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Ultrasound 7 score and serum chemerin in rheumatoid arthritis: Relation to disease activity

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ABSTRACT

Background and objectives. Chemerin is an adipokine associated with inflammation. Musculoskeletal ultrasonography is now widely used for detecting and monitoring RA due to its availability, practicality, and cost-effectiveness. The aim of the study is to determine how accurate serum chemerin levels are as a biomarker of active rheumatoid arthritis (RA) disease and to find a link between these levels and ultrasonographic findings.

Materials and methods. This case-control study included 44 RA cases and 44 matched-age and sex-healthy controls. Seven joints in the hand and foot were assessed by the German-ultrasound 7 (GUS 7) score through greyscale (GSUS) and power Doppler US (PDUS) in all cases. Disease activity score 28 (DAS28) evaluated RA activity, and serum chemerin levels were measured in cases and controls. Both DAS28-CRP and DAS28-ESR were used in the assessment of the disease.

Outcomes. The mean age of patients was 43.48 years versus 39.18 years of controls. 86.4% of patients were females; versus 75% of the control group. 47.7% of the studied patients had moderate disease activity, 31.8% had high disease activity, and 20.5% had low disease activity. There was a statistically significant higher median chemerin serum level among RA cases compared to the control group (898.94 versus 247.81 ng/ml, p <0.001). There was a significant difference in median chemerin between inactive and active patients (352.1 versus 1032.6 ng/ml (p <0.001). The serum chemerin can differentiate between RA patients and controls with a higher sensitivity of 81.8%, a specificity of 88.6%, and an accuracy of 85.2%. There was a statistically significant positive association between chemerin and RA activity (p <0.001). The combination of serum chemerin level and tenosynovitis GSUS score and DAS28-ESR to differentiate between active and inactive RA patients was highly significant with the highest sensitivity of 100%.

Conclusions. Chemerin can serve as an advantageous marker for assessing RA activity. The US-7 score is a complementary method used in standard assessment to determine synovial inflammation in RA. The combined use of serum chemerin and the US 7 score could be of high value for detecting disease activity in RA.

Keywords: rheumatoid arthritis, chemerin and ultrasonography

Abbreviations (in alphabetical order):

DAS – disease activity score
GSUS-B mode – Greyscale US
GUS 7 – German- ultrasound -7
PDUS – Power Doppler US
RA – Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is one of the chronic autoimmune diseases (AID) that affects the joints. It is typically having an onset of symmetric joint swelling and reaching a peak incidence in the fourth and fifth decades. It is typified by synovial inflammation

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that leads to erosions of the bones, cartilage degeneration, and disability. It is noted that female/male ratio was ranging from 2:1 to 4:1, RA is an insidious disease [1]. It's critical to accurately assess RA activity to make early treatment decisions. Numerous indices measure RA activity using physical, laboratory, and clinical data [2].

Many researchers recommended that disease activity could be followed up by rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA). Of note is that RF is more stable during RA; however, anti-citrullinated peptide antibodies (ACPA) may even vanish over time in certain RA cases [3,4].

Clinically, RA activity might be evaluated by the simple disease activity index (SDAI) and disease activity score 28 (DAS28) [5]. However, there are numerous shortcomings with the DAS28-ESR criterion, as many cases of DAS28-ESR relapse may still show very slight levels of RA activity [6].

Johnson and his colleagues conducted a study to evaluate the validity of the multi-biomarker disease activity (MBDA) score in determining RA activity [7].

In a test comprising the combination of 12 biomarkers, the MBDA shows poorer correlations with the SDAI and Routine Assessment of Patient Index Data, but moderate validity with the DAS28-CRP and DAS28-ESR [7]. On the other hand, all the utilized biomarkers in RA appeared to be the best modality in the context of RA disease activity evaluation [8].

Chemerin is defined as a retinoic acid receptor responder 2 (RARRES2) and specified as a potent chemoattractant protein. In addition, it is considered as a natural ligand for chemokine-like receptor 1 (CMKLR1). The defined receptors for chemerin are CMKLR1, chemokine (C-C motif) receptor-like 2 (CCRL2) and G protein-coupled receptor 1 (GPR1). They are commonly expressed in various immune cell types, such as monocytes/macrophages, dendritic cells (DC), neutrophils, and natural killer (NK) cells [9].

Akhverdyan et al. (2022) found that the average chemerin level in RA cases significantly increased compared to that of normal individuals. Chemerin is likely to be one of the possible indicators of inflammatory activity in RA patients [10]. There is no conclusive data support that high chemerin levels increase the activity of rheumatoid arthritis. Supporting its accuracy in identifying activity is still crucial. A correlation with a reliable indicator of disease activity is required in order to identify this objective.

These days, musculoskeletal ultrasonography (MSUS) is a mainstay in RA since it is readily available, useful, and affordable. It aids in illness detection and monitoring. EULAR guidelines emphasize that when it comes to identifying inflammation, MSUS is more effective than clinical examination [11].

Power Doppler (PD) allows for detecting both active inflammation and neo-angiogenesis. The two factors are crucial for following up RA cases. It has also been shown to be a reliable indicator when determining the presence of subclinical synovitis, bone erosions, and recurrence prediction [12].

Thus, this study aimed to determine the precision of serum chemerin levels as a biomarker of RA disease activity and to establish a relationship between their level and ultrasonographic results. Recently, the US has been used as a confirmatory and mandatory tool for disease activity in RA cases.

MATERIALS AND METHODS

This case-control study included patients referred to the outpatient rheumatology, rehabilitation, and physical medicine departments from December 2021 to June 2023. It got approval from the Institutional Research Board (IRB), the code number being MS.21.11.1730.

Forty-four consecutive RA cases were diagnosed in the study using the ACR/EULAR 2010 criteria [13]. As controls, 44 age and sex-matched healthy volunteers were randomly chosen and asked to participate in the research. After guaranteeing confidentiality, all participants provided written informed consent.

Patients with connective tissue disorders, septic arthritis, and other autoimmune disorders such as psoriatic arthritis, reactive arthritis, and overlap syndromes were not included in the study. Additionally, patients with morbid obesity, malignancy, chronic kidney, coronary, and liver diseases, lactation, pregnancy, thyroid disease, and blood transfusion within the previous three months were not allowed to participate in the study.

In this study, we examined seven joints in the hand and foot (the most affected side) by the German-US 7 score using PDUS and grayscale Ultrasonography-B (GSUS-B) mode [14] and EULAR guidelines [15] to detect and grade synovitis and to determine the presence of tenosynovitis, paratendonitis, and erosions. These seven joints were the wrist joint, the second and third metacarpophalangeal (MCP) joints, the second and third proximal interphalangeal (PIP) joints, and the second and fifth metatarsophalangeal (MTP) joints. Synovitis was analyzed semi-quantitatively: zero = no, I = mild, II = moderate, and III = severe synovitis. Erosion, paratendonitis, and tenosynovitis were evaluated and recorded as present = I and absence = 0.

The features of PDUS activities for synovitis, tenosynovitis or paratendonitis were scored as follows: Grade zero: no intraarticular color signal was present. Grade I: the intraarticular area contains up to three color signals, or two singles and one confluent signal; Grade II: the intraarticular area contains more

than three color signals but less than 50% of them; Grade III: the intraarticular area contains more than or equal to 50% of it. Erosion, paratendonitis, and tenosynovitis were evaluated and recorded as presence = I and absence = 0.

Lastly, the total synovitis scores in PDUS and GSUS vary from 0 to 39; the total tenosynovitis and paratendonitis scores in GSUS and PDUS range from 0 to 21; and the total erosive scores in GSUS and PDUS range from 0 to 14 [16].

Utilized device: Siemens Medical Solutions U.S.A. Inc. device, model No. 10852646 ACUSON P300, 685 East Middlefield Road, Mountain View, CA, USA.

Utilized probe: linear probe with 12 to 18 MHZ.

Patients underwent a full, detailed joint examination for swelling, tenosynovitis, and deformities. DAS28-ESR and CRP were done to evaluate RA activity, in which the assessment of disease activity includes the swollen joint count (out of 28), the tender joint count (out of 28), the measurement of the CRP, and the global patient assessment. The records of the four variables will then be fed to an automated calculator, and the activity score can be graded into Low ≤3.2, Moderate >3.2: ≤5.1 and High >5.1 [17].

Measurement of the serum chemerin levels for RA patients and control groups were done by collecting 3 ml of venous blood. The chemerin was measured using ELISA (Human Chemerin ELISA Kit) in compliance with the manufacturer's guidelines (Sun Red International Trade Company, Shanghai, China). Catalogue number: (201-12-1436).

Statistical analysis

SPSS was used to handle and evaluate the collected data (SPSS 26.0, IBM/SPSS Inc.). For numerical parametric data, such as mean, SD, min, and max, and numerical nonparametric data, such as median and first and third IQR, descriptive analyses were conducted; in contrast, they were conducted on categorical data, such as number and percentage. Inferential analysis was performed in quantitative variables using an independent sample t-test with parametric data and a Mann-Whitney U-test with nonparametric data. Inferential analyses were performed for qualitative data using the Chi-square test regarding independent groups. The linear link between two continuous variables with non-normal distribution was examined using Spearman's correlation to determine its direction and strength. The test's precision in differentiating between instances that were diseased and those that weren't was assessed using Receiver Operating Characteristic (ROC) curve analysis. To determine specificity and sensitivity, a ROC curve was utilised. Additionally, cross-tabulation was used to determine accuracy, negative predictive value (NPV), and positive predictive value (PPV). For all prior tests, a P-value of less than 0.050 indicates significance. Box and Whisker plot visually displaying groups of numerical data through their quartiles.

RESULTS

Table1 demonstrates - comparing 44 patients with RA (patients group) to 44 normal individuals (control group) - that the mean age of the patient group was 43.48 ± 12.85, while the mean age of normal individuals was 39.18 ± 10.35. In the patients group, 86.4% were females, while in the control group only 75%. The smoking history among the studied patients was 6.8% versus 0% in the control group. Regarding age, sex, and frequency of smoking, there was no significant difference between the study group patients and control group.

TABLE 1. Comparison of demographic and smoking history among studied groups

	Patient group (n=44)	Control group (n=44)	t/χ2/ FET	P value
Age/years	43.48±12.85	39.18±10.35	1.723	0.09
Sex Male Female	n(%) 6(13.6) 38(86.4)	n(%) 11(25.0) 33(75.0)	1.82	0.177
Smoking -ve +ve	n(%) 41(93.2) 3(6.8)	n(%) 44(100) 0	3.11	0.241

t: Student t test, χ2 : Chi-Square test, FET: Fischer exact test, n: number

Table 2 shows the laboratory findings of the patients group included that the mean haemoglobin (Hb) concentration was 10.7 ± 1.6 (g/dl) with a range between (7.2 – 15 g/dl). The mean red blood cell (RBC) count was 4.2 ± 0.6, ranging between 3.2 and 6.56 ($\times 10^6$ /mm^3). The mean white blood cell (WBC) count was 7.01 ± 2.04, ranging between 3.9 and 13.1 ($\times 10^3$/mm^3). The mean platelets count was 257.7 ± 66.9, ranging between 150 and 427 ($\times 10^3$/mm^3). The median ESR among studied patients was 45, ranging from 5 to 97 mm/hr, and the mean CRP was 12.23 ± 5.01, ranging from 6 to 96 mg/dl. The mean serum RF was 32.49 ± 9.12 U/ml, ranging from 8 to 128 U/ml, and the mean anti-CCP antibody levels were 52.76 ± 12.93 U/ml, ranging from 9 to 239 U/ml.

Additionally, among the patients, 28.4% were taking steroids, 28.4% were taking methotrexate, and 28.4% were using hydroxychloroquine, whereas leflunomide was taken by 27.3%. Just three cases were receiving biological therapy (adalimumab and etanrecept). The average daily dose of hydroxychloroquine was 256 mg with a standard deviation of 187.26096, the average daily dose of leflunomide was 10 mg with a standard deviation of 10.21508 and the average daily dose of steroid was 8.2 mg with a standard deviation of 6.43558, and the average weekly dose of methotrexate was 11.4 mg with a standard deviation of 9.94987. Only one patient was taking 50

mg of etanercept each week, whereas two patients were receiving 50 mg of adalimumab every other week.

The median DAS28-CRP value was 4.4, ranging from 1.1 to 6.85. It was found that 47.7% of the studied patients had moderate disease activity, 31.8% had high disease activity, and 20.5% had low disease activity.

TABLE 2. The laboratory findings of the RA patients

	Mean ± SD	min-max
Hb (g/dl)	10.7 ± 1.6	7.2-15
RBCs count ($x10^6/mm^3$)	4.2 ± 0.6	3.2-6.56
WBCs count ($x10^3/mm^3$)	7.01 ± 2.04	3.9-13.1
Platelets ($x10^3/mm^3$)	257.7 ± 66.9	150-427
ESR (mm/h)	45 ± 8.91	5-97
CRP (mg/dl)	12.23 ± 5.01	6-96
Serum RF (U/ml)	32.49 ± 9.12	8-128
Serum anti-CCP (U/ml)	52.76 ± 12.93	9-239

Table 3 demonstrates that the mean synovitis GSUS was 11.73 ± 2.49, ranging from 1 to 20. The mean synovitis PDUS was 13.42 ± 2.6, ranging from 2 to 24. The mean tenosynovitis GSUS was 1.67 ± 0.44, ranging from 0 to 5. The mean tenosynovitis PDUS was 2.56 ± 1.06, ranging from 0 to 7. The mean erosions score was 2.58 ± 1.27, ranging from 0 to 7.

TABLE 3. Value of the musculoskeletal ultrasound seven scores among RA patients

	R	Mean ±SD
Synovitis GSUS	1 – 20	11.73 ± 2.49
Synovitis PDUS	2– 24	13.42 ± 2.6
Tenosynovitis GSUS	0 – 5	1.67 ± 0.44
Tenosynovitis PDUS	0 – 7	2.56 ± 1.06
Erosions score	0 – 7	3.58 ± 1.27

SD: standard deviation, GSUS (greyscale ultrasound), PDUS (power Doppler ultrasound), R Range

The serum level of chemerin among studied patients ranged from 196.26 ng/ml to 2486 .1 ng/ml, and the median level was 898.94 ng/ml. While the serum level of chemerin among the control group ranged from 177 to 479.96.1 ng/ml, and the median level was 247.81 ng/ml.

The serum level of chemerin among the inactive RA patients ranged from 229.4 to 737.32 ng/ml, and the median level was 352.10 ng/ml. While the serum level of chemerin among the active RA patients ranged from 196.26 to 2,486.1 ng/ml, and the median level was 1032.60 ng/ml.

Mann-Whitney U test was used, and it was noted that statistically significantly higher serum chemerin levels among the studied patients than in the control group (898.94 ng/ml versus 247.81 ng/ml, p <0.001). In addition, there is a higher significant difference in median serum chemerin in active RA patients compared to inactive patients (1,032.6 ng/ml versus 352.1 ng/ml, p <0.001).

There was no statistically significant association between serum chemerin levels in males and females (p = 0.452). There was no statistically significant association between chemerin levels with morning stiffness durations (p = 0.440). Non statistically significant correlation between serum chemerin levels and Hb, RBCS, WBCS, and platelets. (P <0.878, 0.833, 0.272 and 0.475). A significant positive correlation existed between the serum chemerin levels and ESR (P <0.001) and CRP (P <0.031). Besides, a statistically significant positive correlation was detected between serum chemerin levels and BMI (r = 0.389) (p = 0.04).

We performed a ROC curve for DAS28-ESR and for the combination of serum chemerin, DAS28-ESR and GSUS to differentiate between active and inactive RA patients. The fact that DAS28-ESR was used in assessing the activity of the disease was mentioned in Table 4. Both DAS28-CRP and DAS28-ESR were used in the assessment of the disease.

From the results presented in Table 4 it is obvious that there were no significant correlations between serum chemerin levels and all types of used drugs.

Table 5 demonstrates that there was a statistically significant positive correlation between RA pa-

TABLE 4. Correlation between serum chemerin levels and both clinical characteristics of studied cases and as well as the immunosuppressive medications employed in these cases

	Chemerin	
	R	p-value
Age/years	0.151	0.159
Morning stiffness/minute	0.248	0.109
Disease duration/years	0.265	0.082
DAS28-CRP	0.709	0.001*
DAS28-ESR	0.664	0.001*
Serum RF (U/ml)	0.280	0.114
Serum anti-CCP (U/ml)	0.411	0.013*
VAS	0.237	0.121
BMI (kg/m^2)	0.269	0.078
MSUS total score	0.241	0.114
Steroid dose	0.052	0.806
Methotrexate dose	0.021	0.921
Hydroxychloroquine dose	0.306	0.137
Leflunomide	-0.048	0.823

r:Spearman correlation coefficient, Significant at P<0.05

TABLE 5. Correlation between the serum chemerin level with US findings in studied patients

	R	P
Synovitis GSUS	0.723	<0.001*
Synovitis PDUS	0.624	<0.001*
Tenosynovitis GSUS	0.304	0.05
Tenosynovitis PDUS	0.305	0.05
Erosions score	0.321	0.05

GSUS (greyscale ultrasound), PDUS (power Doppler ultrasound). Spearman's correlation. Significant at P<0.05.

tients' serum chemerin levels and their synovitis PDUS score (p ≤0.001) and GSUS score (p <0.001). Additionally, serum chemerin levels were positively correlated with the GSUS score (p = 0.05) and PDUS score (p = 0.05) for tenosynovitis and erosions score (p = 0.05), but this correlation was not statistically significant.

Figure 1 shows the median serum chemerin levels according to disease activity degree.

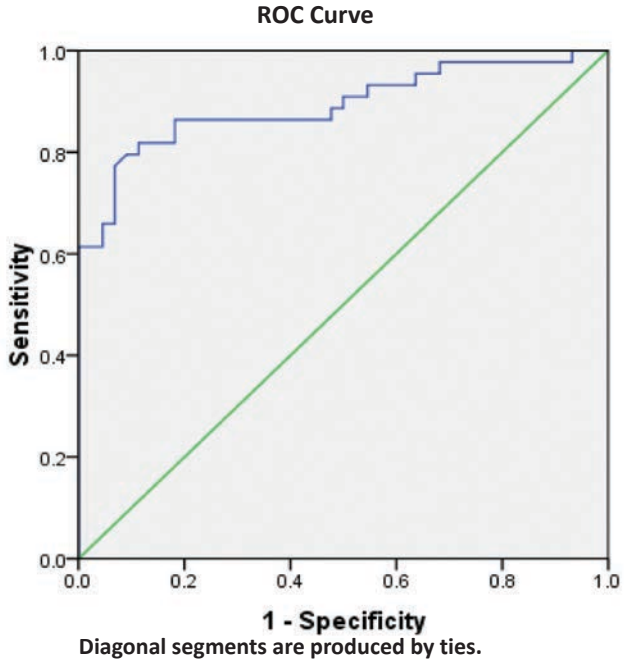

FIGURE 2. ROC curve shows the validity of the serum chemerin level in differentiating RA patients from control groups

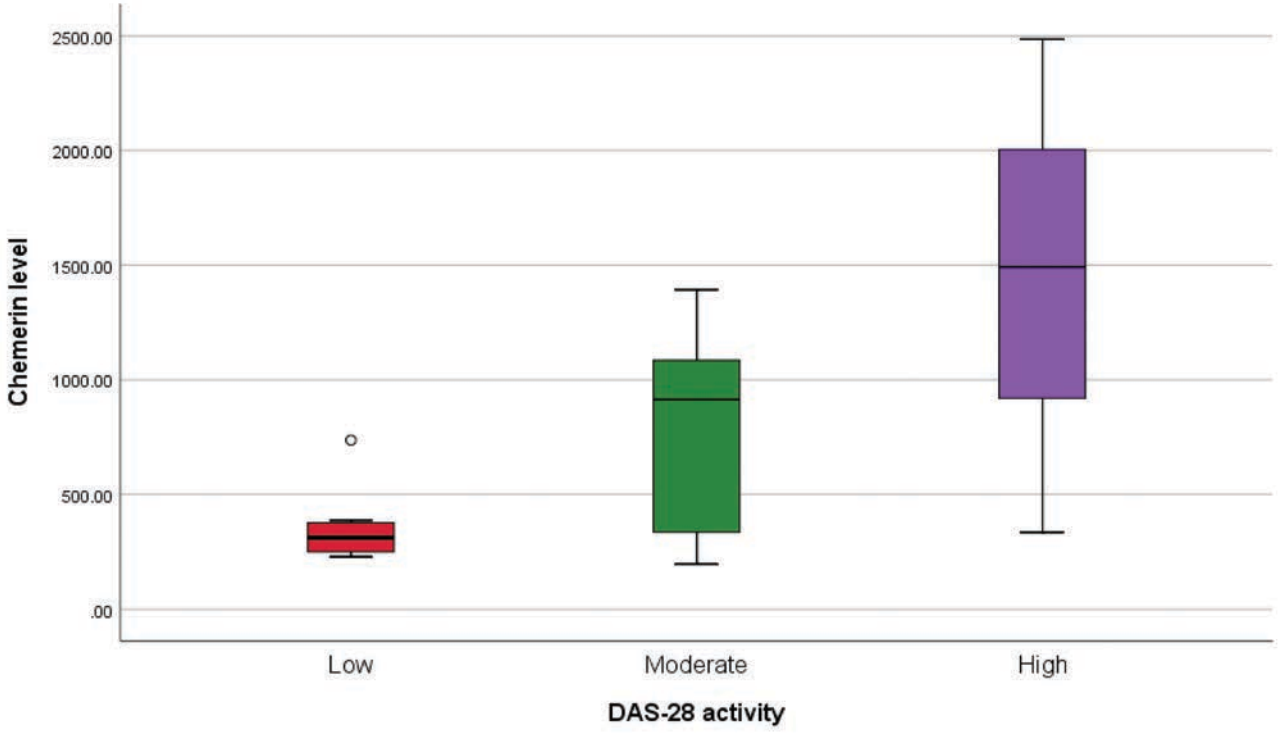

FIGURE 1. Box and Whisker plot shows median serum chemerin level according to disease activity degree

Figure 2 shows the area under the curve for the serum chemerin levels in differentiating patient from the control group was 0.892, with the best-detected cut-off point being 323.93 ng/ml, yielding a sensitivity of 81.8%, specificity of 88.6% and total accuracy of 85.2%.

Figure 3 shows the area under the curve for the serum chemerin levels to differentiate between active and inactive patients was excellent, with the best-detected cut-off point being 469.57 ng/ml, revealing sensitivity of 88.9%, specificity of 74.3% and total accuracy of 77.3%.

Figure 4 clearly shows the area under the curve for tenosynovitis GSUS score to differentiate between active and inactive RA patients, with the best-detected cut-off point being 1, revealing a sensitivity of 33.7% and a specificity of 62.9%.

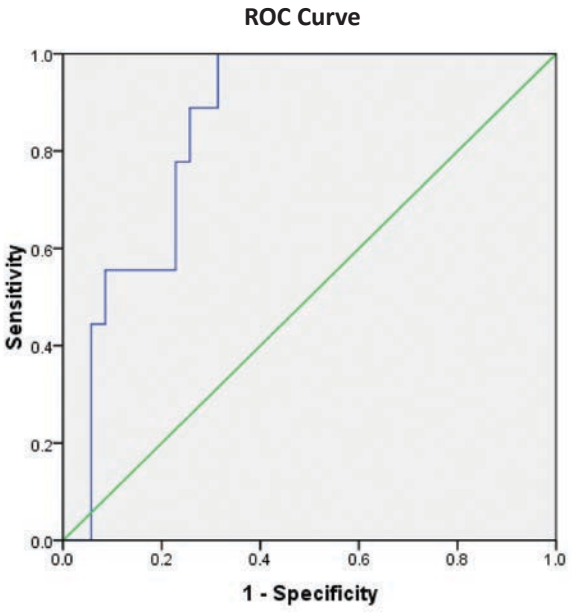

FIGURE 3. ROC curve shows the validity of serum chemerin level in differentiating active from inactive RA patients

GSUS score and DAS28-ESR as well, were extremely significant in differentiating between active and non-active RA patients. This combination had the highest sensitivity and specificity rate of 100%.

DISCUSSION

RA is an AID where the immune system attacks the joints and different tissues. Joint inflammation is associated with swelling, pain, and stiffness that could accompany joint damage if not appropriately treated. RA could affect many joints, especially the joints of the hands, wrists, and feet. In addition, the inflammation could interfere with different body tissues [1,18].

Chemerin is thought to be a unique protein mediator that takes part in the initiation of the pro-resolving responses as well as the early stages of inflammation. It is known to have a chemotactic activity, supporting cellular migration in inflammatory conditions. It can play a role in the expression of adhesion molecules on endothelial cells and monocytes. Previous experimental and clinical research has demonstrated that interleukins (IL) can initiate the creation of chemerin, and it has been linked to CRP, TNF-α, and IL-6 in RA [19,20].

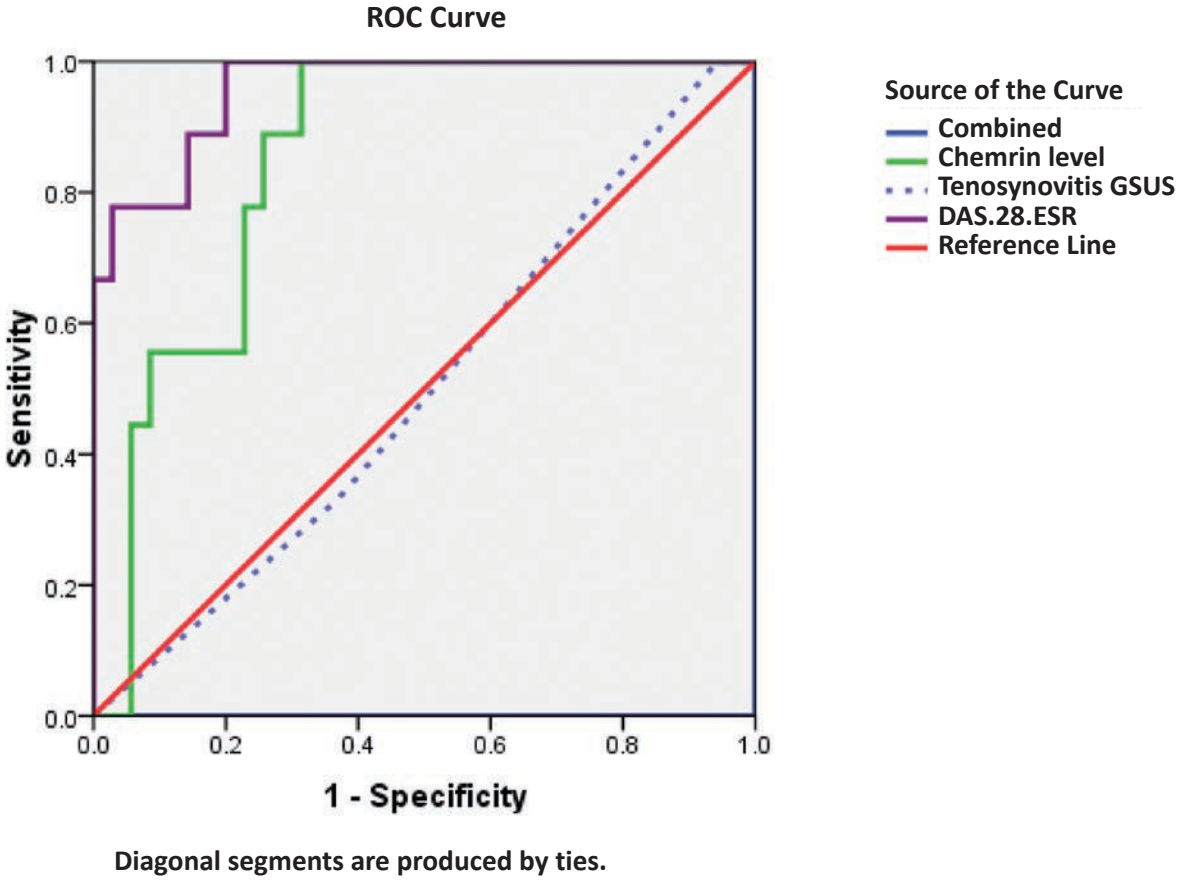

FIGURE 4. ROC curve shows the validity of the serum chemerin, GSUS score, DAS28-ESR.and the combined three parameters in differentiating active from inactive RA patients

Additionally, DAS28-ESR's area under the curve for distinguishing between active and inactive individuals shows a sensitivity of 88.9% and specificity of 85.7%, with the best-detected cut-off point being 4.57 mmHg.

Also, it was found in this curve that the combination of serum chemerin levels and tenosynovitis

It was reported that ultrasonography is of great sensitivity in defining synovitis, tenosynovitis and bony erosions in RA. The validity of PDUS in describing synovial angiogenesis was demonstrated to play a main function in RA pathogenesis. So, it plays a great role in the diagnosis and follow-up of RA disease. Additionally, the German US7 score is of great sensitivity in demonstrating active joint inflammation compared to DAS28. on the other hand, ultrasonography changes, which include synovitis and bony erosions, aren't distinctive to RA and could also be detected in different rheumatologic diseases. Clinically, the topography of the lesions and the biological evaluation are still the most appropriate ways to distinguish an incipient RA from other chronic inflammatory rheumatologic diseases [21]. Abdelhafiz et al. (2022) reported that anti-CCP wasn't accompanied by disease activity but by a significant increase in radiological damage. Rheumatoid Factor was associated with US-detected bone degradation but did not accompany joint injury [22].

Thus, the current study aimed to detect the accuracy of serum chemerin values as a biomarker of RA activity through its correlation with ultrasonographic findings, which is considered a good tool for evaluating RA cases.

Regarding our study, no previous studies have correlated serum chemerin and ultrasonographic findings in RA patients.

In the current study, there was no statistically significant difference among the studied groups regarding age, sex, and smoking.

Our study revealed a statistically significant rise in chemerin serum levels in RA patients compared to the control group. This was in the same line with Vazquez-Villegas et al. (2021), Jebur et al. (2022) and Jeong et al. (2023), who revealed that chemerin serum concentration in RA cases was greater than the control group (P value <0.0001) [23-25].

In terms of the association between chemerin levels and RA activity, our results showed a statistically significant difference in median chemerin levels between inactive and active patients (p = 0.001) that agreed with Vazquez-Villegas et al. (2021) who reported that there was a positive correlation between RA activity and the increase in chemerin value (p = 0.05) [23]. Furthermore, Akhverdyan et al. (2022) concluded that chemerin in RA cases could be used as one of the potential markers of inflammation activity [10].

A few studies have demonstrated the utility of serum chemerin levels as indicators of active illness. These levels can be used to predict the activity of RA. Gonzalez-Ponce et al. (2021) examined the efficacy of chemerin using cutoff values of ≥103 ng/mL, which is comparable to the cutoff value of ≥469.57 ng/ml used in our investigation [26].

In our study, there was no significant correlation between serum chemerin levels and the used drug doses.

In our study, we found a statistically significant positive correlation between RA patients' serum chemerin levels and PDUS and GSUS scores for synovitis.

This can be explained by Yang et al. (2019), who showed that there were significant differences between RA cases and healthy controls regarding thicknesses of the synovial membrane and tendon sheaths (P<0.001) which in turn increase the grade of GSUS and PDUS score [27].

This finding is in harmony with Ganeb et al. (2020), who reported significant associations between disease activity and USGS and PD synovitis scores [28]. It also goes with Hamdy et al. (2022) who found a positive correlation between disease activity and US findings, synovitis (p <0.0001), tenosynovitis (p = 0.05), and erosion score (p = 0.05) [29].

In addition, we demonstrated that the tenosynovitis GSUS score can distinguish active RA from inactive patients, with a sensitivity of 33.7% and a specificity of 62.9%. This can be explained by a study that has , in line with Ali et al. (2020), findings that chemerin had good sensitivity and specificity (p = 0.001) in the context of RA diagnosis. We found that the serum chemerin levels in our study distinguished the RA patients from the control with a sensitivity of 81.8%, a specificity of 88.6%, and a total accuracy of 85.2% [30]. With the best-detected cut-off point of 469.57 ng/ml, the serum chemerin levels also showed a good ability to distinguish between active and inactive RA patients. with a sensitivity of 88.9%, specificity of 74.3% and overall accuracy of 77.3%. However, in the case of a combination of serum chemerin levels and tenosynovitis, GSUS score and DAS 28 ESR level can differentiate between active and non-active RA patients with the highest sensitivity and specificity rate of 100%.

According to these findings, this is the first study investigating the relationship between chemerin serum concentration and ultrasound findings considering the disease activity of RA.

Additional research is required to accurately confirm the role of chemerin in the context of RA pathogenesis and to search for a novel therapeutic target.

In addition, further research is required in many cases to confirm our results regarding the role of chemerin levels as a promising indicator in the context of RA severity. A precise assessment of joint inflammation using the US could facilitate early diagnosis, ultimately ending in a better prognosis.

CONCLUSION

The serum chemerin levels are higher in the serum of RA cases than in healthy subjects. Serum chemerin levels are positively accompanied by activ-

ity parameters DAS28, CRP, and synovitis assessed by the US. These findings indicate that serum chemerin could be an advantageous marker for evaluating RA activity.

The US Seven Score is a method complementary to standard assessment for determining synovial inflammation in RA that could help the physician in proper decision-making. Serum chemerin and the US 7 score may be useful for RA disease activity detection.

Authors's contributions:
Conceptualization, Atif Elghaweet and Eman Hafez; methodology, Rana Menessy; software, Rana Menessy; validation, Eman Hafez; formal analysis, Rana Menessy; investigation, Rasha Elzehery; resources, Rana Menessy; data curation, Rana Menessy.; writing—original draft preparation, Rana Menessy; writing—review and editing, Eman Hafez; visualization, Atif Elghaweet; supervision, Eman Hafez. All authors have read and agreed to the published version of the manuscript.

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