

## Predictive Value of the Red Cell Distribution Width to Albumin Ratio For Hospitalization due to Inflammatory Bowel Disease Flares

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### Abstract

**Background:** Hospitalizations for inflammatory bowel disease (IBD) flares remain common despite advances in biologic therapy and outpatient monitoring. Clinicians still lack simple, low-cost tools that identify patients at imminent risk for severe flare before clinical deterioration occurs.

**Objective:** To evaluate whether the red cell distribution width to albumin ratio (RAR), a composite biomarker derived from routine laboratory testing, predicts hospitalization for IBD flare when measured weeks to months prior to presentation.

**Methods:** We performed a retrospective cohort study of adults with ulcerative colitis (UC) or Crohn's disease (CD) admitted between 2021 and 2023. The most recent outpatient or emergency department RDW (%) and serum albumin (g/dL) obtained within three months prior to admission were used to calculate RAR. The primary predictor was  $RAR \geq 4.3$ . The primary outcome was hospitalization for IBD flare confirmed by detailed chart review.

**Results:** Among 41 patients (mean age  $47.9 \pm 18.8$  years; 46.3% female), 22 (53.7%) were hospitalized for IBD flare. Mean RAR was  $4.57 \pm 1.93$ , and 16 patients had  $RAR \geq 4.3$ . Elevated RAR was strongly associated with flare related hospitalization (OR 9.9, 95% CI 1.52–64.24;  $p=0.01$ ). Other demographic and behavioral variables were not significantly associated with hospitalization.

**Conclusion:** An elevated RDW to albumin ratio measured up to three months prior to presentation was strongly associated with hospitalization for IBD flare. RAR represents a pragmatic, low-cost biomarker that may enable earlier outpatient intervention and offers a promising foundation for prospective, biomarker-guided flare prevention strategies.

**Keywords:** RDW and Albumin ratio; IBD Flare; Ulcerative colitis; Crohn's disease

### Introduction

For patients suffering from Inflammatory bowel disease (IBD) either Ulcerative colitis (UC) or Crohn's disease, unexpected onset of flare episode can drastically affect quality of life with some extreme flare episodes leading to hospitalizations with some patients requiring colectomies. There have been many clinical tools that have shown prognostic values in course of flare episode but little data has been known to predict an onset of flare. With this study we hoped to demonstrate a simple and cost-effective tool: Red cell distribution width/albumin ratio (RAR) obtained through routine blood work

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**Citation:** Kumari Priya Yadav, Scott Golden, Zaid Sameer Jaber Weher, Pramita Prem, Vipin Gupta, Mayuri Gupta. Predictive Value of the Red Cell Distribution Width to Albumin Ratio For Hospitalization due to Inflammatory Bowel Disease Flares. *Journal of Surgery and Research*. 9 (2026): 122-127.

**Received:** January 24, 2026

**Accepted:** February 02, 2026

**Published:** March 09, 2026

during follow-up visits to predict an onset of flare requiring hospitalization.

## Methods

We conducted a dual center retrospective cohort study of adult patients ( $\geq 18$  years) with established ulcerative colitis or Crohn's disease who had at least one hospital admission between January 2021 and December 2023. IBD diagnosis was confirmed through prior endoscopic, histologic, or gastroenterology clinic documentation.

For each patient, the most recent RDW (%) and serum albumin (g/dL) obtained in the outpatient clinic or emergency department within three months prior to admission were recorded. All the laboratory blood values ranged from a month to 3 months prior to the flare episode. The RDW to albumin ratio (RAR) was calculated as RDW divided by albumin. Based on cohort distribution and emerging literature, RAR was dichotomized at a cutoff of  $\geq 4.3$  based on clinical judgement and article review by investigators.

The primary outcome was hospitalization for an IBD flare. Flare related admissions were confirmed by detailed chart review, incorporating symptom escalation, objective inflammatory markers, imaging or endoscopic findings when available, and treating gastroenterologist assessment.

Patients were excluded if they had conditions likely to independently alter RDW or albumin, including pregnancy, active malignancy, recent chemotherapy, sepsis, advanced liver disease, nephrotic syndrome, severe malnutrition, hematologic malignancy, hemolytic anemia, or recent blood transfusion.

## Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Logistic regression was performed to evaluate the association between elevated RAR and hospitalization for IBD flare. Odds ratios with 95% confidence intervals were reported, with statistical significance defined as  $p < 0.05$ .

## Results

A total of 41 patients met inclusion criteria (See Table 1). The mean age was  $47.9 \pm 18.8$  years, and 46.3% were female. Twenty-two patients (53.7%) were admitted for an IBD flare. The mean RAR across the cohort was  $4.57 \pm 1.93$ , with 16 patients (39%) exhibiting  $\text{RAR} \geq 4.3$ . Patients with elevated RAR had nearly tenfold higher odds of hospitalization for IBD flare compared with those with lower RAR values (OR 9.9, 95% CI 1.52–64.24;  $p = 0.01$ ). (See Table 2) (Graph 1). Female sex demonstrated a non-significant trend toward increased risk, while alcohol use, tobacco use, and marijuana use were not associated with hospitalization. Our study had sensitivity of 54.5% and specificity of 78.9% (See

Table 3). The ROC curve analysis demonstrated that  $\text{RAR} \geq 4.3$  predicted hospitalization for inflammatory bowel disease flare with an AUC of 0.70 (95% CI, 0.50–0.83), indicating acceptable discrimination (Graph 2).

## Discussion

For patients living with inflammatory bowel disease, the most disruptive moments are often not gradual symptom changes, but sudden flares that escalate rapidly and culminate in hospitalization [1]. Despite regular clinic visits, laboratory monitoring, and increasingly sophisticated biologic therapies, clinicians are frequently surprised by the severity and timing of these events.

Existing tools for assessing IBD activity including symptoms, C-reactive protein, fecal calprotectin, and endoscopy are invaluable, yet imperfect [2-4]. Many are reactive rather than predictive, costly, invasive, or difficult to deploy consistently in outpatient and telehealth settings. Some even though cost-effective have not yet been studied in prediction of a flare. As a result, opportunities for early, pre-emptive intervention are often missed.

The biological rationale underlying RAR supports its predictive capacity. RDW reflects chronic inflammation driven disturbances in erythropoiesis, cytokine mediated marrow stress, and impaired red blood cell maturation, processes that evolve over time rather than acutely. Albumin, conversely, reflects systemic inflammatory burden, nutritional status, and hepatic synthetic function. By integrating these complementary domains, RAR may act as a cumulative marker of inflammatory and metabolic stress, capturing disease trajectories that are not apparent through symptoms alone.

Red cell distribution width (RDW), a routinely reported component of the complete blood count, has emerged as a marker of systemic inflammation across a wide range of gastrointestinal diseases [5]. In IBD, multiple studies have shown RDW to be higher during active disease than remission, even in the absence of overt anemia [6]. RDW has also shown disease activity in Crohn's Disease [7]. Serum albumin, on the other hand, reflects nutritional status, hepatic synthetic function, and chronic inflammatory burden factors closely linked to disease severity and outcomes in IBD hospitalizations in adults and children [8,9]. Lower albumin levels have also to an extent predicted IBD flare hospitalizations leading to colectomy [10]. Also, non-traditional formulas such as LimG, bowel thickness involving albumin and CRP/albumin ratio have secured more promising results in disease course [11,12]. A fairly new player: Monocyte/high-density lipoprotein ratio has also been accurate but would need additional lipid profile and complete blood count differential tests [13].

The red cell distribution width-to-albumin ratio (RAR) integrates two biologically complementary markers into a single index found in routine blood labs. RAR has demonstrated prognostic value in multitude of diseases, including chronic metabolic diseases [14-17], cognitive diseases [18], neurological diseases [19,20], oncologic populations [21,22], acute care settings [23-26] often outperforming RDW or albumin alone. Amongst gastrointestinal diseases, its study has been limited to fewer organ pathologies [27-29]. However, its role in IBD particularly as an early predictor of clinically meaningful flares requiring hospitalization has not been established.

We hypothesized that RAR measured during routine outpatient care could identify patients on a trajectory toward severe flare before overt clinical deterioration. Our study was designed to test this hypothesis and to explore whether RAR could serve as a practical, scalable, single composite surveillance tool in real world IBD care index and repositioning them from reflections of current disease activity to indicators of future risk. This shift is clinically meaningful, as the inability to reliably anticipate severe flares remains a major limitation of symptom-based disease monitoring.

We began this study, by retrospectively reviewing patient data from two outpatient gastroenterology clinics. We included all patients more than or equal to 18 years of age who had an IBD flare episode. Data was deidentified and charted. Inclusion and exclusion criteria selectively weeded out patients liable to skew the dataset.

From previous study that have explored RAR in either acute or chronic care settings, we found multiple prognosticating levels of RAR. Most studies deduced cut-offs for acute care diseases and settings: post-myocardial infarction, coronary care unit, respiratory failure and sepsis with values ranging from  $\geq 4.3$  to  $\geq 5.2$  predicting worsening outcomes [30-34]. For gastroenterological diseases studied so far RAR  $> 3.8$ ,  $> 4.3$  and  $> 0.36\%$  have shown worsening outcomes [27-29]. Taking inspiration, our team decided that a value  $\geq 4.2$  would be best suited for sensitivity in our clinical setting.

Our population, even though modest was well distributed for age, and almost equally distributed for gender, providing our study a firm baseline. Slightly more than half required a hospitalization, confirming the fact that IBD flares hamper quality of life with almost half of them being severe. The mean RAR was  $4.57 \pm 1.93$ , similar to previous studies, in line with the notion that elevated RAR does confirm itself as a robust biomarker in inflammatory conditions [27-34]. 39% of patients had elevated RAR  $\geq 4.3$ . Our team does acknowledge that this percentage calculated with a fairly lower threshold of RAR value and detect as many as patients as possible, and that further in-depth studies are required to determine better cut-off levels. Further studies with stratification of threshold level shall also yield better sensitive results. Our

overall study model achieved a specificity level of 78.9% even with a modest cohort, thus implying that RAR can be used to evaluate probability of a hospitalization. The AUC for our model was 0.7 for RAR  $\geq 4.3$  predicting a flare leading to hospitalization, suggesting a moderate ability of RAR to discriminate between patients who did and did not require hospitalization for IBD flare.

In this retrospective cohort study, we demonstrate that an elevated red cell distribution width to albumin ratio (RAR), measured as early as three months before clinical presentation, is almost ten times associated with hospitalization for inflammatory bowel disease (IBD) flare. The strength of this association suggests that RAR may capture early biological signals of disease instability that precede overt clinical deterioration, offering a window into the preclinical phase of severe flares. This observation that RAR was predictive weeks to months before hospitalization suggests that subclinical inflammation may be measurable well in advance of clinical decompensation. In our study use of alcohol, smoked tobacco and marijuana use did not show any significant affect, owing to their minority effect. This could also be due to potential underreporting in the community.

From a practical standpoint, RAR has several advantages that distinguish it from existing biomarkers. It is derived entirely from routine laboratory tests already embedded in standard outpatient care and requires no additional cost, specialized assays, or patient effort. Unlike fecal biomarkers or imaging, RAR can be calculated automatically during routine clinic visits or telehealth encounters, making it highly scalable and well suited for real-world implementation. These characteristics are particularly relevant as IBD care increasingly emphasizes remote monitoring and proactive disease management.

Our team does acknowledge that the cohort for this study was modest, and a larger cohort may yield different outcomes. For future explorations a standard level of cutoff with formal AUC evaluations for each cutoff and subclinical stratifications for other comorbidities are definitely needed. We also believe that incorporating more patient data from wider health establishments and comparatively including other biomarkers may help further refine threshold value of RAR with better ROC/AUC analysis. Accordingly, these findings should be viewed as hypothesis-generating rather than definitive. Our study's limitations include its retrospective design, modest sample size, and dual center setting. While the observed effect size was large, confidence intervals were wide, underscoring the need for prospective validation. Nonetheless, the strength and consistency of the association support the role of RAR as a hypothesis generating biomarker worthy of further study.

RAR could serve as an early warning signal to identify patients at increased risk for severe flare, prompting closer surveillance or pre-emptive outpatient intervention.

Such a strategy has the potential to reduce preventable hospitalizations, lower healthcare utilization, and improve patient-centered outcomes key priorities in contemporary IBD management. Notably, RAR represents a rare example of a biomarker that is inexpensive, biologically grounded, and immediately deployable in routine clinical practice. We do encourage primary care physicians and gastroenterologists to use their best clinical judgement for IBD patients and monitor them clinically if there is a significant RAR based on our study.

In conclusion, the RDW to albumin ratio is a novel and accessible composite biomarker that identifies patients with IBD at increased risk for hospitalization due to disease flare. By enabling earlier recognition of high-risk disease trajectories using routinely available data, RAR has the potential to support a more anticipatory and preventive approach to IBD care.

Further prospective studies and clinical trials are warranted to validate these findings and to determine whether RAR-guided interventions can meaningfully improve clinical outcomes. One potential pathway involves identifying patients with elevated RAR during routine care and offering short-course, evidence-based outpatient prophylactic oral steroid therapy tailored to disease location and severity as steroids are the first line for a diagnosed IBD flare [34]. Such an approach could interrupt progression to severe flare and reduce hospitalization rates an outcome with meaningful implications for patients and healthcare systems alike.

**Table 1:** Patient demographics.

Total, N= 41	
Age (Mean ±SD) in years	47.9 ± 18.8 years
Gender; Female: Male	19: 22
Flare leading to admissions (%)	22(53.65%)
RDW/ albumin ratio [RAR ratio] (Mean ±SD)	4.57±1.93
RDW/ albumin ratio (RAR) ≥ 4.3	16
Consumed alcohol	8
Smoked tobacco	6
Marijuana	1

**Table 2:** Flare requiring hospital admission predictors.

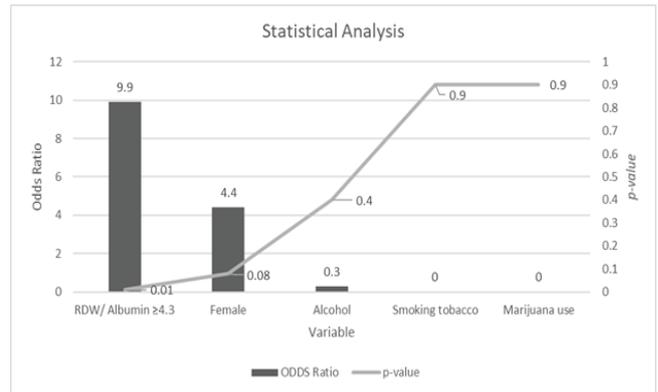
Variable	Odds ratio	p-value	C.I [L.L, U.L]
<b>RDW/ Albumin ≥4.3</b>	<b>9.9</b>	<b>0.01</b>	<b>[1.52, 64.24]</b>
Female Gender	4.4	0.08	[0.82, 23.90]
Alcohol	0.3	0.4	[0.02, 4.6]
Smoking tobacco	0.0	0.9	[0.00, 0.00]
Marijuana use	0.0	0.9	[0.00, 0.00]

Sensitivity =54.5%; Specificity=78.9%

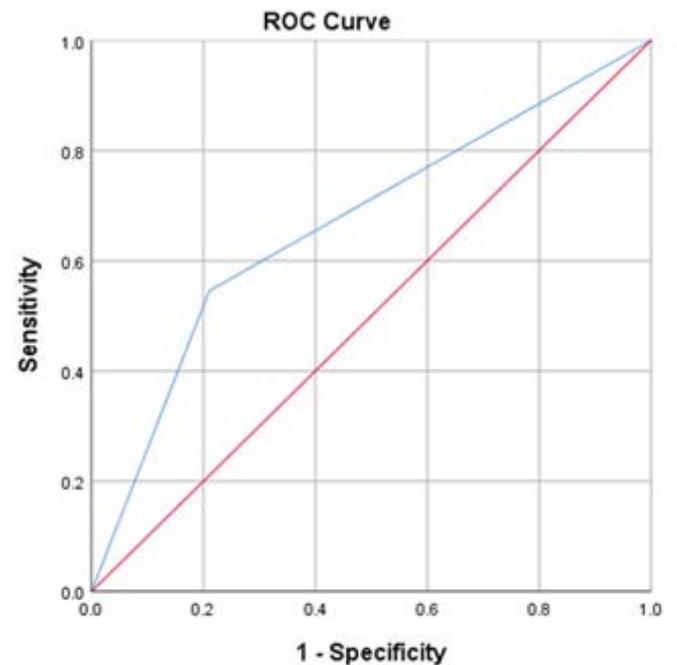
**Table 3:** Sensitivity and specificity.

	Hospitalization	No Hospitalization	
RAR ≥ 4.3	12	4	16
RAR <4.3	10	15	25
	22	19	41

Sensitivity =54.5%; Specificity=78.9%



**Graph 1:** Logistic regression analysis showing odds ratios (bars) and corresponding p-values (line) for predictors of hospitalization due to inflammatory bowel disease flare. An RDW-to-albumin ratio ≥4.3 was independently associated with markedly increased odds of hospitalization (OR 9.9, p=0.01), whereas female sex showed a non-significant trend toward higher risk. Alcohol use, tobacco smoking, and marijuana use were not significantly associated with hospitalization.



Diagonal segments are produced by ties.

AUC (RAR ≥4.3) =0.7 (95% CI, 0.50-0.83).

**Graph 2:** ROC and AUC statistics.

## Ethics, consent to participate, and consent to publish declarations

“This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study involved retrospective analysis of de-identified data; therefore, formal ethical approval and informed consent were not required in accordance with institutional policies.”

## Funding declaration

This research received no external funding. The authors declare that no financial support was obtained for the conduct of this study or the preparation of this manuscript.

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