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A Cross-Sectional Study of Role of C Reactive Protein in Determining Remission of Inflammation in Acute Gout

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Abstract

Background: Gout is characterized by the deposition of monosodium urate (MSU) crystals in joints, leading to acute inflammatory arthritis. C-reactive protein (CRP) is a widely used biomarker for systemic inflammation, but its utility in monitoring remission in acute gout remains underexplored.

Objectives: To evaluate the role of CRP in determining remission of inflammation in acute gout, assessed by clinical examination and ultrasonography at 4 weeks post-treatment, and to examine its correlation with patient-reported pain.

Methods: A cross-sectional study was conducted in a tertiary care hospital in Pune, enrolling 113 adult patients diagnosed with acute gout per ACR/EULAR 2015 criteria. At 4 weeks post-treatment, CRP levels, clinical joint assessments, ultrasonography (OMERACT scoring), and pain scores (VAS) were recorded. Remission was defined as CRP <6 mg/L and OMERACT joint inflammation score ≤1. Statistical analysis included Student's t-test, Pearson correlation, and ROC curve analysis.

Results: The mean age was 53.21 ± 14.92 years; 77% were male. At 4 weeks, 58.4% had CRP <6 mg/L. Remission (OMERACT 0/1) was present in 52.2%. There was a significant association between low CRP and remission by OMERACT ($p<0.001$). CRP showed a weak but significant positive correlation with pain scores ($r=0.247$, $p=0.008$). CRP at 4 weeks demonstrated a sensitivity of 74.58% and specificity of 59.26% for detecting remission.

Conclusions: CRP is a moderately sensitive marker for remission of inflammation in acute gout at 4 weeks, correlating with ultrasonographic and clinical findings. Its use may aid in monitoring disease activity and guiding management.

Keywords: Gout, C-reactive protein, Remission, Ultrasonography, Inflammation

Introduction

Gout is a common inflammatory arthritis marked by monosodium urate (MSU) crystal deposition in joints and periarticular tissues, leading to acute and often severe inflammation [1,2]. Although hyperuricemia is required for gout development, most individuals with elevated serum urate do not progress to clinical gout, even when MSU crystals are present in their joints [1,2]. Differentiating gout from other chronic arthritides, such as osteoarthritis, can be challenging in patients with persistent joint symptoms but without classic acute attacks. In these cases, detecting urate deposits is crucial for diagnosis [3].

Musculoskeletal ultrasonography (USG) has become a valuable, non-invasive, and cost-effective tool for identifying MSU crystal deposits. USG avoids ionizing radiation and is increasingly available in clinical practice [4,5]. Characteristic USG findings in gout include tophi, hyperechoic aggregates, and the double contour sign (DCS), all reflecting MSU deposition. USG can also reveal bone erosions and synovial pathology, aiding both diagnosis and disease activity assessment [2]. The presence of tophi on USG is linked to greater disability and increased pain [6]. Notably, inflammatory changes seen on USG generally resolve within four weeks of appropriate therapy.

C-reactive protein (CRP) is a well-established biomarker for systemic inflammation, rapidly rising in response to tissue necrosis [7]. Despite its role as an inflammation marker, longitudinal data on CRP kinetics in gout are limited [7]. CRP usually normalizes within four weeks post-flare, though delays may occur despite clinical improvement.

Given that acute gouty arthritis usually resolves within four weeks, this study aims to assess the role of CRP in determining remission. Specifically, it compares CRP levels, global pain scores, and USG findings after four weeks of therapy to evaluate CRP's utility as a biomarker for monitoring disease activity and therapeutic response.

Methods

Study Design and Setting

This cross-sectional study was conducted at Bharati Vidyapeeth Deemed to be University Medical College, Dhankawadi, Pune, a tertiary care hospital, from 2023 to 2025. Ethical approval (BVDUMC/IEC/15) was obtained from the Institutional Ethics Committee prior to study initiation, and all participants provided informed consent.

Study Population

The study included adult patients (>18 years) with acute gout undergoing 4-week treatment and meeting the ACR/EULAR gout categorization criteria (2015). Patients with asymptomatic hyperuricemia, those with haematological malignancies, and individuals with a prior diagnosis of other crystal-related arthropathies such as calcium pyrophosphate deposition disease were excluded from the study.

Sample size

The sample size for the study was calculated using the formula:

$n = (Z\alpha/2)^2 \times p \times (100 - p) / d^2$,

where the prevalence (p) was assumed to be 50% due to the lack of prior studies, the allowable error (d) was set at 10 (20% of p), and the standard normal deviate (Zα/2) was 1.96 for a 95% confidence interval. Based on these parameters, the final sample size was determined to be 97 participants.

Data Collection

At the four-week follow-up, all participants underwent a detailed clinical examination of symptomatic joints, measurement of serum C-reactive protein (CRP) levels, and musculoskeletal ultrasonography (USG) of the joint with maximum symptoms. Ultrasonography was performed to assess for synovitis and other signs of inflammation, including power Doppler signal, synovitis greater than grade 2 as per the OMERACT (Outcome Measures in Rheumatology Clinical Trials) joint scoring system, and inflammation within tophi. The following joints were evaluated based on clinical involvement: metatarsophalangeal (MTP), ankle, knee, elbow, wrist, and others as indicated.

Remission was defined as the complete resolution of joint inflammation both clinically and radiologically, corresponding to an OMERACT joint inflammation score of ≤1 and a CRP level <6 mg/L. Patients not meeting these criteria were classified as having active joint inflammation. Demographic and clinical data—including age, gender, disease duration, comorbidities, social and dietary history—were collected for all participants. Symptom severity was graded using the global pain scale (Visual Analog Scale).

CRP levels were correlated with clinical and ultrasonographic findings of joint inflammation. Statistical analysis was performed using SPSS software. Comparisons between groups were made using Student's t-test, and the correlation between CRP and pain scale was assessed using Pearson's correlation coefficient. The sensitivity of CRP in detecting remission was evaluated using receiver operating characteristic (ROC) curve analysis.

Statistical analysis

Data were collected and entered into Microsoft Excel, then analyzed using Statistical package for social sciences (version 28). Descriptive statistics were used to summarize demographic and clinical variables, and results were presented as tables and graphs.

Comparisons of C-reactive protein (CRP) levels and ultrasonography findings at four weeks post-acute gout were performed using Student's t-test. The correlation between CRP levels and patient global pain scores (Visual Analog Scale, VAS) was assessed using the Pearson correlation coefficient to evaluate the strength and direction of association between these continuous variables.

The diagnostic performance of CRP in detecting remission of inflammation was evaluated using receiver operating characteristic (ROC) curve analysis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated based on the optimal CRP cut-off value for remission. A p-value of <0.05 was considered statistically significant for all analyses.

Results

Demographic and Baseline Characteristics

The study included a total of 113 patients with mean age of 53.21 ± 14.92 years. There was a male predominance, with 87 men (77.0%) and 26 women (23.0%). Hypertension was the most prevalent comorbidity, reported in 71 patients (62.8%), followed by chronic kidney disease in 38 patients (33.6%) and diabetes mellitus in 37 patients (32.7%). Other comorbidities included ischemic heart disease in 11 patients (9.7%), hypothyroidism in 5 patients (4.4%), and cerebrovascular accident (CVA) in 1 patient (0.9%). A

total of 12 patients (10.6%) had no comorbidities (Table 1).

Regarding social habits, 55 patients consumed alcohol, 40 were smokers, and 24 chewed tobacco. As for dietary patterns, 92 patients followed a mixed diet, while 21 were vegetarians.

Polyarticular joint involvement was present in 85.8% patients, while monoarticular involvement was seen in 14.2% patients. Joint swelling was observed in 62 patients (54.9%), and joint tenderness was present in 73 patients (64.6%). The most commonly involved joint was the metatarsophalangeal (MTP) joint (86.7%), followed by the ankle joint (45.1%), knee joint (15.0%), wrist joint (4.4%), and other joints (0.9%) (Table 2).

CRP Levels and Ultrasound (OMERACT) Findings

CRP levels measured at 4 weeks were <6 mg/L in 66 patients (58.4%) and ≥6 mg/L in 47 (41.6%). According to the OMERACT scoring system, 5 patients (4.4%) were in Grade 0, 53 (46.9%) in Grade 1, 25 (22.1%) in Grade 2, and 30 (26.5%) in Grade 3. Grouping the grades, 59 patients (52.2%) fell under OMERACT Grade 0 & 1, and 54 (47.8%) were in Grade 2 & 3.

Association Between CRP, Pain Scale, and OMERACT Scores

A statistically significant association was found between CRP levels and OMERACT scores ($p < 0.001$). Among patients with CRP <6 mg/L, 44 (66.7%) had OMERACT Grade 0 & 1, while 22 (33.3%) had Grade 2 & 3. In contrast, among those with CRP ≥6 mg/L, 15 (31.9%) were in Grade 0 & 1, and 32 (68.1%) were in Grade 2 & 3.

A significant relationship was also observed between pain scale scores and OMERACT grades ($p < 0.0001$). Among patients with pain scores <2, 40 (68.97%) had Grade 0 & 1, and 18 (31.03%) had Grade 2 & 3. Conversely, among those with pain scores >2, 19 (34.55%) were in Grade 0 & 1, and 36 (65.45%) were in Grade 2 & 3.

Correlation Analysis

There was a weak but statistically significant positive correlation between CRP levels at 4 weeks and pain scale scores ($r = 0.247$, $p = 0.008$), indicating that higher CRP levels were associated with greater pain intensity.

Diagnostic Performance of CRP and Pain Scale

The diagnostic accuracy of CRP levels at 4 weeks in predicting remission was 66.58%, with a sensitivity of 74.58%, specificity of 59.26%, positive predictive value (PPV) of 62.63%, and negative predictive value (NPV) of 71.79%.

For the pain scale, the diagnostic accuracy was 67.21%, with a sensitivity of 67.80%, specificity of 66.67%, PPV of 65.05%, and NPV of 69.33%.

Discussion

Gout is a crystal-induced inflammatory arthropathy characterized by the deposition of monosodium urate crystals in joints, resulting in acute, painful flares. While the inflammatory phase is typically self-limiting, assessing remission is essential for treatment decisions and preventing recurrence. C-reactive protein (CRP), a hepatic acute-phase reactant, has emerged as a useful biomarker for evaluating ongoing inflammation, therapeutic response, and disease resolution.

In our study of 113 patients with acute gout, the mean age was 53.21 ± 14.92 years, comparable to the findings of Huang et al. (2023)[8], who reported a mean age of 54.6 years. A strong male predominance was observed (77.0%), consistent with the gender distribution reported by both Huang et al. (91.8%) [8] and Roseff et al. (1987) [9]. Hypertension (62.8%) and chronic kidney disease (33.6%) were the most common comorbidities in our

cohort, supporting the link between hyperuricemia and renal dysfunction highlighted by Huang et al. [8]. Lifestyle factors such as alcohol use (48.7%) and smoking (35.4%) were also prevalent. These are important considerations, as Roseff et al. [9] and other researchers have shown that alcohol use may elevate CRP independently, potentially confounding interpretations of disease activity.

Dietary patterns, particularly purine-rich mixed diets (81.4% in our cohort), are recognized contributors to gout flares. Prior studies have highlighted the difficulty of standardizing dietary interventions in clinical research involving gout patients [8,10,11].

Joint involvement followed the classical pattern, with the MTP joint most frequently affected (86.7%), followed by the ankle (43.4%) and knee (15.0%). Although knee involvement was less frequent in our cohort, Huang et al.[8] emphasized the knee joint's importance in musculoskeletal ultrasonography (MSKUS) evaluations, identifying key intra-articular features such as synovial proliferation and joint effusion.

At four weeks post-flare, CRP levels were <6 mg/L in 58.4% of participants. Notably, higher CRP levels (≥6 mg/L) were significantly associated with increased OMERACT scores (Grades 2 & 3), which represent greater inflammatory burden on ultrasound ($p < 0.001$). These results align with the findings of Huang et al. [8], Yu et al. (2023)[12], and Roseff et al. (1987)[9], who reported CRP elevation during active inflammation in gout.

The diagnostic performance of CRP in detecting ongoing inflammation (OMERACT Grades 2 & 3) was modest, with a sensitivity of 74.58%, specificity of 59.26%, and overall accuracy of 66.58%. Zhang et al. (2023)[13] also observed a marked decline in CRP following anti-inflammatory therapy, highlighting CRP's value as a dynamic marker of response.

CRP levels also demonstrated a weak but statistically significant correlation with pain scores ($r = 0.247$, $p = 0.008$) in our study. Although pain is a subjective measure, its diagnostic performance was comparable, with an accuracy of 67.21%. Schlesinger et al. (2019) [14] noted reductions in both CRP and pain scores following anti-inflammatory interventions, suggesting parallel improvement in clinical and biochemical markers. Urano et al. (2002)[10] found that CRP levels dropped significantly from 2.92 mg/dL during the acute phase to 0.41 mg/dL after two weeks, further supporting its utility in tracking disease resolution.

The pain scale showed a sensitivity of 67.80% and specificity of 66.67%, indicating that it can modestly discriminate between those in remission and those with persistent inflammation. However, because CRP can be influenced by other systemic factors—including comorbid conditions and addictions—it should not be used in isolation. Its interpretation must be integrated with clinical presentation and imaging findings.

Overall, our results support CRP as a moderately reliable marker for inflammation remission in acute gout, especially when used in conjunction with the OMERACT scoring system and clinical symptoms. However, lifestyle and comorbid factors may confound its interpretation, underscoring the need for a multimodal assessment strategy in managing gout.

Conclusion

This study demonstrates that CRP serves as a practical and effective biomarker for monitoring inflammation in patients with acute gout. CRP levels reliably reflect both the onset and resolution of disease activity, rising during acute flares and returning to normal as symptoms

subside. This makes CRP a useful adjunct to clinical assessment for determining remission status. However, clinicians should consider other possible sources of inflammation when interpreting CRP values. Further research is needed to establish standardized CRP thresholds for use in gout management.

Limitations

The study's cross-sectional design captures CRP at a single time point, limiting the ability to observe changes throughout the entire course of a gout flare and remission. The relatively small sample size and single-center setting may affect the generalizability of the findings. Despite exclusion criteria, confounding factors such as undetected infections or comorbidities may have influenced CRP levels. Additionally, other inflammatory markers like ESR and interleukin-1 were not assessed, which could have provided a more comprehensive inflammatory profile. Finally, the subjective nature of clinical remission assessment may introduce observer bias in correlating CRP with disease resolution.

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List of Abbreviations

- ACR – American College of Rheumatology
- CKD – Chronic Kidney Disease
- CRP – C-reactive protein
- DCS – Double Contour Sign
- ESR – Erythrocyte Sedimentation Rate
- HAG – Hyperechoic Aggregates
- HUA – Hyperuricemia
- MTP – Metatarsophalangeal
- MSU – Monosodium Urate
- NPV – Negative Predictive Value
- OMERACT – Outcome Measures in Rheumatology Clinical Trials
- PPV – Positive Predictive Value
- ROC – Receiver Operating Characteristic
- USG – Ultrasonography
- VAS – Visual Analog Scale

Legend Tables:

Table 1: Demographic, Clinical, and Social Characteristics of Patients (N = 113)

Characteristic	Category	Number of patients
Age (Years)	Mean ± SD	53.21 ± 14.92 years
Gender	Male	87 (77.0)
	Female	26 (23.0)
Comorbidities	Hypertension	71 (62.80)
	Chronic Kidney Disease	38 (33.62)
	Diabetes Mellitus	37 (32.74)
	Other Comorbidities	26 (23.00)
	Ischemic Heart Disease	11 (9.70)
	Hypothyroidism	5 (4.40)

Characteristic	Category	Number of patients
	Cerebrovascular Accident	1 (0.90)
	No Comorbidities	12 (10.62)
Social History	Alcohol Consumption	55 (48.7)
	Smoking	40 (35.4)
	Tobacco Chewing	24 (21.2)
Dietary History	Mixed Diet	92 (81.4)
	Vegetarian	21 (18.6)

Table 2: Joint Involvement and Examination

Parameter	Category	Number of patients (%)
Joint Involvement Type	Monoarticular	16 (14.2)
	Polyarticular	97 (85.8)
Joint Swelling	Present	62 (54.9)
	Absent	51 (45.1)
Joint Tenderness	Present	73 (64.6)
	Absent	40 (35.4)
Specific Joints Involved	MTP Joint	98 (86.7)
	Ankle Joint	51 (45.1)
	Knee Joint	17 (15.0)
	Wrist Joint	5 (4.4)
	Other Joints	1 (0.9)

Table 3: Inflammatory Marker (CRP) and Ultrasound (OMERACT) Assessment

Marker/Score	Category	Number of patients (%)
CRP at 4 weeks	<6 mg/L	66 (58.4)
	≥6 mg/L	47 (41.6)
OMERACT Score	Grade 0	5 (4.4)
	Grade 1	53 (46.9)
	Grade 2	25 (22.1)

Marker/Score	Category	Number of patients (%)
	Grade 3	30 (26.5)
OMERACT Category	Grade 0 & 1	59 (52.2)
	Grade 2 & 3	54 (47.8)

Table 4: Associations of CRP and Pain Scale with OMERACT Category

Parameter	OMERACT 0&1	OMERACT 2&3	P value
CRP <6 mg/L	44	22	<0.001
CRP ≥6 mg/L	15	32	
Pain Scale <2	40	18	<0.0001
Pain Scale >2	19	36	

Table 5: Correlation and Diagnostic Performance at 4 weeks

Variable	Mean ± SD	R value	P value
CRP (mg/L)	8.09 ± 9.44	0.247	0.008
Pain Scale	2.8 ± 2.3		

Table 6: Diagnostic Accuracy of CRP and Pain Scale for Remission

Marker	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
CRP at 4 weeks	74.58	59.26	62.63	71.79	66.58
Pain Scale	67.80	66.67	65.05	69.33	67.21