



Article

Enteric Infections in Relapsing Ulcerative Colitis Patients in Albania: The Predictive Value of CRP/Albumin Ratio

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Abstract

Background and Aim: Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease (IBD) associated with increased susceptibility to enteric infections, which may mimic or exacerbate disease flares. The C-reactive protein (CRP)-to-albumin ratio (CAR) has emerged as a simple indicator of systemic inflammation in UC. This study aimed to assess the prevalence of stool infections in active UC and to further evaluate CAR as a potential predictive marker. **Methods:** This retrospective study included 42 patients with active UC (Mayo score ≥ 6) from April 2024 to February 2025. Stool samples were analyzed using multiplex polymerase chain reaction (PCR) for 25 bacterial, viral, and parasitic pathogens. Serum CRP and albumin levels were measured to calculate the CAR. Patients were categorized as infected or non-infected. Logistic regression and receiver operating characteristic (ROC) analyses were performed to evaluate CAR predictive performance. **Results:** Enteric infections were identified in 35.7% of patients, with *Escherichia coli* species predominating. CAR was significantly higher in infected than in non-infected patients [0.21 (0.02–0.62) vs. 0.06 (0.02–0.15), $p = 0.028$]. CAR was significantly associated with enteric infection in logistic regression analysis (OR = 240.0, 95% CI 2.7–21,555.6; $p = 0.017$). ROC analysis yielded an AUC of 0.706, with a cut-off value of 0.669 providing 100% specificity and 40% sensitivity. **Conclusion:** Enteric infections are prevalent in patients with active UC. CAR may serve as a simple, rapid, and accessible adjunctive marker to identify patients who warrant further evaluation for enteric infection. Thus, it may aid in differentiating UC flares from superimposed infection.

Keywords: ulcerative colitis; coeliac disease; CAR; stool infection; Albania; gastrointestinal disorder; inflammatory bowel disease

Academic Editor: Tamara Čačev

Received: 21 May 2026

Revised: 27 June 2026

Accepted: 1 July 2026

Published: 6 July 2026

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1. Introduction

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease (IBD) that primarily affects the colon and rectum. UC flares are unpredictable, and prompt therapeutic intervention is essential to optimize both short-term outcomes and long-term goals, including mucosal and histologic remission [1]. Its pathogenesis involves disruption of the intestinal mucosal barrier and immune dysregulation, and it often requires immunosuppressive therapy. The long-term use of immunosuppressive medications for the treat-

ment of UC, such as immunomodulators and corticosteroids, particularly when these agents are used in combination, contributes to an increased susceptibility to secondary infections, including enteric pathogens [2–4]. These infections are clinically significant, as they can mimic or exacerbate disease activity, complicating both diagnosis and management [5]. With the advent of multiplex stool polymerase chain reaction (PCR) assays, the detection of enteropathogens has markedly improved clinical decision-making and overall disease management [6].

Previous studies have reported variable prevalence rates of enteric infections in IBD patients, ranging from 10% to 31%, depending on the population studied and the diagnostic method applied [1–4]. Among the pathogens identified, *Clostridioides difficile* has consistently been reported as the most frequent, often linked to prior antibiotic exposure and associated with worse clinical outcomes [2,4,7].

During disease flares, patients commonly present with abdominal pain, diarrhea, and rectal bleeding, symptoms that significantly overlap with those caused by enteric infections. This overlap poses a major diagnostic challenge in clinical practice, as misclassification may delay appropriate treatment, lead to unnecessary antibiotic use, or complicate therapeutic decisions regarding immunosuppressive and biologic agents. Given these limitations, there is a growing need for accessible and reliable biomarkers that can aid in distinguishing UC flares from superimposed infections.

C-reactive protein (CRP) and serum albumin are widely available laboratory markers reflecting systemic inflammation and nutritional status, respectively [7]. The CRP/albumin ratio (CAR) has recently gained attention as a reliable biomarker of disease activity and prognosis in several inflammatory conditions, including IBD. While elevated CAR values have been associated with increased inflammatory burden in IBD [7,8], CAR's role in distinguishing IBD flares from concurrent enteric infections has not been fully elucidated.

The aim of this study was to determine the prevalence and spectrum of enteric infections in patients with active UC and to evaluate the diagnostic utility of the CAR as a predictor of enteric infection in this patient population.

2. Results

2.1. Baseline Characteristics

A total of 42 patients with active UC were enrolled, comprising 25 females (59.5%) and 17 males (40.5%), with a mean age of 46.1 ± 15.6 years. The median disease duration was 6.0 years (IQR 2.0–11.25 years). The median total Mayo score at enrollment was 7.0 (IQR 6.0–8.0), consistent with moderate-to-severe disease activity (Table 1).

Table 1. Demographic and clinical characteristics of the patients.

	Infected (n = 15)	Non-Infected (n = 27)	Total (n = 42)	p-Value
Age (years), mean $\pm$ SD	47.20 $\pm$ 16.09	45.44 $\pm$ 15.67	46.07 $\pm$ 15.65	0.366
Gender, n (%)				
Male	7 (46.7)	10 (37.0)	17 (40.5)	0.542
Female	8 (53.3)	17 (63.0)	25 (59.5)	
Disease duration (years), median (IQR)	2.00 (2.00–11.00)	6.00 (2.00–12.00)	6.00 (2.00–11.25)	0.234
Medications, n (%)				
Corticosteroids	10 (66.7)	16 (59.3)	26 (61.2)	0.636
Azathioprine	4 (26.7)	11 (40.7)	15 (35.7)	0.362

Antibiotics	2 (13.3)	4 (14.8)	6 (14.3)	0.895
Disease Activity n (%)				
Moderate	15 (100)	24 (88.9)	39 (92.9)	0.372
Severe	0 (0)	3 (11.1)	3 (7.1)	
Total Mayo score, median (IQR)	8.00 (7.00–8.50)	7.00 (6.00–8.00)	7.00 (6.00–8.00)	0.168
WBC ($\times 10^9/L$), mean $\pm$ SD	9.39 $\pm$ 3.41	9.20 $\pm$ 2.57	9.27 $\pm$ 2.87	0.844
Albumin (g/dL), median (IQR)	4.40 (3.90–4.50)	4.40 (4.20–4.50)	4.40 (4.20–4.50)	0.210
CRP (mg/dL), median (IQR)	0.80 (0.11–2.48)	0.24 (0.07–0.67)	0.27 (0.10–0.96)	0.028
CAR, median (IQR)	0.21 (0.02–0.62)	0.06 (0.02–0.15)	0.06 (0.02–0.22)	0.028

Based on stool PCR analysis, 15 patients (35.7%) were classified as infected and 27 (64.3%) as non-infected. No significant differences were observed between infected and non-infected groups in terms of age (47.20 ± 16.09 vs. 45.44 ± 15.67 years; $p = 0.366$), gender distribution ($p = 0.542$), or disease duration [6.00 (2.00 – 12.00) vs. 2.00 (2.00 – 11.00); $p = 0.234$]. Similarly, no significant differences were observed in the use of corticosteroids ($p = 0.636$), azathioprine ($p = 0.362$), or antibiotics in the preceding month ($p = 0.895$).

2.2. Disease Activity

Disease activity, assessed by the total Mayo score, was comparable between groups. The majority of patients in both infected and non-infected cohorts had moderate disease activity, with no significant difference in distribution ($p = 0.372$). Median total Mayo scores were also similar between infected and non-infected patients [8.0 (7.0 – 8.5) vs. 7.0 (6.0 – 8.0); $p = 0.168$] (Table 1).

2.3. Laboratory Findings

Laboratory parameters were largely comparable between groups. White blood cell (WBC) counts did not differ significantly between infected and non-infected patients (9.39 ± 3.41 vs. $9.20 \pm 2.57 \times 10^9/L$; $p = 0.844$), nor did albumin levels [4.40 (3.90 – 4.50) vs. 4.40 (4.20 – 4.50) g/dL; $p = 0.210$].

In contrast, inflammatory markers were significantly elevated in patients with enteric infection. CRP levels were higher in infected patients compared to non-infected patients [0.80 (0.11 – 2.48) vs. 0.24 (0.07 – 0.67) mg/dL; $p = 0.028$]. Similarly, the CAR was significantly increased in infected patients. [0.21 (0.02 – 0.62) vs. 0.06 (0.02 – 0.15); $p = 0.028$] (Table 1).

2.4. Enteric Pathogens

Overall, 15 of the 42 patients (35.7%) tested positive for enteric infection by stool PCR. Among these, six (40%) cases had multiple concurrent pathogens.

Bacterial pathogens were the most frequently identified group, predominantly non-*Clostridioides* species. The most commonly detected organisms were *Escherichia coli* (*E. coli*) pathotypes, including enteropathogenic *E. coli* (EPEC; $n = 5$), Shiga toxin-producing *E. coli* (STEC; $n = 2$), enterohemorrhagic *E. coli* (EHEC; $n = 1$), and enteroaggregative *E. coli* (EAEC; $n = 1$). *Clostridioides difficile* was identified in three patients, while *Aeromonas* spp. and *Salmonella* spp. were each detected in two patients.

Parasitic infections included *Dientamoeba fragilis* ($n = 2$), *Blastocystis* spp. ($n = 2$), and *Giardia lamblia* ($n = 1$). Viral pathogens were less frequent and included Norovirus in two patients. The full distribution of detected pathogens is shown in Figure 1.

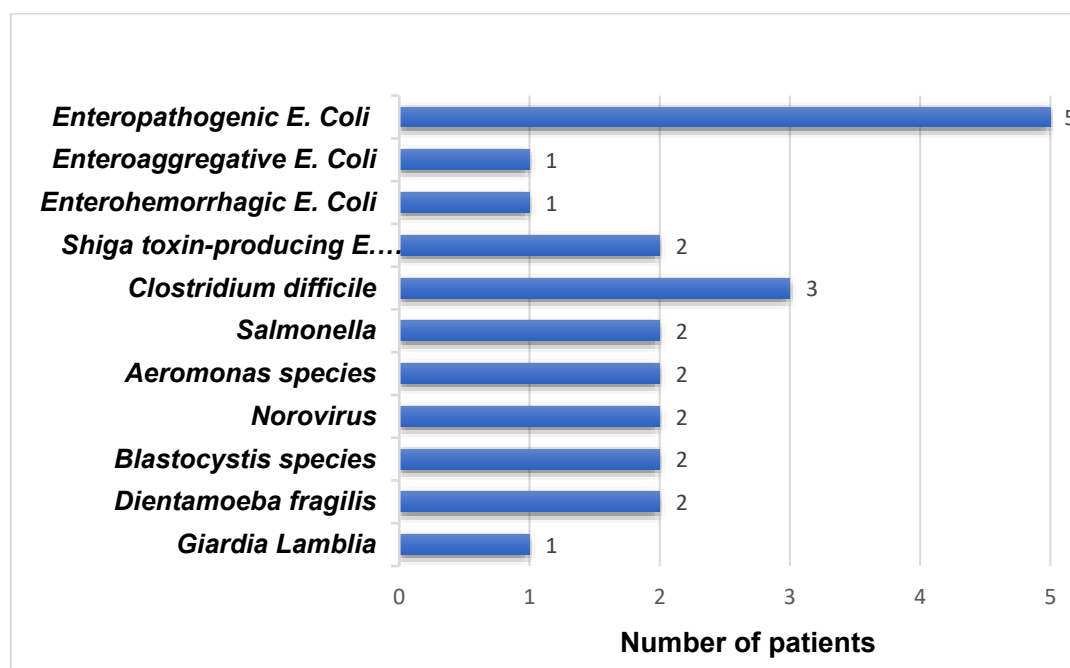


Figure 1. Identified enteric pathogens.

2.5. Association Between CAR and Enteric Infection

A significant positive correlation was observed between CAR and enteric infection status ($r = 0.407$, $p = 0.008$), indicating higher CAR values in infected patients.

CAR was not significantly correlated with total Mayo score (Spearman's $\rho = 0.188$, $p = 0.295$).

2.6. Univariate Logistic Regression Analysis

In univariate logistic regression analysis, CAR was significantly associated with enteric infection ($B = 5.481$, $SE = 2.295$, $p = 0.017$), corresponding to an OR of 240.0 (95% CI: 2.7–21,555.6). The Wald statistic confirmed statistical significance (Wald = 5.704) (Table 2). This indicates a strong unadjusted association between higher CAR values and the presence of enteric infection.

Table 2. Logistic regression analysis: CAR as a predictor of infection.

Predictor	B	SE	Wald	p-Value	OR (Exp(B))	95% CI for OR
CRP/albumin ratio	5.481	2.295	5.704	0.017	240.00	2.70–21,555.60

2.7. Multivariable Logistic Regression Analysis

A multivariable logistic regression model including CAR and total Mayo score was used to assess whether the association between CAR and enteric infection was independent of UC disease activity.

CAR remained positively associated with enteric infection but did not reach statistical significance after adjustment ($B = 5.588$, $SE = 3.025$, $OR = 267.16$, 95% CI: 0.71–100,475.64; $p = 0.065$). In contrast, the total Mayo score was not independently associated with infection ($B = 0.155$, $SE = 0.289$, $OR = 1.17$, 95% CI: 0.66–2.06; $p = 0.592$) (Table 3).

Table 3. Multivariable logistic regression analysis of predictors of enteric infection.

Predictor	B	SE	Wald	p-Value	OR (Exp(B))	95% CI for OR
CAR	5.59	3.03	3.41	0.065	267.16	0.71–100,475.64
Total Mayo score	0.16	0.29	0.29	0.592	1.17	0.66–2.06

2.8. Linear Regression Analysis of CAR

Multiple linear regression was performed to further assess determinants of CAR, with enteric infection status and total Mayo score included as predictors.

The model was statistically significant ($F = 4.793$, $p = 0.016$), explaining 24.2% of the variance in CAR ($R^2 = 0.242$; adjusted $R^2 = 0.192$). Enteric infection was independently associated with higher CAR values ($B = 0.441$, $SE = 0.178$, $\beta = 0.399$, $p = 0.019$), whereas total Mayo score was not significantly associated with CAR ($B = 0.074$, $SE = 0.053$, $\beta = 0.225$, $p = 0.174$) (Table 4).

Table 4. Multivariable linear regression analysis identifying factors associated with CAR.

Predictor	B	SE	Standardized β	t	p-Value	95% CI for B
Enteric infection	0.441	0.178	0.399	2.473	0.019	0.077–0.805
Total Mayo score	0.074	0.053	0.225	1.394	0.174	−0.034–0.182
Constant	−0.446	0.397	—	−1.124	0.270	−1.257–0.364

2.9. ROC Curve Analysis

ROC curve analysis demonstrated an AuROC of 0.706 (95% CI: 0.525–0.888), indicating moderate discriminatory ability of CAR in detecting enteric infection (Figure 2).

The optimal cut-off value of 0.669 yielded a specificity of 100% and a sensitivity of 40%, with a Youden's J statistic of 0.40 (Table 5).

At this cut-off, CAR demonstrated a high specificity profile, suggesting potential utility as a complementary marker for risk stratification.

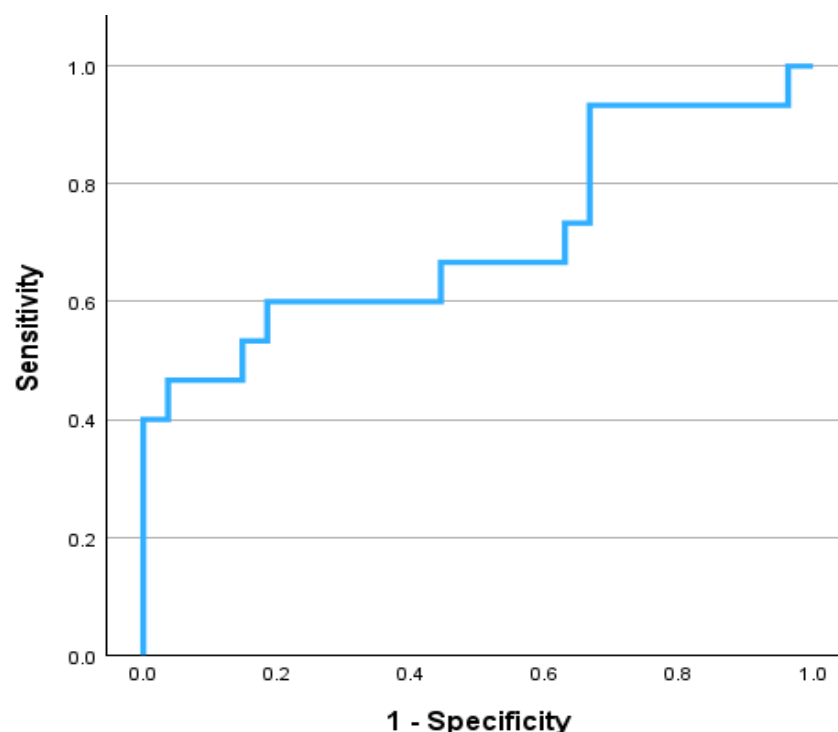


Figure 2. ROC curve analysis of CAR in predicting enteric infections.

Table 5. Discriminatory power of CAR for enteric infection by ROC curve.

Variable	AuROC (95% CI)	Cut-Off Value	Sensitivity (%)	Specificity (%)	Youden's J Statistic
CAR	0.706 (0.525, 0.888)	0.669	40	100	0.40

3. Discussion

In our study, the prevalence of enteric infections among patients with active UC was 35.7%, which is higher than that reported in some previous studies (12–31.1%). Milonaki et al. observed a rate of 10.5% in active IBD individuals; [2] Antonelli et al. detected enteric pathogens in 12% of active IBD cases, particularly in Crohn's disease. [9] In another cross-sectional analysis of 214 symptomatic IBD patients, 26.8% were diagnosed with enteric infection [10], and Limsrivilai et al. reported a 31.1% rate among active IBD patients [11].

The higher pathogen detection rate observed in our study may be partially attributable to the broad pathogen coverage and high analytical performance of the multiplex PCR panel, which has a reported sensitivity of 98.5% and specificity of 99.2%. By simultaneously screening for a wide range of bacterial, viral, and parasitic pathogens, multiplex PCR enables the identification of microorganisms that may remain undetected with conventional diagnostic methods. Consistent with this, Hong et al. reported significantly higher pathogen detection rates in patients with IBD flares when PCR-based stool testing was used compared with conventional microbiological testing (26% vs. 5%) [12].

However, an important limitation of multiplex PCR is that it detects pathogen nucleic acids rather than active infection [13]. Consequently, positive results may reflect asymptomatic carriage, colonization, co-infection, or persistence of pathogen nucleic acids following a prior infection [14]. This consideration is particularly relevant for organisms such as EPEC, EAEC, *Blastocystis* spp., and *Dientamoeba fragilis*, which may also be identified in asymptomatic individuals. [15,16]. Although stool testing in our study was performed in patients with clinical deterioration and/or endoscopic evidence of active UC, the pathogenic role of some detected organisms remains uncertain. Therefore, PCR-positive findings should be interpreted within the broader clinical, endoscopic, and laboratory context, and the prevalence of clinically relevant enteric infections reported in our cohort may represent an overestimation of true infectious disease.

On the other hand, these findings may also reflect the epidemiology of enteric infections within our general population, suggesting that these pathogens are not only relevant in the context of IBD flares but are also widely circulating in the community.

Most studies have identified a predominance of *Clostridioides difficile* enteric infection [2,5,10]. In contrast, in our patients (13/42, 30%), non-*Clostridioides difficile* bacterial infection was the most common, with *E. coli* species predominating. Our results probably reflect the local situation in which *E. coli* is found in potable and coastal waters [17,18]. Similarly, when Ghosh et al. investigated the prevalence of enteric infection in 75 consecutive patients presenting with UC flare, 48% tested positive. *Aeromonas* was the most frequently identified pathogen, accounting for 22.7% of cases, whereas *Clostridioides difficile* was detected in only 2.7% of patients. The authors attributed these findings to geographical and ethnic variation [19].

Antibiotic use is a well-established risk factor for *Clostridioides difficile* occurrence [20] and was low in our study population (14.3%), with only two individuals among the infected group reporting recent exposure. This limited use may also contribute to our results. However, the detection of multiple concurrent pathogens in 40% of infected cases emphasizes the complexity of microbial interactions in this population and the need for comprehensive diagnostic approaches.

Distinguishing an UC flare from a concurrent enteric infection remains a significant clinical challenge due to overlapping symptomatology. In our cohort, disease activity, as assessed by total Mayo score, did not differ significantly between infected and non-infected patients ($p = 0.168$), suggesting limited discriminatory ability of clinical indices alone.

CRP is one of the most important proteins in acute inflammation. It is produced by the liver within a few hours in response to increases in proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and interleukin-1 (IL-1) [21]. It is a key biomarker in evaluating disease activity in IBD patients [22]. In our study, the non-infected group had a median CRP level of 0.24 mg/dL (IQR 0.07–0.67), and it increased by nearly four times in the infected group, reaching the median value of 0.80 mg/dL (IQR 0.11–2.48).

Albumin, traditionally viewed as a nutritional marker, also decreases during systemic inflammation [23]. In our cohort, serum albumin levels were similar between groups, with median values of 4.40 g/dL (IQR 3.90–4.50) in the infected group and 4.40 g/dL (IQR 4.20–4.50) in the non-infected group, with no statistically significant difference observed ($p = 0.210$).

CAR combines these two indicators and has recently gained attention as a useful index of disease severity and systemic inflammatory burden. It has been shown that CAR had a better correlation with IBD disease activity than each component alone [24,25].

In our study, CAR, already elevated in active disease, was significantly higher in the infected group compared to the non-infected group, with median values of 0.21 (IQR 0.02–0.62) versus 0.06 (IQR 0.02–0.15), respectively ($p = 0.028$). This association aligns with previous findings showing that a heightened CAR value may reflect increased inflammatory activity, potentially facilitating infection onset or indicating an ongoing infection [7,26].

Given that CAR is a marker of systemic inflammation, we specifically explored the potential confounding effect of UC disease activity. CAR was not significantly correlated with the total Mayo score, and disease activity was not independently associated with CAR. In multivariable logistic regression, adjusting for disease activity, CAR showed a positive but borderline association with infection, while the Mayo score was not associated. Consistently, linear regression showed that enteric infection status, but not disease activity, was associated with CAR. Overall, these findings suggest that CAR may be more strongly related to enteric infection than to UC disease activity in this cohort; however, given the limited sample size and borderline statistical significance, residual confounding cannot be excluded.

Although CAR was significantly associated with enteric infection in the logistic regression analysis, the estimated OR showed a very wide CI (OR 240.0; 95% CI 2.7–21,555.6), indicating considerable uncertainty around the effect estimate. This likely reflects the limited sample size and the relatively small number of infection events, resulting in imprecision in the estimated effect size. Therefore, while the findings suggest a potential association between CAR and enteric infection, the magnitude of this association should be interpreted cautiously and validated in larger prospective cohorts.

ROC analysis demonstrated moderate discriminatory performance (AUC 0.706), with limited sensitivity (40%) but high specificity (100%) at the optimal cut-off of 0.669. Therefore, CAR alone is not sufficient to exclude infection, but elevated values may indicate patients requiring further microbiological evaluation. Accordingly, CAR should be considered a complementary marker rather than a standalone diagnostic test. This pattern mirrors observations in Crohn's disease, where specificity is typically higher than sensitivity [7].

Clinically, identifying enteric infections in UC is essential, as they may worsen symptoms, complicate treatment decisions, and increase hospitalization risk [5]. In this context,

CAR may assist in supporting clinical suspicion of infection, but it should always be interpreted alongside clinical and microbiological findings.

Several limitations of this study should be acknowledged. First, the relatively small sample size, particularly the limited number of patients with enteric infection, restricts the generalizability of our findings and may have reduced statistical power, increasing the risk of false-negative errors. In addition, the small number of outcome events limits the robustness of subgroup and multivariable analyses and constrains the number of covariates that can be reliably included, increasing the risk of model overfitting and unstable estimates. As a result, potential confounders such as age, disease duration, disease severity, corticosteroid exposure, azathioprine treatment, antibiotic use, albumin level, and CRP could not be fully adjusted for in multivariable models.

Second, the cross-sectional design limits causal inference, and the absence of longitudinal follow-up does not allow for assessment of CAR dynamics in relation to infection onset, progression, or resolution. Third, although our study focused specifically on patients with clinically active UC presenting with worsening symptoms—where distinguishing disease flare from superimposed enteric infection is particularly relevant—this design limits the applicability of our findings to patients with mild or stable disease managed in general outpatient settings.

Finally, we did not perform a comparative analysis of CAR with its individual components (CRP and albumin) using ROC analysis, which could have clarified the incremental value of the composite marker. However, the primary aim of this study was to evaluate CAR as a composite biomarker in the context of enteric infection in relapsing UC, and such exploratory analyses were not performed due to the limited sample size. Future larger, multicenter, and longitudinal studies are needed to validate our findings and further define the clinical utility of CAR across diverse UC populations.

4. Materials and Methods

4.1. Patients and Disease Data

This retrospective, observational study was conducted at the IBD Unit of the Clinic of Gastroenterology, Tirana, Albania, spanning April 2024 to February 2025. A total of 42 patients with active UC, defined by a total Mayo score ≥ 6 , were included. All patients had a confirmed diagnosis of UC and were under regular follow-up at our unit during the study period. Patients with incomplete records or indeterminate diagnoses were excluded.

Clinical data were extracted from standardized medical records, including disease duration, disease activity (assessed by total Mayo score), smoking status, recent treatment regimens (use of corticosteroids, azathioprine, and antibiotics within the preceding month), and relevant comorbidities. Laboratory, endoscopic, and microbiological findings were obtained from hospital records and laboratory reports.

All patients had provided informed consent for the use of their clinical data for research purposes. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, University of Medicine, Tirana (Decision No. 62, 10 December 2025).

4.2. Laboratory Data

Stool samples from all participants were collected and analyzed using a multiplex gastrointestinal PCR panel capable of detecting 25 bacterial, viral, and parasitic enteric pathogens (Table 6). The assay is based on a two-stage nested PCR technology coupled with melt curve analysis and is performed in a closed, automated system that integrates nucleic acid extraction, amplification, and result interpretation. The assay has an overall sensitivity of 98.5% and specificity of 99.2%, with results reported qualitatively as detected or not detected.

Table 6. GI panel of pathogen organisms identified by multiplex PCR stool test.

Bacterial Pathogens:	
• Enterohemorrhagic <i>E. coli</i> (EHEC) • Enteropathogenic <i>E. coli</i> (EPEC) • Enteroaggregative <i>E. coli</i> (EAEC) • Enterotoxigenic <i>E. coli</i> (ETEC) • Shiga toxin-producing <i>E. coli</i> (STEC stx1/stx2) • <i>Shigella</i> spp. • <i>Clostridioides difficile</i> (Toxin B) • <i>Clostridioides difficile</i> (hypervirulent) • <i>Salmonella</i> spp. • <i>Vibrio</i> spp. • <i>Campylobacter</i> spp. • <i>Aeromonas</i> spp. • <i>Yersinia enterocolitica</i>	
Viral Pathogens:	
• Adenovirus • Rotavirus • Astrovirus • Norovirus GII • Norovirus GI • Sapovirus	
Parasitic Pathogens:	
• <i>Cryptosporidium</i> spp. • <i>Entamoeba histolytica</i> • <i>Giardia lamblia</i> • <i>Blastocystis hominis</i> • <i>Dientamoeba fragilis</i> • <i>Cyclospora cayetanensis</i>	

In addition to microbiological analysis, blood samples were obtained to measure CRP levels (normal range <0.5 mg/dL) and serum albumin concentrations (normal range 3.2–5.5 g/dL). CAR was subsequently calculated for each patient. Stool and blood samples were collected within three days of each other and during the same week that a colonoscopy was performed.

4.3. Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 29.0.2.0. Patients were categorized into two groups based on enteric infection status: infected and non-infected.

The distribution of continuous variables was assessed using the Shapiro–Wilk test. Variables with a normal distribution are presented as mean $\pm$ standard deviation (SD), whereas non-normally distributed variables are reported as median and interquartile range (IQR). Categorical variables are summarized as frequencies and percentages. Comparisons between infected and non-infected patients were performed using the independent-samples *t*-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Associations between categorical variables were evaluated using the Pearson chi-square test or Fisher’s exact test, as appropriate.

The relationship between CAR and enteric infection status was initially assessed using correlation analysis. Univariate logistic regression analysis was performed to evaluate the association between CAR and the presence of enteric infection.

To evaluate whether the relationship between the CAR and enteric infection was independent of UC disease activity, multivariable regression analyses were performed with the total Mayo score included as a covariate. Logistic regression was applied to assess the association between CAR and enteric infection, while multiple linear regression was used to identify factors independently associated with CAR. Results are reported as regression coefficients (B), standard errors (SEs), odds ratios (ORs), standardized coefficients (β), and 95% confidence intervals (CIs), as appropriate. The discriminatory performance of CAR for identifying enteric infection was evaluated using receiver operating characteristic (ROC) curve analysis. The area under the ROC curve (AuROC) and corresponding 95% CI were calculated. The optimal cut-off value was determined using the Youden index, defined as the maximum value of sensitivity plus specificity minus one. Sensitivity, specificity, and Youden index values were reported for the selected threshold.

All statistical tests were two-tailed, and a p -value < 0.05 was considered statistically significant.

5. Conclusions

In this study, we observed a notably high prevalence of enteric infections among biologic-naïve patients with active UC, with non-*Clostridioides difficile* bacterial pathogens—particularly *E. coli* species—emerging as the leading contributors. This pattern likely reflects both the expanded diagnostic yield of multiplex PCR assays and local environmental exposures. The clinical overlap between UC flares and infection-related symptoms highlights the ongoing challenge of achieving diagnostic clarity in routine practice. Our findings suggest that the CAR may serve as a useful complementary biomarker to support clinical suspicion of enteric infection. However, CAR should not be considered a standalone diagnostic tool, given its limited sensitivity. While these results provide preliminary insights, they must be interpreted with caution due to the small sample size and methodological constraints. Larger, prospective, multicenter studies are required to validate these observations and to define the role of CAR within diagnostic algorithms for UC flares complicated by enteric infection.

Author Contributions: Conceptualization, M.S., S.H. and S.P.; methodology, M.S., S.H., X.P., and S.P.; software, S.P., G.Q. and S.P.; validation, M.S., S.H., X.P., G.Q., E.A.M. and S.P.; formal analysis, M.S., S.H., E.A.M. and G.Q.; investigation, M.S., S.H., X.P. and S.P.; resources, M.S., S.H., X.P. and S.P.; data curation, M.S., G.Q., E.A.M. and S.P.; writing—original draft preparation, M.S., S.H., X.P. and S.P.; writing—review and editing, M.S., S.H., X.P., G.Q., E.A.M. and S.P.; visualization, M.S., S.H., X.P., G.Q., E.A.M. and S.P.; supervision, S.P.; project administration, M.S. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki, and ethical approval for the study was obtained from the Ethics Committee of the Faculty of Medicine, University of Medicine, Tirana, Albania (Decision No. 62, 10 December 2025).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The dataset is available upon request from the authors.

Conflicts of Interest: The authors declare no conflicts of interest.

References

1. Monstad, I.L.; Solberg, I.C.; Cvancarova, M.; Hovde, O.; Henriksen, M.; Huppertz-Hauss, G.; Gunther, E.; Moum, B.A.; Stray, N.; Vatn, M.; et al. Outcome of Ulcerative Colitis 20 Years after Diagnosis in a Prospective Population-based Inception Cohort from South-Eastern Norway, the IBSEN Study. *J. Crohn's Colitis* **2021**, *15*, 969–979.
2. Mylonaki, M.; Langmead, L.; Pantes, A.; Johnson, F.; Rampton, D.S. Enteric infection in relapse of inflammatory bowel disease: Importance of microbiological examination of stool. *Eur. J. Gastroenterol. Hepatol.* **2004**, *16*, 775–778.
3. Zabana, Y.; Rodríguez, L.; Lobatón, T.; Gordillo, J.; Montserrat, A.; Mena, R.; Beltrán, B.; Dotti, M.; Benitez, O.; Guardiola, J.; et al. Relevant Infections in Inflammatory Bowel Disease, and Their Relationship with Immunosuppressive Therapy and Their Effects on Disease Mortality. *J. Crohn's Colitis* **2019**, *13*, 828–837.
4. Irving, P.M.; de Lusignan, S.; Tang, D.; Nijher, M.; Barrett, K. Risk of common infections in people with inflammatory bowel disease in primary care: A population-based cohort study. *BMJ Open Gastroenterol.* **2021**, *8*, e000573. <https://doi.org/10.1136/bmjgast-2020-000573>.
5. Dimopoulos-Verma, A.; Hong, S.; Axelrad, J.E. Enteric Infection at Flare of Inflammatory Bowel Disease Impacts Outcomes at 2 Years. *Inflamm. Bowel Dis.* **2024**, *30*, 1759–1766.
6. Beal, S.G.; Tremblay, E.E.; Toffel, S.; Velez, L.; Rand, K.H. A Gastrointestinal PCR Panel Improves Clinical Management and Lowers Health Care Costs. *J. Clin. Microbiol.* **2018**, *56*, 10–1128. <https://doi.org/10.1128/jcm.01457-17>.
7. Qin, G.; Tu, J.; Liu, L.; Luo, L.; Wu, J.; Tao, L.; Zhang, C.; Geng, X.; Chen, X.; Ai, X.; et al. Serum Albumin and C-Reactive Protein/Albumin Ratio Are Useful Biomarkers of Crohn's Disease Activity. *Med. Sci. Monit.* **2016**, *22*, 4393–4400.
8. Nguyen, A.L.; Brick, C.; Liu, D.; Gibson, D.J.; Gibson, P.R.; Sparrow, M.P. Clinical utility of C-reactive protein-to-albumin ratio in the management of patients with inflammatory bowel disease. *JGH Open* **2024**, *8*, e13059.
9. Antonelli, E.; Baldoni, M.; Giovenali, P.; Villanacci, V.; Essatari, M.; Bassotti, G. Intestinal superinfections in patients with inflammatory bowel diseases. *J. Crohn's Colitis* **2012**, *6*, 154–159.
10. Axelrad, J.E.; Joelson, A.; Nobel, Y.R.; Lawlor, G.; Green, P.H.; Lichtiger, S.; Lebowitz, B. Enteric Infection in Relapse of Inflammatory Bowel Disease: The Utility of Stool Microbial PCR Testing. *Inflamm. Bowel Dis.* **2017**, *23*, 1034–1039.
11. Limsrivilai, J.; Saleh, Z.M.; Johnson, L.A.; Stidham, R.W.; Waljee, A.K.; Govani, S.M.; Guterma, B.; Brown, A.M.; Briggs, E.; Rao, K.; et al. Prevalence and Effect of Intestinal Infections Detected by a PCR-Based Stool Test in Patients with Inflammatory Bowel Disease. *Dig. Dis. Sci.* **2020**, *65*, 3287–3296.
12. Hong, S.; Zaki, T.A.; Main, M.; Hine, A.M.; Chang, S.; Hudesman, D.; Axelrad, J.E. Comparative Evaluation of Conventional Stool Testing and Multiplex Molecular Panel in Outpatients With Relapse of Inflammatory Bowel Disease. *Inflamm. Bowel Dis.* **2021**, *27*, 1634–1640.
13. Tansarli, G.S.; Allen, D.R.; Fang, F.C. Multiplex Polymerase Chain Reaction Panels for Gastrointestinal Infections: Current Evidence, Regulatory Hurdles, and the Way Forward. *Open Forum Infect. Dis.* **2025**, *12*, S1418–S1430.
14. Goyal, M.K.; Berinstein, E.; Dutta, P.; Ahuja, V.; Higgins, P.D.; Berinstein, J.; Bishu, S. The role of gastrointestinal PCR in inflammatory bowel disease flares: A double-edged sword or a diagnostic breakthrough? *Indian J. Gastroenterol.* **2026**, *45*, 5–14.
15. Robert-Gangneux, F.; Duval, X.; Cazala, C.; Belaz, S.; Dupuis, A.; Guegan, H.; Autier, B.; Gangneux, J.P. Improvement of the diagnosis of intestinal protozoa using a multiplex qPCR strategy compared to classical microscopy: A prospective study on 3500 stool samples over 3 years. *J. Clin. Microbiol.* **2025**, *63*, e0161024.
16. Aceto, G.M.; Falasca, K.; Berardinucci, D.; Cavallo, L.; Mangiò, A.; Mancuso, G.; Muraro, R.; Ciccocioppo, R.; Catalano, T. Deciphering the Implications of *Escherichia coli* in Inflammatory Bowel Disease: From Symbiont to Pathogen. *Pathogens* **2026**, *15*, 548.
17. Poga Sm, E.; Molla, L.; Bici, E.; Kokali, A.; Zhurka, G. Monitoring the Potable Water Quality in Albania. *Albanian J. Nat. Tech. Sci.* **2024**, *29*, 67–76.
18. Bakalli, M.; Malollari, I.; Selamaj, J. Microbial Indicators of Coastal Water in Albania. *WSEAS Trans. Environ. Dev.* **2021**, *17*, 232–236.
19. Ghosh, C.K.; Mohiuddin, S.A.; Tabassum, N.; Islam, S.; Islam, N.; Bari, A. S1315 Prevalence and Pattern of Infection in Ulcerative Colitis Flare-Ups. *Off. J. Am. Coll. Gastroenterol.* **2024**, *119*, S941.
20. Balram, B.; Battat, R.; Al-Khoury, A.; D'Aoust, J.; Afif, W.; Bitton, A.; Lakatos, P.L.; Bessissow, T. Risk Factors Associated with *Clostridium difficile* Infection in Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. *J. Crohn's Colitis* **2018**, *13*, 27–38.
21. Bencardino, S.; D'Amico, F.; Zilli, A.; Parigi, T.L.; Allocca, M.; Fiorino, G.; Danese, S.; Furfaro, F. Fecal, Blood, and Urinary Biomarkers in Inflammatory Bowel Diseases. *J. Transl. Gastroenterol.* **2024**, *2*, 61–75.

22. Schoepfer, A.M.; Beglinger, C.; Straumann, A.; Trummler, M.; Renzulli, P.; Seibold, F. Ulcerative colitis: Correlation of the Rachmilewitz endoscopic activity index with fecal calprotectin, clinical activity, C-reactive protein, and blood leukocytes. *Inflamm. Bowel Dis.* **2009**, *15*, 1851–1858.
23. Don, B.R.; Kaysen, G. Serum albumin: Relationship to inflammation and nutrition. *Semin Dial* **2004**, *17*, 432–437.
24. Liu, X.; Pan, L.X.; Pei, J.X.; Pu, T.; Wen, H.T.; Zhao, Y. Role of serological biomarkers in evaluating and predicting endoscopic activity in inflammatory bowel disease. *World J. Gastroenterol.* **2025**, *31*, 104206.
25. Chen, Y.H.; Wang, L.; Feng, S.Y.; Cai, W.M.; Chen, X.F.; Huang, Z.M. The Relationship between C-Reactive Protein/Albumin Ratio and Disease Activity in Patients with Inflammatory Bowel Disease. *Gastroenterol. Res. Pract.* **2020**, *2020*, 3467419.
26. Sayar, S.; Kurbuz, K.; Kahraman, R.; Caliskan, Z.; Atalay, R.; Ozturk, O.; Doganay, H.L.; Ozdil, K. A practical marker to determining acute severe ulcerative colitis: CRP/albumin ratio. *North Clin. Istanbul.* **2020**, *7*, 49–55.

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