The results shown in Table 1 show the sera [CRP] elevated in some stages of disease severity, including the moderate and severe forms only; however, reported evidence is insufficient to make a similar association for the mild form of this disease (18).

The liver is responsible for the synthesis of acute phase reactants, which are markers for an inflammatory state (23). Among these is a group of several proteins called positive acute phase reactants [24], like CRP. These are reported to rise significantly during acute inflammatory disease, while the negative acute phase proteins, like albumin, are reported to decrease (18, 24). Such a reduction results from the body saving amino acids to synthesize the positive acute phase proteins in the liver (25). CRP is an acute-phase protein that is produced in response to stimulation by various cytokines induced by infection and inflammatory conditions (23, 26). High CRP levels have been shown by Chai *et al.* (2023) to be associated with the severity of systemic inflammation (27). The plasma half-life of CRP is constant under all conditions of health and disease; therefore, the sole determinant of the circulating levels of CRP is the synthesis rate, which indicates that the intensity of the pathological process stimulates the production of CRP (18). Elevated CRP levels were observed in the

sera of Psoriasis patients (Table 1); such elevations were reported to occur in inflammatory processes and chronic inflammatory diseases (26).

Recently, researchers have reported the C-reactive protein-to-albumin ratio as a novel independent prognostic marker for oxidative stress for many diseases (18, 27). The findings in Figures 2, 3, and 4 indicated that all three parameters are significant tools for differentiating between patients and healthy individuals, with varying degrees of accuracy. The observed increase in [CRP] (as shown in Figure 2) indicates the demonstrated diagnostic accuracy, reiterating its established role as a sensitive marker of systemic inflammation. Elevated CRP levels are commonly associated with inflammatory and pathological processes (24). From Figure 3, it was clear that the serum [albumin] shows an acceptable diagnostic performance. The reduction in [albumin] observed in patients may be explained by the inflammation-induced suppression of the hepatic synthesis, increased vascular permeability, and enhanced protein catabolism (21, 23). Despite its clinical relevance, albumin alone revealed slightly lower diagnostic accuracy compared with that of the CRP. Furthermore, Figure 4 indicates that the [CRP]/[albumin] ratio exhibited the highest AUC, sensitivity, and Specificity. This superior action could be attributed to its capacity to combine a positive acute-phase reactant (CRP) with a negative acute-phase reactant (albumin), offering a more comprehensive reflection of the inflammatory status and disease burden. The results observed thus support the use of the [CRP]-[albumin] ratio as a more reliable diagnostic marker compared with [CRP] or [albumin] alone. Its higher discriminative ability suggests potential clinical value both in disease assessment and risk stratification.

Limitations

The challenges in collecting Psoriasis samples, small sample size, and short follow-up period, which may affect the generalizability of the findings.

Conclusion

The findings of this study highlighted the significance of the CRP/albumin ratio as a marker of chronic inflammation in Psoriasis. Etanercept treatment significantly improved this ratio, suggesting its potential utility for monitoring disease activity. Combined assessment of CRP and albumin levels provides a more accurate evaluation than either biomarker alone. These findings warrant confirmation in larger cohorts and longitudinal studies to validate the clinical application of the CRP/albumin ratio as an inflammatory marker in Psoriasis management.

Authors' declaration:

We confirm that all the Figures and Tables in the manuscript belong to the current study. Authors sign on ethical consideration's approval (Ethical Clearance): The project was approved by the local ethical committee at the College of Science,

University of Baghdad, Baghdad, Iraq, in accordance with the principles of the Declaration of Helsinki. The ethical approval number is (CSEC/0126/0009) and officially issued. Written informed consent was obtained from all participants prior to sample collection.

Conflict of Interest: The authors declare no conflict of interest.

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Data availability: Upon reasonable request, the corresponding author will make the data sets generated and/or analyzed during the current work available.

Authors' contributions:

Study Conception & Design: (Rajaa Jaber Abdel Rasul & Hathama Razooki Hasan). Literature Search: (Rajaa Jaber Abdel Rasul). Data Acquisition: (Rajaa Jaber Abdel Rasul). Data Analysis & Interpretation: (Rajaa Jaber Abdel Rasul). Manuscript Preparation: (Rajaa Jaber Abdel Rasul & Hathama Razooki Hasan). Manuscript Editing & Review: (Rajaa Jaber Abdel Rasul & Hathama Razooki Hasan).

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تأثير علاج إيتانيرسيبت على مستويات الألبومين والبروتين التفاعلي C ونسبتهما لدى مرضى الصدفية العراقيين

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الخلاصة:

الخلفية: الصدفية مرض جلدي مناعي ذاتي مزمن شائع، يتم تشخيصه من خلال التقشر والالتهاب الذي يظهر على الجلد. وتساهم كل من العوامل البيئية والوراثية في نشأته.

الهدف: هدفت هذه الدراسة إلى فحص التغيرات في مستويات الألبومين والبروتين المتفاعل C ونسبتهما، وتأثير علاج إيتانيرسيبت على هذه المؤشرات في مصل مرضى الصدفية العراقيين مقارنةً بأفراد أصحاء.

الطرق: شملت الدراسة مئة مريض مصاب بالصدفية وتمت مطابقتهم مع ثلاث وتسعون شخصًا سليمًا يراجعون قسم الأمراض الجلدية والزهرية في مستشفى بغداد التعليمي خلال الفترة من نوفمبر 2024 إلى أبريل 2025. وقورنت مستويات البروتين المتفاعل C والألبومين، بالإضافة إلى نسبتهما، لدى هؤلاء المرضى مع مستويات المجموعة الضابطة. كما تمت متابعة تأثير العلاج البيولوجي لهذه المؤشرات لدى ثلاثين مريضاً قبل تلقي أي علاج وبعد ثلاثة أشهر من العلاج بالإيتانيرسيبت.

النتائج: أظهر مستوى الألبومين في الدم انخفاضًا ملحوظًا للغاية، مع ارتفاع ملحوظ في تركيز كل من البروتين المتفاعل C في الدم ونسبة البروتين المتفاعل C إلى الألبومين في مجموعة المرضى مقارنةً بمجموعة الضبط. علاوة على ذلك، أدى العلاج بالإيتانيرسيبت لمدة ثلاثة أشهر إلى فرق كبير في مستويات الألبومين، وانخفاض ملحوظ جدًا في كل من تركيز البروتين المتفاعل C ونسبة البروتين المتفاعل C إلى الألبومين.

الاستنتاج: يؤثر مرض الصدفية على تركيز الألبومين والبروتين المتفاعل C، بالإضافة إلى نسبتهما. في الوقت نفسه أدى استخدام العلاج البيولوجي إيتانيرسيبت لمدة ثلاثة أشهر إلى تعديل التغيرات المقاسة حيث وصلت التركيزات إلى مستويات مماثلة تقريبًا لتلك الموجودة لدى الأفراد الأصحاء.

الكلمات المفتاحية: الألبومين، الصدفية، المؤشرات الحيوية، نسبة البروتين التفاعلي C إلى الألبومين، علاج إيتانيرسيبت.