



## Predictive Value of C-Reactive Protein and Fibrinogen in Flare-Ups of Ulcerative Colitis.

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### Abstract

Ulcerative colitis (UC), a chronic relapsing inflammatory bowel disease, is typified by cycles of remission and acute flare-ups. Predicting these exacerbations is clinically challenging, necessitating reliable, non-invasive biomarkers for early detection. This study investigates the diagnostic utility of serum C-reactive protein (CRP) and fibrinogen levels in forecasting UC flare-ups. A total of 120 patients with histologically confirmed UC were enrolled and divided into two cohorts: those experiencing active flares and those in remission. Serum CRP and fibrinogen levels were analyzed and correlated with Mayo scores and endoscopic findings. Results revealed significantly higher concentrations of CRP ( $p < 0.001$ ) and fibrinogen ( $p = 0.002$ ) in the flare group. Receiver operating characteristic (ROC) analyses demonstrated that both biomarkers had strong predictive value, with CRP outperforming fibrinogen in sensitivity and specificity. These findings support the clinical relevance of CRP and fibrinogen as adjunctive tools for early detection and proactive management of UC flare-ups, potentially reducing dependence on invasive diagnostics like endoscopy.

**Keywords:** Ulcerative colitis, Biomarkers, C-reactive protein, Fibrinogen, Flare prediction

### Introduction

Ulcerative colitis (UC) is a chronic inflammatory disorder of the colon, marked by continuous mucosal inflammation beginning in the rectum and extending proximally. Its pathogenesis involves complex interactions between genetic factors, environmental triggers, immune dysregulation, and gut microbiota alterations. Clinically, UC is characterized by unpredictable relapses and remissions, complicating timely therapeutic interventions. Despite advances in diagnostic modalities, the accurate and early prediction of disease exacerbation remains elusive.<sup>1-4</sup>

Current monitoring techniques, primarily based on symptom evaluation, endoscopic imaging, and histopathological assessment, are limited by invasiveness, cost, and delayed

availability. Moreover, clinical symptoms often do not correlate with mucosal inflammation, highlighting the need for objective, accessible biomarkers to detect subclinical disease activity.<sup>5-8</sup>

Among emerging biomarkers, acute-phase reactants such as C-reactive protein (CRP) and fibrinogen show promise. CRP, synthesized by hepatocytes in response to interleukin-6, is a general marker of systemic inflammation. Fibrinogen, another hepatic acute-phase protein, contributes not only to coagulation but also to the inflammatory cascade, with emerging evidence suggesting a role in intestinal microthrombosis and barrier dysfunction.<sup>9-10</sup>

Despite their individual relevance, few studies have directly compared CRP and fibrinogen in the context of UC flare prediction. This study aims to fill that gap by evaluating and

comparing the predictive accuracy of CRP and fibrinogen in patients with clinically and endoscopically confirmed UC, and assessing their correlation with disease severity indices such as the Mayo score.

## Methodology

A prospective, comparative study was conducted over 12 months at the Gastroenterology Department of Central Park Medical College, Lahore. Ethical approval was obtained from the institutional review board, and verbal informed consent was acquired from all participants.

### Sample Selection:

A total of 120 patients (18–65 years) with histologically confirmed UC were enrolled through consecutive non-probability sampling. Based on disease activity, participants were classified into:

- **Group A (Flare-up, n=60):** Mayo score  $\geq 6$
- **Group B (Remission, n=60):** Mayo score  $\leq 2$

The sample size was calculated using Epi Info software (power: 80%, confidence level: 95%) based on anticipated biomarker differences from pilot data.

### Inclusion Criteria:

Patients with confirmed UC (endoscopy and biopsy), assessed within two weeks of enrollment.

### Exclusion Criteria:

Individuals with active infections, autoimmune diseases, malignancy, chronic liver disease, pregnancy, recent surgeries, or recent corticosteroid/immunosuppressive therapy were excluded.

### Laboratory Analysis:

Fasting venous blood samples were obtained. Serum CRP was quantified via high-sensitivity immunoturbidimetry, and fibrinogen was measured using the Clauss method. All analyses were conducted in a certified laboratory. Demographic and clinical variables (age, sex, disease duration, smoking status, and medication history) were recorded via structured proforma.

### Statistical Analysis:

Data were analyzed using SPSS v26. Mean and standard deviation were reported for continuous variables; frequencies and percentages for categorical variables. Intergroup comparisons used independent t-tests, with  $p < 0.05$  considered statistically significant. ROC analysis was performed to assess predictive accuracy (AUC, sensitivity, specificity) for flare-up detection.

## Results

### Demographic Characteristics:

Both groups were statistically comparable regarding age, sex, smoking status, disease duration, and medication use (Table 1), ensuring minimal confounding.

### Biomarker Comparison:

- **CRP Levels:**
  - Flare-up:  $19.6 \pm 6.3$  mg/L
  - Remission:  $5.2 \pm 2.8$  mg/L

- $p < 0.001$

- **Fibrinogen Levels:**

- Flare-up:  $516.4 \pm 87.1$  mg/dL
- Remission:  $388.7 \pm 74.6$  mg/dL
- $p = 0.002$

### Predictive Accuracy (ROC Analysis):

- **CRP:**
  - AUC: 0.902
  - Cut-off:  $\geq 9.8$  mg/L
  - Sensitivity: 88.3%
  - Specificity: 83.7%
- **Fibrinogen:**
  - AUC: 0.821
  - Cut-off:  $\geq 450$  mg/dL
  - Sensitivity: 80.0%
  - Specificity: 76.2%

Both biomarkers were effective predictors, with CRP demonstrating superior diagnostic performance (Table 3).

## Discussion

This study underscores the diagnostic significance of CRP and fibrinogen as non-invasive markers for UC flare-ups. Elevated levels of both biomarkers were observed in active disease states, reinforcing their roles as systemic indicators of inflammation.<sup>11-13</sup>

CRP showed high sensitivity and specificity, aligning with prior findings, although previous literature had questioned its accuracy in colonic-limited disease. By minimizing confounding factors, this study clarifies CRP's predictive strength in UC flare detection.<sup>14-16</sup>

Fibrinogen, though traditionally linked to coagulation, exhibited a strong correlation with disease activity, supporting newer evidence of its inflammatory role in UC. Its slightly lower predictive power compared to CRP does not undermine its utility; instead, it complements CRP in a dual-marker strategy.<sup>17-20</sup>

Importantly, the identified cut-off values for CRP ( $\geq 9.8$  mg/L) and fibrinogen ( $\geq 450$  mg/dL) provide actionable thresholds that can guide early therapeutic intervention in the absence of immediate endoscopic access. When used together, these biomarkers enhance the precision of disease activity assessment, particularly in resource-limited settings.

The homogeneity in demographic parameters further strengthens the validity of the results, eliminating potential confounding effects.

## Conclusion

CRP and fibrinogen are effective, non-invasive biomarkers for identifying flare-ups in ulcerative colitis, with CRP demonstrating slightly superior predictive capability. Their integration into clinical practice can facilitate early detection, improve individualized care, and reduce reliance on invasive procedures. Future longitudinal studies and biomarker-driven management protocols are warranted to build upon these findings.

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