

Original Research Article

C-REACTIVE PROTEIN/ALBUMIN RATIO AND DISEASE ACTIVITY IN CROHN'S DISEASE: A RETROSPECTIVE CROSS-SECTIONAL STUDY FROM SOUTH INDIA

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ABSTRACT

Background: The Crohn's Disease Activity Index (CDAI) depends partly on patient-reported symptoms, and ileo-colonoscopy is invasive and unsuitable for frequent repetition. The C-reactive protein (CRP)/albumin ratio has been proposed as a simple serological marker of disease activity in inflammatory bowel disease, but data specific to Crohn's disease (CD) in South Asian populations are limited.

Materials and Methods: In this retrospective cross-sectional study, 33 patients with CD managed at a tertiary centre in South India between January 2024 and August 2025 were analysed. Active disease was defined as CDAI ≥ 150 . Associations were assessed with Spearman's rank correlation (ρ), differences across activity categories with the Kruskal–Wallis test, and discrimination of active disease from remission with receiver operating characteristic (ROC) analysis; the cutoff was chosen by the Youden index.

Results: Sixteen patients (48.5%) had active disease. The CRP/albumin ratio correlated strongly with CDAI ($\rho = 0.790$, 95% CI 0.58–0.90, $p < 0.001$) and discriminated active disease from remission (area under the curve [AUC] 0.949, 95% CI 0.869–1.000). A cutoff of 0.85 gave a sensitivity of 87.5% (95% CI 61.7–98.4) and a specificity of 100% (95% CI 80.5–100). The median ratio rose from 0.07 in remission to 1.20 in severe disease ($p < 0.001$). CRP alone performed equivalently ($\rho = 0.791$; AUC 0.945).

Conclusion: In this small cohort, the CRP/albumin ratio correlated strongly with CDAI and discriminated active CD from remission, but it did not outperform CRP alone. The cutoff of 0.85 was derived and evaluated in the same sample and requires validation in larger prospective studies with endoscopic assessment.

Keywords: Crohn's Disease, C-Reactive Protein, Serum Albumin, Severity of Illness Index, Biomarkers.

INTRODUCTION

Disease activity in Crohn's disease (CD) is conventionally quantified with the Crohn's Disease Activity Index (CDAI).^[1] The CDAI is laborious to compute in routine practice, relies substantially on

patient-reported symptoms, and correlates imperfectly with mucosal inflammation.^[2] Ileo-colonoscopy remains the reference standard for assessing the mucosa but is invasive and cannot be repeated frequently.^[3] A low-cost serological marker

that reflects disease activity would therefore be of clinical value.

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are the serological markers most widely used for this purpose.^[4] CRP is synthesised by the liver in response to interleukin-6,^[5] whereas serum albumin decreases with systemic inflammation and with the protein loss and impaired nutritional status associated with active intestinal disease.^[6] The CRP/albumin ratio combines these two opposing changes in a single index. It was initially evaluated as a prognostic marker in acutely ill medical patients,^[7] and subsequently in solid tumours.^[8] In CD, Qin et al. reported that serum albumin and the CRP/albumin ratio were useful biomarkers of disease activity.^[9] In a Chinese cohort of 876 patients with inflammatory bowel disease (IBD), 601 of whom had CD, the ratio was associated with disease activity in both ulcerative colitis and CD, with an area under the receiver operating characteristic curve (AUC) of 0.925 and an optimal cutoff of 0.43 in CD.^[10]

Data on the CRP/albumin ratio in South Asian CD cohorts remain limited. The present study therefore evaluated the association of the CRP/albumin ratio with the CDAI, and its ability to discriminate active disease from remission, in a cohort of patients with CD from southern India, in comparison with CRP, albumin, ESR and the haematological ratios derived from the complete blood count. The patients analysed here are the CD subgroup of a larger IBD cohort analysed in a separate manuscript.^[11] The present analysis is restricted to CD and addresses a distinct question: whether a CD-specific cutoff can be derived against the CDAI, and whether the ratio performs better than CRP alone in this disease.

MATERIALS AND METHODS

Study Design and Setting: This retrospective cross-sectional study was conducted at the Department of Medical Gastroenterology, Chettinad Hospital and Research Institute, Kelambakkam, Tamil Nadu, India. Electronic and paper medical records from January 2024 to August 2025 were reviewed. The study was approved by the Institutional Human Ethics Committee for Student Research (CARE IHEC-I; IHEC-I/4148/25, 23 August 2025), which waived the requirement for informed consent because the data were pre-existing and anonymised. The study was conducted in accordance with the Declaration of Helsinki and is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.^[12]

Participants. Adults aged 18 years or older with a diagnosis of CD established by clinical, endoscopic, radiological and histological criteria,^[3,13] were eligible. Patients were excluded if they had active infection, malignancy, another chronic inflammatory disease, or Child-Pugh class B or C liver disease, or

if CRP, albumin or CDAI data were missing. Patients receiving biologic therapy were retained. The 33 patients who met these criteria formed the CD subgroup of a cohort of 110 patients with IBD, of whom 77 had ulcerative colitis.^[11]

Variables and definitions. Disease activity was assessed with the CDAI and categorised as remission (<150), mild (150–220), moderate (221–450) or severe (>450).^[1] Active disease was defined as a CDAI of 150 or above. The CDAI was derived retrospectively from clinical records. The following variables were extracted: age, sex, body mass index, smoking status, disease location, disease duration, treatment, haemoglobin, platelet, neutrophil, lymphocyte and monocyte counts, ESR, CRP and albumin. CRP was expressed in mg/L and albumin in g/L, and the CRP/albumin ratio was calculated as CRP (mg/L) divided by albumin (g/L). The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) were calculated from the complete blood count.

Statistical analysis

Data were analysed using IBM SPSS Statistics 22.0 and Python 3.10 (SciPy 1.11.4, scikit-learn 1.3.2). Normality was assessed with the Kolmogorov–Smirnov test. Continuous variables are presented as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR), and categorical variables as number (percentage). Associations with the CDAI were quantified with Spearman's rank correlation coefficient (ρ), with 95% confidence intervals (CIs) from the Fisher z-transformation using the Bonett–Wright standard error. The CRP/albumin ratio was compared across CDAI categories with the Kruskal–Wallis test. Discrimination of active disease (CDAI $\geq$ 150) from remission was evaluated by receiver operating characteristic (ROC) analysis, and the optimal cutoff was determined by the Youden index. Sensitivity and specificity are given with exact (Clopper–Pearson) 95% CIs. All tests were two-tailed, and $p < 0.05$ was considered statistically significant. No adjustment for multiple comparisons was made across the exploratory comparator markers, and the AUCs of the markers were not formally compared with one another.

RESULTS

Participant characteristics. The cohort comprised 33 patients with CD, with a mean age of 41.2 ± 13.4 years; 20 (60.6%) were male. [Table 1] Disease location was ileocolonic in 16 (48.5%), colonic in 10 (30.3%) and ileal in 7 (21.2%), and 10 patients (30.3%) had perianal disease. Sixteen patients (48.5%) had active disease and 17 (51.5%) were in remission. By CDAI category, 17 patients were in remission, 4 had mild, 8 moderate and 4 severe disease. Twenty patients (60.6%) were receiving biologic therapy.

Table 1: Characteristics of the 33 patients with Crohn's disease

Variable	Value
Age, years, mean $\pm$ SD	41.2 $\pm$ 13.4
Male, n (%)	20 (60.6)
BMI, kg/m ² , mean $\pm$ SD	20.5 $\pm$ 1.8
Disease duration, months, median (IQR)	17 (12–20)
Ever smoked, n (%)	8 (24.2)
Location: ileal / colonic / ileocolonic, n (%)	7 (21.2) / 10 (30.3) / 16 (48.5)
Perianal disease, n (%)	10 (30.3)
Active disease (CDAI $\geq$ 150), n (%)	16 (48.5)
Remission / mild / moderate / severe, n	17 / 4 / 8 / 4
Biologics, n (%)	20 (60.6)
Immunomodulators, n (%)	17 (51.5)
Corticosteroids, n (%)	16 (48.5)
5-aminosalicylates, n (%)	16 (48.5)

Abbreviations: BMI, body mass index; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; IQR, interquartile range; SD, standard deviation. Remission, CDAI <150; mild, 150–220; moderate, 221–450; severe, >450. Treatment categories are not mutually exclusive.

Correlation with disease activity. The CRP/albumin ratio was strongly correlated with the CDAI ($\rho = 0.790$, 95% CI 0.58–0.90, $p < 0.001$), equivalent to CRP alone ($\rho = 0.791$). Albumin showed a weaker inverse correlation ($\rho = -0.440$, $p = 0.010$). The absolute correlation coefficients of ESR, PLR, NLR and LMR ranged from 0.541 to 0.709. [Table 2]

Discrimination of active disease. The CRP/albumin ratio discriminated active disease from remission with an AUC of 0.949 (95% CI 0.869–1.000). The cutoff identified by the Youden index was 0.85, with a sensitivity of 87.5% (14/16; 95% CI 61.7–98.4) and a specificity of 100% (17/17; 95% CI 80.5–100). The AUCs of the comparator markers were 0.945 for CRP, 0.939 for ESR, 0.938 for PLR, 0.893 for NLR, 0.886 for albumin and 0.820 for LMR. The cutoff was derived and assessed in the same sample and was not internally validated.

Table 2: Correlation with CDAI and discrimination of active Crohn's disease (n = 33)

Marker	Spearman ρ with CDAI (95% CI)	p	AUC
CRP/albumin ratio	0.790 (0.58 to 0.90)	<0.001	0.949
CRP, mg/L	0.791 (0.58 to 0.90)	<0.001	0.945
ESR, mm/h	0.669 (0.39 to 0.84)	<0.001	0.939
PLR	0.709 (0.45 to 0.86)	<0.001	0.938
NLR	0.541 (0.22 to 0.76)	0.001	0.893
Albumin, g/L	-0.440 (-0.69 to -0.10)	0.010	0.886
LMR	-0.608 (-0.80 to -0.31)	<0.001	0.820

Abbreviations: AUC, area under the ROC curve for discrimination of active disease (CDAI $\geq$ 150) from remission; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio. 95% CIs for ρ were

computed with the Fisher z-transformation and the Bonett–Wright standard error.

Ratio across activity categories. The CRP/albumin ratio increased with CDAI category (Kruskal–Wallis $H = 21.85$, $p < 0.001$; Table 3). Median values were 0.07 in remission ($n = 17$), 0.88 in mild ($n = 4$), 0.93 in moderate ($n = 8$) and 1.20 in severe disease ($n = 4$).

Table 3: CRP/albumin ratio by CDAI category

Marker, median	Remission (n = 17)	Mild (n = 4)	Moderate (n = 8)	Severe (n = 4)
CRP/albumin ratio	0.07	0.88	0.93	1.20

CDAI categories as defined in [Table 1]. Values are medians. Kruskal–Wallis $H = 21.85$, $p < 0.001$.

DISCUSSION

In this cohort of 33 patients with CD, the CRP/albumin ratio correlated strongly with the CDAI and discriminated active disease from remission with high accuracy. The AUC of 0.949 is comparable to the value of 0.925 reported for CD in a Chinese IBD cohort.^[10] The optimal cutoff in the present study (0.85) was nearly twice the 0.43 reported in that cohort.^[10] The ratio is sensitive to

the units used for CRP and albumin (for example, CRP in mg/L with albumin in g/dL gives a value ten times larger than CRP in mg/L with albumin in g/L), so cutoffs are comparable only when units are identical; the units used in the earlier cohort are not stated in the source article. Differences in CRP assay methods and in the inflammatory burden of the study populations may also contribute, although the present data do not allow these explanations to be distinguished. The cutoff was derived from 16

patients with active disease and 17 in remission and was evaluated in the same patients. The reported specificity of 100% is therefore likely to be overestimated, its lower 95% confidence limit being 80.5%, and the cutoff should not be applied clinically before external validation.

The CRP/albumin ratio did not outperform CRP alone. The correlation coefficients (0.790 and 0.791) and AUCs (0.949 and 0.945) were virtually identical, and albumin alone performed less well. In the full 110-patient IBD cohort, the haematological ratios performed clearly worse than the CRP/albumin ratio,^[11] but in the CD subgroup their performance was closer, with AUCs of 0.938 for PLR and 0.893 for NLR. Within this subgroup the ratio therefore showed no clear advantage over CRP or PLR, and a larger sample would be required to determine whether one exists. This is consistent with the practical point that CRP, which is already widely available and inexpensive, may be sufficient for this purpose in routine care.

The ratio increased across CDAI categories, but the increase occurred predominantly between remission (median 0.07) and any level of activity (medians of 0.88 or higher). Median values in mild (0.88) and moderate (0.93) disease were similar, and the mild and severe categories each comprised only four patients. These data therefore do not demonstrate that the ratio grades severity within active CD.

Biologic therapy is a relevant confounder. Twenty of the 33 patients (60.6%) were receiving biologics, which may lower CRP independently of mucosal disease activity. The sensitivity analysis in the parent cohort excluded all biologic users,^[11] applied to the present subgroup it would leave only 13 patients with CD, so it cannot be interpreted as a CD-specific assessment, and a separate comparison of biologic-treated and biologic-naïve patients was not undertaken because of the small numbers. Albumin is influenced by nutritional status, and both markers by corticosteroid use (16 patients, 48.5%) and perianal disease (10 patients, 30.3%), none of which could be adjusted for in this sample. Given the emphasis on objective, treat-to-target assessment in current guidance,^[14,15] biomarkers of this kind are most useful as adjuncts to, not substitutes for, endoscopic or imaging assessment.

This study has further limitations. Its retrospective, single-centre design and small sample size limit precision and generalisability, as reflected in the wide confidence intervals. The CDAI was the sole reference standard and was derived retrospectively from clinical records, so misclassification of activity status cannot be excluded; no endoscopic scoring (such as the Simple Endoscopic Score for Crohn's Disease, SES-CD), imaging or histology was used, so it cannot be determined whether the ratio reflects mucosal healing. The CDAI was also not independent of the index test, because systemic inflammation influences some of its components. The AUCs of the markers were not formally compared within the CD subgroup, and the cutoff of

0.85 was not internally validated. CRP assays were not standardised across the study period. Prospective studies with larger samples and endoscopic assessment, in which biologic-treated and untreated patients are analysed separately, are required to establish the diagnostic value of the CRP/albumin ratio in CD.

CONCLUSION

In this cohort of 33 patients with CD, the CRP/albumin ratio correlated strongly with the CDAI and discriminated active disease from remission with high accuracy, but it did not perform better than CRP alone. The proposed cutoff of 0.85 requires validation in a larger prospective cohort with endoscopic assessment.

Ethics approval: Institutional Human Ethics Committee for Student Research, Chettinad Academy of Research and Education (IHEC-I/4148/25, 23 August 2025); informed consent was waived because the data were anonymised and retrospective.

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