e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(7); 874-877

Original Research Article

A Comparative Cross-Sectional Study of Serum Calreticulin and ESR in Rheumatoid Arthritis and Its Correlation with Disease Activity

Neethu D. S.[1], Sangita Paneri[2], Deepasha Shahi[3], Sanjay Dubey[4], Rajeev Lohokare[5]

[1]PG Resident, Department of Biochemistry, M.G.M. Medical College & M.Y. Hospital, Indore, Madhya Pradesh, 452001, India

[2]Professor, Department of Biochemistry, M.G.M. Medical College & M.Y. Hospital, Indore, Madhya Pradesh 452001, India

[3]Assistant Professor, Department of Biochemistry, M.G.M. Medical College & M.Y. Hospital, Indore, Madhya Pradesh 452001, India

[4]Associate Professor, Department of Medicine, M.G.M. Medical College & M.Y. Hospital, Indore, Madhya Pradesh 452001, India

[5]Associate Professor, Department of Biochemistry, M.G.M. Medical College & M.Y. Hospital, Indore, Madhya Pradesh 452001, India

Received: 01-04-2026 / Revised: 15-05-2026 / Accepted: 21-06-2026

Corresponding author: Dr. Neethu D S

Conflict of interest: Nil

Abstract

Background: Rheumatoid arthritis is a chronic systemic autoimmune disease characterized by persistent inflammation, progressive joint destruction, and extra-articular manifestations. The present study aimed to compare serum calreticulin and ESR levels between RA patients and healthy controls and to evaluate their association with disease activity.

Materials and Methods: Study comprises a total of 100 participants comprising 50 patients with rheumatoid arthritis came to Medicine department, M.Y. Hospital, Indore, Madhya Pradesh, India and 50 age and gender matched healthy controls. Participants are enrolled as per inclusion criteria. Disease activity was assessed using DAS28-ESR. Serum calreticulin levels were measured by ELISA, while ESR was estimated using the standard method.

Results: Serum Calreticulin and ESR demonstrated a progressive increase from remission to high disease activity. Serum calreticulin showed a strong positive correlation with DAS28 across all disease activity categories, including remission and low disease activity, whereas ESR showed relatively weaker association in remission. Serum calreticulin also correlated positively with ESR.

Conclusion: We conclude that, compared with ESR, calreticulin appears to be a more sensitive biomarker and potentially useful as an adjunct marker for disease activity assessment and monitoring in rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Calreticulin, Erythrocyte sedimentation rate, Disease Activity Score-28.

DOI: 10.25258/ijcpr.18.7.134

Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disorder characterized by persistent synovial inflammation, progressive joint destruction, and functional disability.[1] It affects nearly eighteen million individuals worldwide and out of these, about 70% were women, and 55% of them were aged above 55 years.[2] In India, the prevalence varies from 0.28 to 0.7%.[3]

Hereditary determinants and the interactions between gene and environment are greatly influencing RA. The combined effect of HLA-DRβ1 alleles and tobacco consumption are main reason for Anti-Citrullinated Protein/peptide Antibody (ACPA) production, persistent synovial inflammation and progressive joint damage.[4] In addition to joint involvement RA can affect other organs also, leads to extra-articular manifestations.[5] RA patients are also highly prone to develop cardiac problems and also other comorbidities, which collectively results in reduced life expectancy.[6,7]

The assessment of level of disease status in RA patients is done with the help of the Disease Activity Score based on 28 joints (DAS28), it is essential for monitoring disease progression,

guiding treatment, and preventing irreversible joint damage.[8,9] Erythrocyte sedimentation rate (ESR) is routinely incorporated into DAS28 because it is a simple and inexpensive marker of systemic inflammation. Calreticulin (CRT) is a calcium-binding molecular chaperone predominantly located in the endoplasmic reticulum, where it regulates calcium homeostasis and protein folding.[10] In addition to its intracellular functions, calreticulin has been identified as an autoantigen in rheumatoid arthritis and plays an important role in immune activation and inflammatory signalling.[11]

In the present study, we investigated serum calreticulin and ESR levels in RA patients and compared with the normal control group. In addition, we have evaluated the correlation between disease activity and these parameters.

Materials and Methods

The present cross-sectional study was conducted in the Departments of Biochemistry and General Medicine at M.G.M. Medical College and M.Y. Hospital, Indore, Madhya Pradesh, India.

The study included 100 participants including 50 patients diagnosed with RA attending the outpatient department or admitted to the Department of General Medicine in period between June 2024 to May 2025 aged ≥18 years and willing to participate in the study were selected as the case group. Age and gender matched 50 healthy volunteers were included as control group.

Patients with other autoimmune diseases like SLE, secondary Sjogren's syndrome, inflammatory bowel disease and patients who have history of carcinoma (gastric cancer, breast cancer, pancreatic cancer, oesophageal squamous cell carcinoma) were excluded. An informed written consent was taken from all the participants and the study protocol was approved by Institutional Ethics Committee.

Disease activity was assessed using the Disease Activity Score-28 based on ESR (DAS28-ESR), and patients were classified into four groups, Remission group with DAS28 score < 2.6, low disease activity group with DAS28 score 2.6 < 3.2, moderate disease activity group with DAS28 score 3.2 < 5.1, and high disease activity group with DAS28 score > 5.1.

Collection and Preparation of Sample: 5 mL of venous blood was collected from each participant under full aseptic precautions and transferred into clot activator tube for serum analysis and to EDTA tube for ESR measurement. Blood collected in clot activator tubes was allowed to clot. Clotted blood was centrifuged and the separated serum was collected and stored at −20°C until analysis. Serum calreticulin levels were estimated using a commercially available Human Calreticulin ELISA kit using Sandwich-ELISA principle. ESR was measured by the Westergren method.

Statistical Analysis: Data were entered into Microsoft Excel spread sheet and analysed using Jamovi software. Normality was assessed using the Shapiro–Wilk test. Variables were expressed as mean ± standard deviation. Differences between two groups were analysed using the Independent t-test or Mann–Whitney U test, while comparisons among disease activity groups were performed using one-way ANOVA with Games–Howell post hoc analysis. Correlation between serum calreticulin, ESR, and DAS28 score was assessed using Spearman correlation coefficient. A p value <0.05 was considered statistically significant and highly significant at p<0.001.

Results

In our study, among 50 RA patients, 12 (24%) were in remission, 11 (22%) had low disease activity, 11 (22%) had moderate disease activity, and 16 (32%) had high disease activity according to DAS28-ESR. Analysis of serum biomarkers showed that patient with RA had elevated levels of ESR and calreticulin levels as compared to control.

Table 1: Basic characteristics of study population

Characteristics	Healthy Controls (n=50)	Cases (n=50)
Age (yrs)	52.5 ± 6.92	52.5 ± 6.77
Male: Female	13 : 37	14 : 36
Urban : Rural	26 : 24	28 : 22

Both the RA cases and Healthy controls are well matched and comparable in terms of age and gender.

Table 2: Comparison of parameters between Controls and RA Patients

Parameters	Healthy Controls	RA Cases	p-value
ESR (mm/hr)	11 ± 3.74	32 ± 24.8	< 0.001
Calreticulin (ng/mL)	3.12 ± 0.25	6.01 ± 1.69	< 0.001

According to Shapiro-Wilk p values, the ESR data is not normally distributed so Mann–Whitney U test is used to compare RA cases and Healthy controls. ESR and calreticulin levels in cases are significantly elevated when compared to controls and their difference was statistically highly significant (p < 0.001).

Table 3: Distribution of parameters across different disease activity levels of RA

Parameters	Remission (n=12)	Low (n=11)	Moderate (n=11)	High (n=16)	Overall p-value
ESR (mm/hr)	6.83 ± 2.29	12.18 ± 2.04	32.73 ± 8.78	63.88 ± 8.74	< 0.001
Calreticulin (ng/mL)	4.07 ± 0.25	4.99 ± 0.18	5.98 ± 0.23	8.17 ± 0.69	< 0.001

The mean ESR and Calreticulin levels have increased markedly with disease activity, thus demonstrated a clear increasing trend with worsening disease activity, suggesting their potential role as markers of disease severity in rheumatoid arthritis.

Table 4: Post hoc pairwise comparison of parameters according to DAS-28 in RA

Parameters	p- value	
	ESR	**Calreticulin**
Remission vs Low	0.002	< 0.001
Remission vs Moderate	< 0.001	< 0.001
Remission vs High	< 0.001	< 0.001
Low vs Moderate	< 0.001	< 0.001
Low vs High	< 0.001	< 0.001
Moderate vs High	< 0.001	< 0.001

ESR shows significant statistical differences ($p < 0.05$) between all RA disease activity groups, indicating progressive increase with increasing disease severity. For Calreticulin, all comparisons between disease activity groups demonstrated a high statistically significant difference ($p < 0.001$). These findings indicates that CRT have a strong association with disease activity in RA.

Table 5: Correlation table: Spearman correlation analysis

Variables	**r value**	**p value**
ESR vs Disease activity category (DAS28)	0.963	< 0.001
Calreticulin vs Disease activity category (DAS28)	0.999	< 0.001
ESR vs Calreticulin	0.965	< 0.001

Spearman correlation analysis demonstrated a strong positive correlation between serum calreticulin and DAS28 score and ESR with DAS28 score. In addition, serum calreticulin was strongly correlated with ESR.

Discussion

Although previous studies have reported altered calreticulin levels and their correlation with DAS28 scores but such data are limited in the Indian context. Currently, there is limited evidence from India that integrates calreticulin, ESR, and DAS28 score within a single study framework. The present study demonstrated significantly higher serum ESR and calreticulin levels in patients with rheumatoid arthritis compared with healthy controls. ESR remains a widely used marker of inflammation and has been shown to increase with disease activity in rheumatoid arthritis. Similar findings have been reported by Smolen et al., who demonstrated that ESR reflects inflammatory burden, particularly in patients with moderate to high disease activity.[12] Mishra et al. also reported significantly elevated ESR levels in rheumatoid arthritis patients compared with healthy controls and observed a positive association with disease activity.[13] Serum calreticulin levels were significantly elevated in rheumatoid arthritis patients and increased progressively from remission to high disease activity. Calreticulin have strong positive correlation between serum calreticulin and DAS28 score across all disease activity categories, including remission and low disease activity. These observations are in agreement with Lee et al., who identified calreticulin as an emerging biomarker closely associated with disease activity indices in rheumatoid arthritis.[14] Zhang et al. further reported that increased calreticulin expression reflects immune activation and chronic inflammation, supporting its usefulness in disease monitoring.[15] Calreticulin is involved in immune regulation, antigen presentation, calcium homeostasis, and activation of inflammatory signalling pathways. Increased extracellular calreticulin enhances immune-cell activation and promotes the production of pro-inflammatory cytokines, thereby contributing to persistent synovial inflammation in rheumatoid arthritis.[16,17] The strong correlation observed between serum calreticulin and ESR in the present study further supports the association between calreticulin and systemic inflammatory activity.

The findings of the present study suggest that, compared with ESR, calreticulin demonstrated a more consistent association with disease activity, particularly in patients with remission and low disease activity. Thus, serum Calreticulin may serve as a valuable adjunct biomarker for assessing disease activity in rheumatoid arthritis.

However, the study was limited by its cross-sectional design, relatively small sample size, and single-centre setting. Further multicentric studies with larger sample sizes and longitudinal follow-up are required to establish the clinical utility of serum calreticulin in routine assessment and monitoring of rheumatoid arthritis.

Conclusion

Rheumatoid arthritis is characterised with persistent inflammation, progressive joint damage, and also extra-articular manifestations, which adversely affects the physical function and quality of life. ESR is a broad, nonspecific marker of inflammation that can be elevated in numerous disease conditions. Hence, calreticulin estimation may serve as a valuable tool for predicting disease progression and monitoring disease activity in rheumatoid arthritis. It facilitates early identification of patients with increasing inflammatory burden and helps to provide therapeutic strategies timely to prevent adverse disease outcomes.

Acknowledgements: The authors gratefully acknowledge the institutional leadership and the laboratory staff of the Department of Biochemistry, MGM Medical College, Indore, for providing the facilities and support essential for the successful completion of this study.

Ethical Approval: The study was approved by the Institutional Ethics Committee

References

1. Lin YJ, Anzaghe M, Schülke S. Update on the patho-mechanism, diagnosis, and treatment options for rheumatoid arthritis. Cells (2020) 9(4):880. doi:10.3390/ cells9040880
2. GBD 2019: Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. https://vizhub.healthdata.org/gbd-results/.
3. Malaviya, A. N., Kapoor, S. K., Singh, R. R., Kumar, A. & Pande, I. Prevalence of rheumatoid arthritis in the adult Indian population. Rheumatol. Int. 13, 2021;131–134.
4. Firestein GS. Etiology and pathogenesis of rheumatoid arthritis. In: Ruddy S, Harris ED, Sledge CB, Kelley WN, eds. Kelley's Textbook of Rheumatology. 7th ed. Philadelphia: W.B. Saunders, 2005:996-1042
5. Turesson, C. (2013). Extra-articular rheumatoid arthritis. Current Opinion in Rheumatology 25(3) 360-366
6. Smitten, A. L., Simon TA, Hochberg MC, Suissa S. (2008). A meta-analysis of the incidence of malignancy in adult patients with rheumatoid arthritis. Arthritis Research & Therapy 10(2) R45, doi: 10.1186/ar2404.
7. 7.Sodergren A, Stegmayr B, Lundberg V, Ohman ML, Wallberg-Jonsson S. (2007). Increased incidence of and impaired prognosis after acute myocardial infarction among patients with seropositive rheumatoid arthritis. Annals of the Rheumatic Diseases 66(2) 263-266.
8. Farheen K and Agarwal SK (2011): Assessment of disease activity and treatment outcomes in rheumatoid arthritis. J Manag Care Pharm; 17: S09–13.
9. Nishimoto N, Takagi N. Assessment of the validity of the 28-joint disease activity score using erythrocyte sedimentation rate (DAS28-ESR) as a disease activity index of rheumatoid arthritis in the efficacy evaluation of 24-week treatment with tocilizumab: sub analysis of the SATORI study. Mod Rheumatol. 2021;20:539–47
10. Zhang Y, Li X, Wang J, Chen Z, Zhang L. Calreticulin: multifunctional roles in immune regulation and disease. Front Immunol. 2021;12:680194.
11. Liu R, Gong J, Chen J, et al. Calreticulin regulates inflammatory signaling pathways. J Immunol. 2020;205(8):2065–2076.
12. Smolen JS, Aletaha D, McInnes IB.: Rheumatoid arthritis. The Lancet, Volume 388, Issue 10055, October 2016, Pages 2023–2038.
13. Mishra R, Singh A, Kaur H, et al. Evaluation of ESR and CRP as markers of disease activity in rheumatoid arthritis. J Family Med Prim Care. 2022;11(6):2850 2855.
14. Lee HS, Kim KW, Park SH, Lee SH.: Emerging biomarkers in rheumatoid arthritis: focus on calreticulin. Journal of Autoimmunity, Volume 128, 2022, Article 102802
15. Zhang QY, Liu H, Wang X, Chen Y, Li J.: Calreticulin in immune activation and chronic inflammatory diseases. Immunology Letters, Volume 256, 2023, Pages 28-35.
16. Liu R, Gong J, Chen J, et al. Calreticulin regulates inflammatory signaling pathways. J Immunol. 2020;205(8):2065–2076.
17. Firestein GS & McInnes IB: Immunopathogen esis of Rheumatoid Arthritis. Immunity, Volume 46, Issue 2, February 2017, Pages 183–196.