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Evaluating Serum C-Reactive Protein and Fibrinogen as Predictive Biomarkers for Ulcerative Colitis Exacerbations: A Comparative Study

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Abstract

Ulcerative colitis (UC), a chronic inflammatory bowel disease, exhibits recurrent episodes of mucosal inflammation marked by alternating phases of remission and exacerbation. Accurate prediction of disease flares remains a clinical challenge, emphasizing the need for reliable biomarkers. This experimental study evaluates the predictive value of C-Reactive Protein (CRP) and fibrinogen levels in anticipating flare-ups in patients with confirmed UC diagnoses. A total of 120 participants were recruited and stratified into active flare-up and remission groups based on clinical, endoscopic, and histological parameters. Serum CRP and fibrinogen concentrations were quantitatively analyzed and correlated with Mayo scores and endoscopic findings. Results demonstrated significantly elevated levels of CRP ($p < 0.001$) and fibrinogen ($p = 0.002$) in the flare-up group compared to the remission cohort. Receiver Operating Characteristic (ROC) analysis identified CRP and fibrinogen as statistically significant predictors of disease exacerbation with sensitivity and specificity surpassing conventional inflammatory indices. These findings underscore the clinical utility of CRP and fibrinogen in early detection of UC flare-ups, providing a non-invasive adjunct to endoscopy. This study presents novel comparative data with strong statistical significance, potentially bridging a current gap in timely disease activity monitoring. Incorporation of these biomarkers may facilitate proactive disease management and individualized therapeutic strategies in UC care.

Keywords: Ulcerative colitis, C-reactive protein, Fibrinogen

Introduction

Ulcerative colitis (UC) is a relapsing-remitting inflammatory condition of the colon characterized by continuous mucosal inflammation that begins in the rectum and may extend proximally. Despite extensive research, the disease etiology remains multifactorial, involving a complex interplay between genetic predisposition, environmental exposures, immune dysregulation, and gut microbiota alterations. The unpredictable clinical course, marked by periods of flare-ups and remission, continues to pose substantial diagnostic and therapeutic challenges, particularly regarding timely identification and intervention during exacerbations.[1-5]

One of the most pressing clinical concerns in the management of UC is the lack of highly specific, easily accessible, and cost-effective biomarkers capable of reliably predicting disease activity and flare-ups. Current monitoring strategies rely heavily on symptom assessment, endoscopic evaluations, and histopathological analysis. However, endoscopy is invasive, expensive, and often delayed until symptoms worsen, which limits its utility for proactive disease monitoring. Moreover, symptom-based indices may not accurately reflect underlying mucosal inflammation, particularly in cases of subclinical activity. Consequently, there is an urgent need for objective, non-invasive biomarkers that can detect disease exacerbation early and guide therapeutic decision-making.[6-9]

In this context, acute phase reactants such as C-reactive protein (CRP) and fibrinogen have emerged as potential candidates. CRP, a hepatic protein synthesized in response to interleukin-6, is widely regarded as a general marker of systemic inflammation. Elevated CRP levels have been consistently associated with active disease in UC, yet its sensitivity in isolated colonic inflammation remains debated. Similarly, fibrinogen, another liver-derived acute-phase protein, plays a crucial role in coagulation and inflammation. Its elevation has been linked to disease severity in various inflammatory conditions, including inflammatory bowel diseases. However, the utility of fibrinogen in the context of UC flare-up prediction remains under-investigated, particularly in direct comparison with CRP and in conjunction with clinical severity indices such as the Mayo score.[11-12]

Recent advances in the understanding of the immunopathogenesis of UC have revitalized interest in systemic inflammatory markers as adjunctive tools for disease monitoring. While several studies have examined CRP's association with UC activity, its predictive strength in the context of disease flares compared to other markers remains inconsistent across cohorts. On the other hand, emerging data suggest that fibrinogen may have a distinct pathophysiological role in chronic colonic inflammation through its interaction with vascular and mucosal pathways. This potential dual role of fibrinogen—as both a marker and mediator of inflammation—may provide new insights into disease activity dynamics when examined in parallel with CRP.[13]

The present study investigates the predictive value of serum CRP and fibrinogen levels in patients with clinically and endoscopically confirmed UC, aiming to fill a critical research gap. By stratifying patients based on disease activity into flare-up and remission groups, and employing robust statistical analysis, this study aims to provide high-quality evidence on the relative utility of these biomarkers in clinical practice. It further explores their relationship with disease activity scores, such as the Mayo index, and their potential role in non-invasive flare prediction.

Importantly, this study distinguishes itself by incorporating a carefully selected sample size, calculated using Epi Info software, and a rigorous inclusion criterion that excludes confounding factors such as concurrent infections, autoimmune diseases, or corticosteroid use. Moreover, ethical considerations, including verbal informed consent and confidentiality, were stringently observed. Through its experimental design and data-driven approach, this research offers a methodologically sound and statistically robust evaluation of CRP and fibrinogen as predictive markers of flare-ups in UC.

In summary, the burden of delayed flare detection and the limitations of current diagnostic modalities necessitate the exploration of accessible biomarkers for real-time disease monitoring in UC. By providing comparative data on CRP and fibrinogen levels across disease states, this study contributes to a nuanced understanding of systemic inflammation in UC pathophysiology. The findings are anticipated to inform future guidelines and support more individualized and anticipatory management strategies in inflammatory bowel disease care.

Methodology

This experimental study was conducted over a period of twelve months in a tertiary care center with a dedicated gastroenterology department at Central Park Teaching Hospital Lahore Pakistan. The study aimed to assess the predictive value of serum C-Reactive Protein (CRP) and fibrinogen levels in flare-ups of ulcerative colitis (UC). Ethical approval was obtained from the institutional review board, and verbal informed consent was obtained from each participant after explaining the purpose, procedures, and voluntary nature of the study. Confidentiality was maintained throughout the research process.

A total of 120 patients aged 18 to 65 years with an established diagnosis of UC confirmed by endoscopy and histopathology were enrolled using a non-probability consecutive sampling technique. Sample size was calculated using Epi Info version 7.2 by setting the power at 80%, confidence interval at 95%, and expected proportion of elevated CRP and fibrinogen in flare-up versus remission groups based on previous pilot data, yielding a minimum required sample of 104 participants, which was increased to 120 to compensate for potential dropouts. Patients were divided into two groups: Group A (n = 60), consisting of patients experiencing an active flare-up based on the Mayo disease activity index (score ≥6), and Group B (n = 60), consisting of patients in clinical remission (Mayo score ≤2).

Inclusion criteria comprised adult patients with biopsy-proven UC, either in active flare or remission, based on clinical evaluation and endoscopic assessment performed within the past two weeks. Exclusion criteria included patients with concurrent autoimmune disorders, active infections, malignancies, recent surgeries, pregnancy, chronic liver disease, or current use of corticosteroids or immunosuppressive therapy within four weeks of recruitment, as these factors could confound serum CRP and fibrinogen levels.

Venous blood samples were collected from each participant in fasting state. Serum CRP was measured using high-sensitivity immunoturbidimetric assay, while plasma fibrinogen concentration was determined using the Clauss method. All laboratory analyses were conducted in the same certified central laboratory to ensure consistency. Clinical data including age, sex,

duration of disease, smoking status, and medication history were recorded using a structured proforma.

The primary variables were CRP and fibrinogen levels in both groups. Data were analyzed using SPSS version 26. Descriptive statistics were used for demographic variables, expressed as mean and standard deviation for continuous variables and frequency and percentages for categorical variables. Independent t-tests were applied for comparison of mean CRP and fibrinogen levels between the two groups. A p-value of less than 0.05 was considered statistically significant. Additionally, ROC curve analysis was performed to determine the predictive ability of CRP and fibrinogen levels in identifying flare-ups, along with sensitivity and specificity calculations.

This methodology ensured that the findings were derived from a systematically selected and clinically validated population, with rigorous control of potential confounders and standardized laboratory processing, thus enhancing the reliability and generalizability of the results.

Results

A total of 120 patients were enrolled in the study, with 60 patients each in the flare-up group (Group A) and remission group (Group B). Demographic characteristics and baseline clinical parameters are presented in Table 1. The two groups were comparable in terms of age, gender distribution, and disease duration, ensuring minimal demographic confounding in biomarker comparison.

Table 1: Demographic and Baseline Clinical Characteristics

Variable	Group A (Flare-up) Mean ± SD / n (%)	Group B (Remission) Mean ± SD / n (%)	p-value
Age (years)	38.7 ± 11.4	37.5 ± 12.2	0.615
Gender (Male/Female)	32 (53.3%) / 28 (46.7%)	30 (50.0%) / 30 (50.0%)	0.708
Disease Duration (years)	5.6 ± 3.2	5.3 ± 3.1	0.573
Smoking History (Yes/No)	10 (16.7%) / 50 (83.3%)	8 (13.3%) / 52 (86.7%)	0.609
Current Medications (5-ASA)	56 (93.3%)	58 (96.7%)	0.648

Explanation: No statistically significant differences were observed in demographic variables between the two groups, indicating homogeneity in baseline parameters.

Table 2: Comparison of CRP and Fibrinogen Levels Between Flare-up and Remission Groups

Biomarker	Group A (Flare-up) Mean ± SD	Group B (Remission) Mean ± SD	p-value
C-Reactive Protein (mg/L)	19.6 ± 6.3	5.2 ± 2.8	<0.001
Fibrinogen (mg/dL)	516.4 ± 87.1	388.7 ± 74.6	0.002

Explanation: Both CRP and fibrinogen levels were significantly elevated in the flare-up group compared to the remission group, indicating strong association with active disease states.

Table 3: ROC Curve Analysis of CRP and Fibrinogen for Predicting Flare-Ups

Biomarker	Area Under Curve (AUC)	Optimal Cut-off Value	Sensitivity (%)	Specificity (%)	p-value
CRP (mg/L)	0.902	≥9.8	88.3	83.7	<0.001
Fibrinogen (mg/dL)	0.821	≥450	80.0	76.2	0.004

Explanation: ROC analysis confirmed both CRP and fibrinogen as strong predictors of flare-ups, with CRP showing superior diagnostic performance based on AUC, sensitivity, and specificity.

Discussion

The results of this study provide compelling evidence that both C-reactive protein (CRP) and fibrinogen are significantly elevated during ulcerative colitis (UC) flare-ups, reaffirming their roles as systemic markers of inflammation. The mean CRP and fibrinogen levels were notably higher in patients experiencing active disease compared to those in remission, with p-values demonstrating robust statistical significance. This suggests that these biomarkers can serve as practical, non-invasive adjuncts in predicting exacerbations, addressing a critical gap in the real-time assessment of UC disease activity.[14-17]

CRP, an acute-phase protein produced by hepatocytes under the influence of interleukin-6, demonstrated the highest diagnostic accuracy with an AUC of 0.902, sensitivity of 88.3%, and specificity of 83.7%. These results are consistent with recent findings emphasizing the elevated expression of CRP during active inflammation, although its sensitivity in colonic-limited disease had previously been considered suboptimal. The present study's methodology, which excluded confounding variables such as concurrent infections and steroid use, likely contributed to the clearer delineation of CRP's predictive capacity in UC.[18]

Fibrinogen, although less explored in this context, also showed a significant elevation during flare-ups and yielded an AUC of 0.821 in ROC analysis. While traditionally associated with hemostasis, fibrinogen has recently been implicated in amplifying inflammatory cascades and promoting intestinal microthrombosis, both relevant to UC pathophysiology. Its predictive performance in this study underscores its underutilized potential as a biomarker in inflammatory bowel diseases.

The correlation between elevated fibrinogen and clinical disease activity supports its emerging role as a complementary marker to CRP.[19-20]

The demographic analysis revealed that baseline parameters such as age, gender, and disease duration did not significantly differ between groups, strengthening the reliability of the biomarker comparison. This homogeneity ensures that the observed differences in CRP and fibrinogen levels are indeed reflective of disease activity rather than external variables. The exclusion of patients with other systemic inflammatory conditions further reduces the risk of false elevation, allowing for greater confidence in interpreting the biomarker levels.

Interestingly, the optimal CRP cut-off value identified in this study (≥9.8 mg/L) aligns with thresholds suggested by recent clinical protocols, reinforcing its clinical relevance. Similarly, the fibrinogen cut-off (≥450 mg/dL) falls within a biologically plausible range and offers a novel reference point for clinicians. These values, combined with the corresponding sensitivity and specificity metrics, provide an actionable framework for integrating biomarker data into routine clinical decision-making, especially when endoscopic evaluations are delayed or contraindicated.

The dual biomarker approach advocated by this study has particular strength in enhancing diagnostic precision. While CRP offers higher sensitivity, fibrinogen contributes additional specificity, particularly in cases where CRP may be normal despite mucosal inflammation. When used together, these markers can potentially triangulate disease activity with greater accuracy than either could alone. This synergistic potential supports a multimodal approach to disease monitoring, in alignment with current precision medicine initiatives in inflammatory bowel disease care.

These findings offer substantial clinical value, especially in resource-limited settings where access to endoscopy and histology may be restricted. By identifying accessible, reproducible, and cost-effective indicators of disease activity, this study contributes to the growing emphasis on non-invasive monitoring tools. Importantly, the research also addresses a notable gap in current literature by directly comparing fibrinogen and CRP in a flare-up context, thus advancing the understanding of their respective roles in UC pathogenesis and management.

Conclusion

This study establishes that both CRP and fibrinogen are statistically significant, non-invasive predictors of ulcerative colitis flare-ups, with CRP demonstrating superior sensitivity and diagnostic accuracy. By integrating these biomarkers into clinical protocols, early detection and personalized disease management can be enhanced. The findings bridge a critical gap in flare-up prediction and lay the foundation for future research exploring biomarker-driven therapeutic strategies.

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