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CLINICAL UTILITY OF CIRCULATING GALECTIN-3 AS A BIOMARKER IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Inflammatory bowel disease (IBD) requires accurate diagnosis and ongoing activity assessment, yet endoscopy and fecal calprotectin have limitations. Circulating Galectin-3 has emerged as a candidate serum biomarker for IBD, but studies report inconsistent diagnostic performance and activity associations. To systematically review and synthesize the diagnostic performance and clinical utility of circulating Galectin-3 as a biomarker in patients with inflammatory bowel disease, including its association with disease activity. A systematic review and meta-analysis followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines across five databases. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool. Pooled estimates for circulating Galectin-3 concentrations in patients with IBD versus healthy controls were calculated as standardized mean differences (SMDs) with 95% confidence intervals (CIs) using a fixed-effect inverse-variance model. Six cross-sectional studies were included. Most studies reported significantly higher circulating Galectin-3 levels in patients with IBD than in healthy controls, although findings regarding disease activity were inconsistent. Meta-analysis demonstrated significantly elevated circulating Galectin-3 in both Crohn's disease (CD) (SMD = 0.81, 95% CI: 0.44–1.18; $p < 0.0001$) and ulcerative colitis (UC) (SMD = 0.62, 95% CI: 0.26–0.97; $p = 0.0006$), with no observed statistical heterogeneity ($I^2 = 0\%$). Diagnostic accuracy varied considerably across studies, with sensitivity ranging from 53% to 100% and specificity from 47% to 97%. This variability likely reflects differences in assay methods, cut-off values, patient characteristics, and study design. These findings suggest Galectin-3 may better serve as a diagnostic biomarker than as a marker of disease activity. Circulating Galectin-3 shows promise as a biomarker for the diagnosis of IBD. However, evidence regarding its utility for disease activity assessment and treatment monitoring remains inconsistent.

Keywords: biomarkers; crohn disease; galectin 3; inflammatory bowel diseases; ulcerative colitis

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INTRODUCTION

Inflammatory bowel disease (IBD), comprising ulcerative colitis (UC) and Crohn's disease (CD), is a chronic immune-mediated inflammatory disorder of the gastrointestinal tract that requires accurate diagnosis and continuous assessment of disease activity to optimize patient management. Although endoscopy remains the gold standard for diagnosis and evaluation of mucosal inflammation, its invasiveness, high cost, and limited patient acceptability make repeated examinations impractical for routine monitoring (Górecka dkk., 2025; Salama dkk., 2026). Consequently, considerable efforts have been directed toward identifying non-invasive biomarkers that can support diagnosis and disease monitoring. While C-reactive protein (CRP) and fecal calprotectin are widely used, CRP shows inconsistent correlations with endoscopic activity and fecal calprotectin is limited by the need for stool sample collection, highlighting the need for more

practical serum biomarkers (Salama dkk., 2026; Volarevic dkk., 2019). Among emerging candidates, galectin-3 (Gal-3), a β-galactoside-binding lectin involved in immune regulation and inflammatory responses, has attracted increasing attention (Brzački dkk., 2025; Frol'ová dkk., 2009; Górecka dkk., 2025; Maaser dkk., 2019; Salama dkk., 2026; Yu dkk., 2020).

Growing evidence suggests that Gal-3 plays an important role in IBD pathogenesis and may have diagnostic value. Early studies demonstrated increased Gal-3 expression in inflamed intestinal mucosa and elevated circulating levels in patients with UC and CD compared with healthy controls (Frol'ová dkk., 2009). Experimental studies further showed that Gal-3 exerts context-dependent immunomodulatory effects, promoting inflammatory responses during the acute phase while facilitating immune regulation and mucosal healing during recovery (Volarevic dkk., 2019). More recent clinical investigations have reported promising diagnostic performance, with some studies showing high sensitivity and specificity for distinguishing IBD from healthy individuals and positive associations with inflammatory markers, endoscopic findings, and disease severity (Cibor dkk., 2019; Frol'ová dkk., 2009; Górecka dkk., 2025; Salama dkk., 2026; Volarevic dkk., 2019).

Despite these encouraging findings, the clinical utility of Gal-3 remains uncertain because published studies have reported inconsistent results. While several investigations found significantly elevated Gal-3 levels in patients with IBD, others observed no meaningful differences between patients and controls or reported limited ability to distinguish active from inactive disease(Cibor dkk., 2019; Yu dkk., 2020). Furthermore, substantial methodological heterogeneity including differences in biological specimens, assay methods, diagnostic cut-off values, comparator groups, and study populations may contribute to the variability in reported diagnostic performance. To date, these inconsistencies have not been comprehensively synthesized, making it difficult to determine the true diagnostic and disease-monitoring value of Gal-3 in clinical practice (Górecka dkk., 2025; Salama dkk., 2026).

Therefore, this systematic review aims to synthesize the available clinical evidence on circulating Gal-3 as a biomarker for IBD by evaluating its diagnostic performance, including sensitivity, specificity, area under the receiver operating characteristic curve (AUC), and reported cut-off values, as well as its association with disease activity in patients with UC and CD. In addition, this review critically examines methodological heterogeneity across studies to identify factors that may explain conflicting findings and to clarify the potential role of Gal-3 in the diagnosis and monitoring of inflammatory bowel disease.

METHOD

Study Methodology

This study was conducted as a systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This research was performed to evaluate, summarize, and present a structured synthesis of the available evidence on the clinical utility of circulating Galectin-3 as a diagnostic biomarker in patients with inflammatory bowel disease (IBD) (Page dkk., 2021).

Eligibility Criteria

Study Type

Included studies were observational studies (cross-sectional or case-control) that measured circulating Galectin-3 concentrations in serum or plasma of patients with Crohn's disease (CD) and/or ulcerative colitis (UC) compared with a healthy control group, and that reported extractable quantitative concentration data and/or diagnostic performance measures. Studies must be available in full-text.

Inclusion and Exclusion Criteria

Studies were included if they involved human participants diagnosed with CD and/or UC based on standard clinical, endoscopic, histological, or radiological criteria; measured circulating Galectin-3 concentrations in serum or plasma; evaluated Galectin-3 as a diagnostic biomarker or as a marker associated with disease activity; included a healthy control comparison group; and reported at least one diagnostic performance parameter (sensitivity, specificity, area under the receiver operating characteristic curve [AUC], or diagnostic cut-off value) or sufficient quantitative data for meta-analysis. Only full-text articles published in English were considered. Studies were excluded if they were review articles, systematic reviews, meta-analyses, editorials, letters, conference abstracts without complete data, animal or in vitro studies, studies assessing Galectin-3 exclusively in tissue, biopsy, or stool specimens, studies without a healthy control comparison, or duplicate publications.

Study Search and Selection

The literature search process was conducted using five electronic databases: PubMed, Scopus, Europe PMC, ScienceDirect, and Epistemonikos, from database inception through July 2026. Keywords were compiled using the Boolean operator method: [("Galectin-3" OR "LGALS3" OR "Mac-2") AND ("Inflammatory Bowel Disease" OR "IBD" OR "Crohn's disease" OR "Ulcerative Colitis")], adapted to the indexing syntax of each database. Reference lists of eligible articles were additionally screened by hand to identify further relevant studies, which yielded one additional record. All studies obtained from the databases were stored in Rayyan.ai, which then underwent study selection. Duplicate articles were removed, and the remaining articles were screened based on their titles and abstracts by two independent reviewers. Potentially eligible full-text articles were thoroughly assessed using the pre-defined inclusion and exclusion criteria(Page dkk., 2021).

Risk of Bias Assessment

Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool, applied to the studies reporting diagnostic accuracy data, across four domains: patient selection, index test, reference standard, and flow and timing. The assessment was conducted independently by two reviewers, and any discrepancies were resolved through discussion to reach consensus (Deeks dkk., 2023; Whiting dkk., 2011).

Data Extraction and Analysis

Two independent reviewers extracted data from all eligible studies using a standardized data extraction form. Discrepancies were resolved through discussion and consensus. Extracted variables included author and year of publication, country, study design, sample size, diagnostic criteria for IBD, biological specimen type, Galectin-3 assay method, diagnostic cut-off value, and diagnostic performance or disease-activity outcomes. For quantitative synthesis, standardized mean differences (SMDs) with corresponding 95% confidence intervals (CIs) were calculated for circulating Galectin-3 concentrations in patients with IBD compared with healthy controls. Pooled estimates were calculated using a fixed-effect inverse-variance model, and heterogeneity was assessed using the I^2 statistic. Subgroup analyses were performed according to IBD subtype (CD and UC). Diagnostic accuracy outcomes (sensitivity, specificity, and AUC) were synthesized narratively and illustrated using forest plots and a summary receiver operating characteristic (SROC) curve, given the limited number of studies with comparable diagnostic accuracy data (Deeks dkk., 2023; Page dkk., 2021).

RESULT

Study Selection

Preliminary search identified 194 records from five databases: PubMed (n = 54), Scopus (n = 108), Europe PMC (n = 19), ScienceDirect (n = 11), Epistemonikos (n = 2), and one additional record through citation searching. After removing 64 duplicate records, 130 records underwent title and

abstract screening, of which 115 were excluded. Fifteen full-text articles were assessed for eligibility, and 10 were excluded for the following reasons: wrong study design (n = 6), wrong population (n = 1), wrong outcome (n = 1), wrong study objective (n = 1), and ineligible study design and outcomes (n = 1). Finally, six studies met the inclusion criteria and were included in the systematic review. The study selection process is presented in Figure 1.

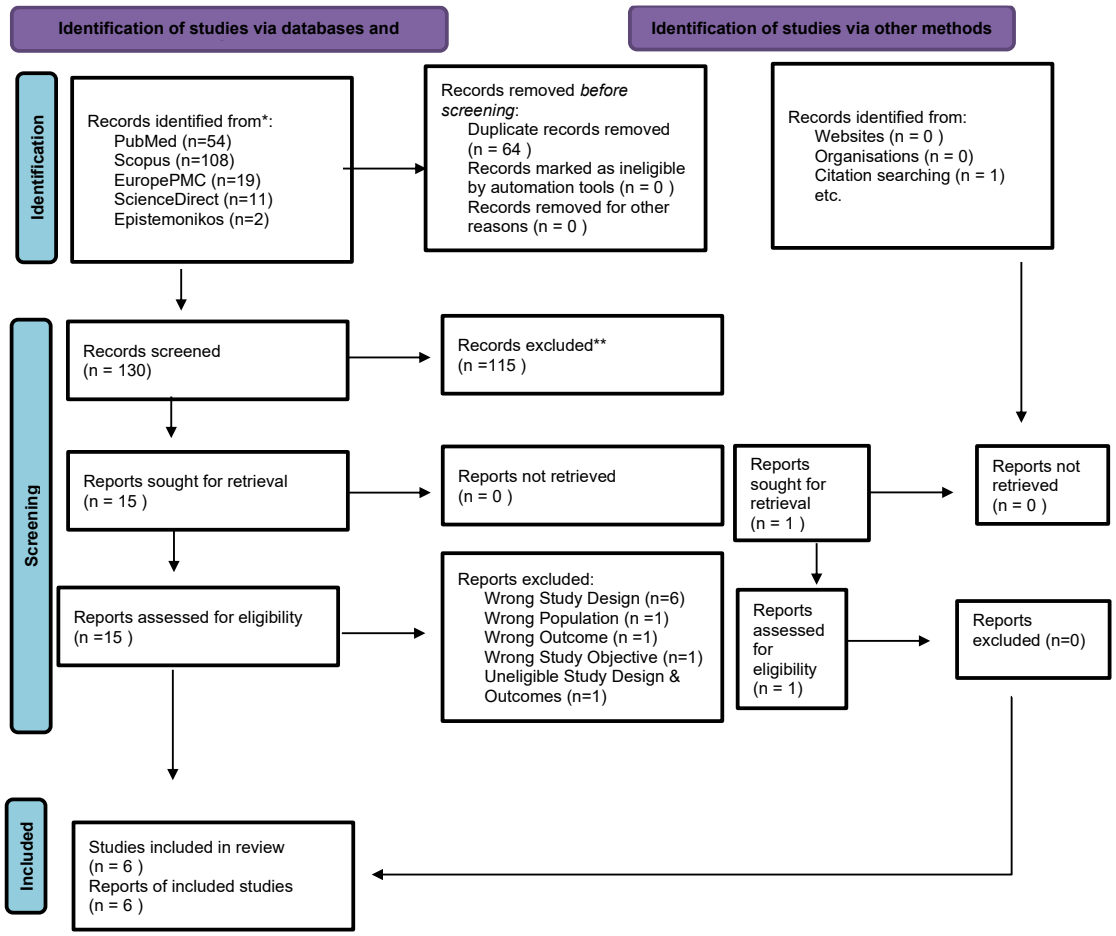


Figure 1. PRISMA 2020 Flow Diagram

Risk of Bias

The high risk of bias and variability observed in the first two QUADAS-2 domains were primarily attributable because all of the studies compared patients with established, often severe, inflammatory bowel disease (IBD) to healthy controls instead of symptomatic non-IBD individuals. This study design can artificially enhance diagnostic accuracy, resulting in inflated estimates of sensitivity and specificity. Additionally, in many studies, diagnostic cutoffs were determined after data analysis rather than being pre-specified, increasing the risk of overestimating test performance (Deeks dkk., 2023; Whiting dkk., 2011).

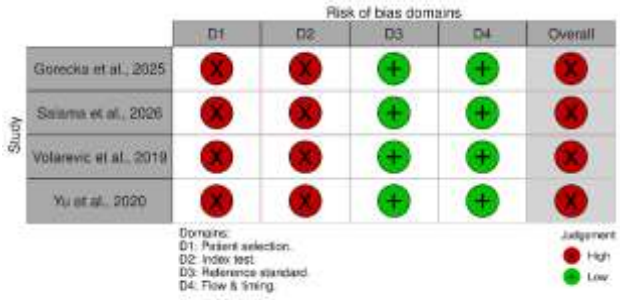


Figure 2. QUADAS-2 Assessment

Study Characteristics

The included studies predominantly utilized a cross-sectional design to evaluate the clinical utility of circulating Galectin-3 in patients with Inflammatory Bowel Disease (IBD). Geographically, the research is primarily centered in Europe (Poland, Czech Republic, Serbia, and the United Kingdom), with additional data emerging from Egypt. Across all cohorts, IBD was diagnosed using conventional clinical, endoscopic, histological, and radiological criteria, ensuring a standardized approach to patient selection (Cibor dkk., 2019; Frol'ová dkk., 2009; Górecka dkk., 2025; Salama dkk., 2026; Volarevic dkk., 2019; Yu dkk., 2020).

The assessment of Galectin-3 demonstrated high methodological homogeneity regarding the biological specimen, with 100% of the studies utilizing serum for analysis. Similarly, the enzyme-linked immunosorbent assay (ELISA) was the universal assay method employed across all trials. However, significant heterogeneity was observed in reported Galectin-3 cut-off values, which varied widely between studies (ranging from 0.75 ng/mL to 94.8 ng/mL), while some investigators did not report a specific diagnostic threshold. This variability suggests a lack of standardization in defining "elevated" circulating Galectin-3 across different clinical settings. The detailed characteristics of the included studies are presented in table 1 (Cibor dkk., 2019; Frol'ová dkk., 2009; Górecka dkk., 2025; Salama dkk., 2026; Yu dkk., 2020).

Table 1.
Study Characteristics

Author, Year	Country	Study Design	Sample Size	Diagnostic criteria for IBD	Galectin-3 Assessment
Cibor et al., 2019	Poland	Cross-sectional	125 IBD patients (77 CD, 48 UC); 30 healthy controls	Standard clinical, radiological, endoscopic, and histological criteria	• Biological specimen: Serum • Assay method: ELISA • Galectin-3 cutoff value: Not Reported (NR)
Frol'ová et al., 2009	Czech Republic	Cross-sectional	126 IBD patients (68 CD, 58 UC); 71 healthy controls	Confirmed by standard endoscopy and histological criteria	• Biological specimen: Serum • Assay method: ELISA (BMS 279; Bender Medsystems GmbH) • Galectin-3 cutoff value: 3.95 ng/mL
Górecka et al., 2025	Poland	Cross-sectional	49 IBD patients (18 CD, 31 UC); 30 healthy controls	Endoscopic examination, clinical symptoms, and laboratory tests	• Biological specimen: Serum • Assay method: ELISA • Galectin-3 cutoff value: 0.75 ng/mL (UC); 1.22 ng/mL (CD)
Salama et al., 2026	Egypt	Cross-sectional	40 IBD patients (17 CD, 23 UC); 40 healthy controls	Clinical criteria and colonoscopy with biopsy	• Biological specimen: Serum • Assay method: ELISA • Galectin-3 cutoff value: >5.199 µg/mL (for activity); >94.8 ng/mL (for differentiating active IBD from controls)
Volarevic et al., 2019	Serbia	Cross-sectional	65 IBD patients (0 CD, 65 UC); 30 healthy control	Clinical criteria and colonoscopy with biopsy	• Biological specimen: Serum (and stool) • Assay method: ELISA • Galectin-3 cutoff value: 954 pg/mL (mild-moderate); 580 pg/mL (moderate-severe)
Yu et al., 2020	United Kingdom	Cross-sectional	168 IBD patients (97 CD, 71 UC); 40 healthy control	Conventional clinical, endoscopic and radiological criteria	• Biological specimen: Serum • Assay method: *Sandwich* ELISA • Galectin-3 cutoff value: 38,5 ng/mL

Study Outcomes

The clinical outcomes regarding circulating Galectin-3 in inflammatory bowel disease (IBD) demonstrate a general trend toward diagnostic utility, although significant inconsistencies remain regarding its association with disease activity. Multiple studies reported that serum Galectin-3 levels are significantly elevated in both Crohn's disease (CD) and ulcerative colitis (UC) patients compared to healthy control groups (1,2,4,6). For instance, Yu et al. observed median levels of 41.7 ng/mL in IBD patients versus 14.9 ng/mL in controls (Yu dkk., 2020). In contrast, Cibor et al. found no statistically significant difference in median Galectin-3 levels between IBD patients and healthy volunteers (Cibor dkk., 2019).

The association between Galectin-3 and disease activity is notably inconsistent across the literature. Some evidence suggests that concentrations are significantly higher in active disease states compared to remission (Frol'ová dkk., 2009; Salama dkk., 2026). Salama et al. further reported a strong positive correlation between serum Galectin-3 and clinical Mayo scores, endoscopic scores, and fecal calprotectin (Salama dkk., 2026). However, other investigators found no significant differences between active and inactive disease subgroups in either UC or CD (5,6). Furthermore, Volarevic et al. identified a significant negative correlation between serum Galectin-3 levels and clinical, histological, and endoscopic subscores in UC patients (Volarevic dkk., 2019).

Regarding biochemical correlations and monitoring, Galectin-3 has been shown to correlate positively with C-reactive protein (CRP) in CD patients (Górecka dkk., 2025). Nevertheless, Yu et al. noted that while a combination of Galectin-3 and CRP could distinguish active disease from remission, it did not provide a significant diagnostic advantage over using CRP as a standalone marker (Yu dkk., 2020). In terms of longitudinal monitoring, Górecka et al. reported divergent results following one year of treatment: levels significantly increased in UC patients receiving anti-TNF-α therapy but significantly decreased in CD patients undergoing conventional therapy (Górecka dkk., 2025). Finally, several clinical factors, including disease location, duration, and specific medication types, do not appear to significantly influence median Galectin-3 concentrations (Yu dkk., 2020). The detailed outcomes of the included studies are presented in table 2.

Table 2.
Outcomes Reported

Author, Year	Outcomes Reported	Results
Cibor et al., 2019	Diagnostic performance (comparison with healthy controls), Association with disease activity (active vs. inactive), correlations with biochemical marker	• Median Gal-3 levels did not differ between patients and controls: UC 6.5 (5.3–8.4) ng/mL, CD 6.7 (5.2–8.5) ng/mL, Control 7.1 (6–8.3) ng/mL ($p = 0.58$). • No significant differences between active and inactive CD or UC subgroups. • Very weak correlation with CDAI in CD patients ($r = 0.26$, $p = 0.02$)
Frol'ová et al., 2009	Diagnostic performance (comparison with healthy controls), Association with disease activity (active vs. remission)	• Galectin-3 concentrations significantly higher in active UC (mean: 6.13 ng/mL), UC remission (mean: 4.40 ng/mL), active CD (mean: 5.65 ng/mL), and CD remission (mean: 3.42 ng/mL) compared to controls (mean: 2.38 ng/mL) (all $p < 0.001$)
Górecka et al., 2025	Diagnostic performance (AUC, sensitivity, specificity), Association with disease activity (correlation with CRP), Monitoring treatment response	• Baseline levels significantly higher in UC (median 1.63 ng/mL, $p < 0.0005$) and CD (mean 1.92 ng/mL, $p < 0.05$) vs. controls (median 0.95 ng/mL). • Diagnostic performance (UC vs. Control): AUC = 0.745, sensitivity = 100%, specificity = 46.4%. • Diagnostic performance (CD vs. Control): AUC = 0.691, sensitivity = 76.9%, specificity = 63.0%. • Correlation with CRP in CD: $r = 0.603$ ($p < 0.05$). • Response to treatment (1 year): Significant increase in UC patients on anti-TNF-α (1.63 to 2.42 ng/mL, $p < 0.05$) and significant decrease in CD patients on

Author, Year	Outcomes Reported	Results
		conventional therapy (1.92 to 1.33 ng/mL, $p < 0.05$)
Salama et al., 2026	Diagnostic performance (ROC), Association with disease activity (Clinical and endoscopic Mayo scores, fecal calprotectin)	• Serum levels significantly higher in active IBD vs. normal controls ($p < 0.001$). • Significant positive correlation with: Fecal calprotectin ($r = 0.873$, $p < 0.001$), clinical Mayo score ($r = 0.492$, $p = 0.001$), and endoscopic Mayo score ($r = 0.403$, $p = 0.010$). • Significant negative correlation with serum albumin ($r = -0.428$, $p = 0.006$). • ROC for activity: sensitivity 100%, specificity 92%, accuracy 99.6%. • ROC for active IBD vs. controls: sensitivity 100%, specificity 97.5%.
Volarevic et al., 2019	Diagnostic performance (ROC), Association with disease activity (Clinical, endoscopic, histological scores)	• Serum Gal-3 levels negatively correlated with: Clinical score ($r = -0.667$, $p < 0.0005$), histological score ($r = -0.317$, $p < 0.01$), and endoscopic subscore ($r = -0.256$, $p < 0.05$). • Serum levels significantly higher in mild UC vs. moderate UC vs. severe UC ($p < 0.01$). • ROC for monitoring UC progression: Sensitivity 95%, specificity 91.7%.
Yu et al., 2020	Diagnostic performance (differentiating IBD from healthy controls), the relationship with disease activity (comparing active disease vs. remission), correlation with other biomarkers (specifically C-reactive protein or CRP), and sub-group analyses based on disease location, disease duration, and concurrent medications	• Galectin-3 levels were significantly higher in IBD patients than in healthy controls, with a median of 41.7 ng/mL for IBD vs. 14.9 ng/mL for controls ($p < 0.0001$). • Levels were significantly higher in patients with Crohn's disease (median 42.1 ng/mL) compared to controls ($p = 0.0003$). • Levels were significantly higher in patients with Ulcerative Colitis (median 37.4 ng/mL) compared to controls ($p = 0.0001$). • Diagnostic Performance: Using a cut-off value of 38.5 ng/mL, Gal-3 separated IBD patients from healthy controls with 53% sensitivity and 87% specificity. • Disease Activity: Galectin-3 was unable to significantly distinguish between active disease and remission in either UC ($p = 0.2353$) or CD ($p = 0.1036$). • Combination with CRP: While the combination of Gal-3 + CRP could distinguish active disease from remission ($p = 0.0219$ for UC; $p = 0.0056$ for CD), this combination was not significantly better than using CRP as a standalone marker ($p = 0.4150$). • Other Factors: There were no significant differences in median Gal-3 levels when analyzed by disease location, disease duration, or the type of medications the patients were using.

Meta-Analysis

The meta-analysis of circulating Galectin-3 levels demonstrates a consistent increase in IBD patients compared to healthy controls. For the Crohn's disease subgroup, the pooled Standardized Mean Difference (SMD) was 0.81 [95% CI: 0.44, 1.18], indicating a significant elevation ($p < 0.0001$). Similarly, the Ulcerative Colitis subgroup showed a significant elevation with a pooled SMD of 0.62 [95% CI: 0.26, 0.97] ($p = 0.0006$). The statistical heterogeneity for both subgroups was remarkably low ($I^2 = 0\%$), suggesting high consistency in the direction and magnitude of the effect across the analyzed studies. Diagnostic accuracy data varied more widely, with sensitivity ranging from 0.53 to 1.00 and specificity ranging from 0.47 to 0.97 across the individual studies included in the diagnostic forest plot. The detailed forest plot is presented in **Figure 3** (Górecka dkk., 2025; Salama dkk., 2026; Yu dkk., 2020).

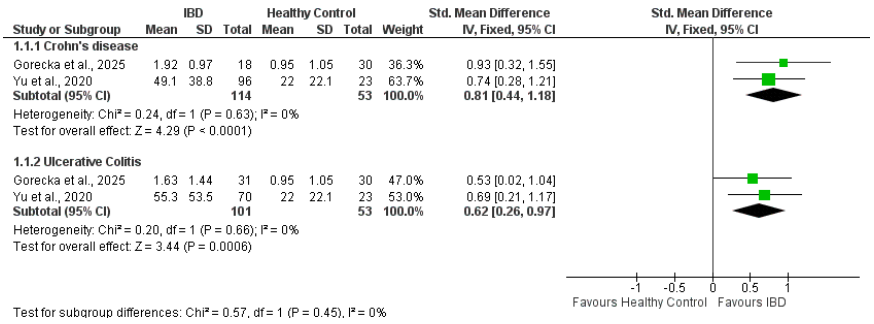


Figure 3. Forest Plot of Circulating Galectin-3 Levels in Inflammatory Bowel Disease Compared to Healthy Control

The Summary Receiver Operating Characteristic (SROC) plot illustrates the diagnostic potential of circulating Galectin-3, though interpretation should be cautious due to the inclusion of only four data points. The distribution of study points is scattered, reflecting the variability in diagnostic performance reported across the literature. While two studies cluster near the upper-left corner, indicating high sensitivity and high specificity, the remaining studies are positioned lower or further to the right. This distribution signifies significant variability in diagnostic accuracy between the studies. The resulting SROC curve follows a trajectory toward the upper-left corner but does not perfectly hug the axes, suggesting that while Galectin-3 holds potential as a biomarker, its overall diagnostic performance may be influenced by the different cut-off values and clinical contexts employed by the researchers. The detailed SROC plot is presented in **Figure 4** (Deeks dkk., 2023; Whiting dkk., 2011).

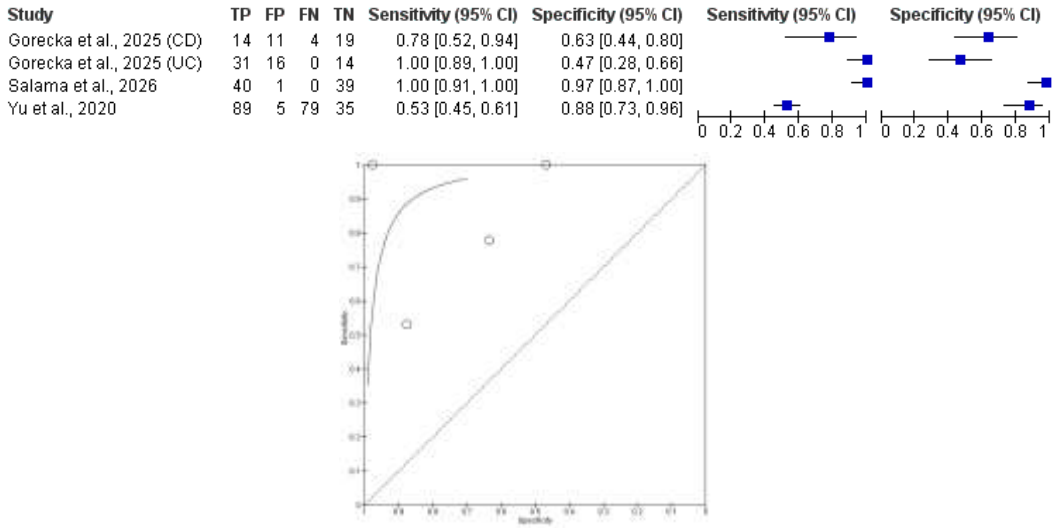


Figure 4. SROC of Circulating Galectin-3 as Potential Diagnostic Biomarker

DISCUSSION

The principal findings of this systematic review and meta-analysis indicate that circulating galectin-3 levels are significantly elevated in patients with inflammatory bowel disease (IBD) compared to healthy control populations (Frol'ová dkk., 2009; Górecka dkk., 2025; Salama dkk., 2026; Yu dkk., 2020). The integrated meta-analysis data confirms a statistically significant increase in serum concentrations for both the CD and UC. From a biological perspective, circulating galectin-3 functions as a multifaceted mediator of intestinal inflammation (Górecka dkk., 2025; Volarevic dkk., 2019). It is a -galactoside-binding lectin that facilitates the activation and polarization of macrophages towards a pro-inflammatory M1 phenotype during the induction phase of colitis,

thereby amplifying the inflammatory cascade Furthermore, galectin-3 is deeply involved in fibrosis and tissue remodeling, as it promotes the proliferation of fibroblasts and the synthesis of extracellular matrix (ECM) components like collagen. This role in chronic remodeling suggests that elevated levels may reflect underlying disease progression and the potential development of complications such as strictures.

A critical evaluation of the included studies reveals significant similarities in initial diagnostic findings but notable discrepancies regarding disease activity and clinical status. Both Frol'ová et al. and Salama et al. identified that galectin-3 concentrations were significantly higher in active disease states compared to remission. Salama et al. further reported a strong positive correlation between serum levels and objective endoscopic Mayo scores. In contrast, studies by Yu et al. and Cibor et al. found that galectin-3 could not significantly distinguish between active and inactive disease in either CD or UC cohorts. Adding to this complexity, Volarevic et al. identified a negative correlation between serum levels and clinical severity, observing higher levels in mild UC compared to severe cases, which might suggest consumption of the protein or altered expression during advanced systemic inflammation.(Freeman dkk., 2019; Lin dkk., 2014; Maaser dkk., 2019; Rokkas dkk., 2018; Sturm dkk., 2019; Turner dkk., 2021; "Utility of PR3-ANCA in patients with inflammatory bowel disease: a systematic review and meta-analysis," 2024; van Rheenen dkk., 2010; Volarevic dkk., 2019; Whiting dkk., 2011)

These inconsistencies are likely attributable to several methodological and clinical factors, such as significant assay variability resulting from the use of different commercial ELISA kits, which often report divergent baseline ranges for healthy control populations. Furthermore, substantial cut-off heterogeneity was observed across studies, with standardized diagnostic thresholds varying drastically from 0.75 ng/mL in the analysis by Górecka et al. to over 94.8 ng/mL in the studied by Salama et al.(Salama dkk., 2026) Differences in study design and patient selection, particularly regarding disease severity at the time of sampling, the influence of concurrent medications, and the limited statistical power of smaller pilot trials, likely restricted the ability to identify consistent associations with disease activity.

This review represents one of the first systematic review and meta-analysis of circulating galectin-3 in IBD. It benefits from a standardized methodology, the evaluation of multiple clinical outcomes (diagnosis, activity, and treatment response), and a meta-analysis that shows high robustness in comparing IBD patients to healthy controls. The primary limitations include the small number of included studies, the predominance of cross-sectional observational designs, and significant methodological heterogeneity regarding assay kits and reported cut-off points. Future research should prioritize multicenter prospective cohorts to establish validated, standardized diagnostic cut-off values. There is also a need for long-term studies to validate its role in prognostic prediction. Looking forward, the clinical utility of galectin-3 may also be significantly enhanced through its integration into multi-marker panels.

CONCLUSION

Circulating Galectin-3 shows promise as a biomarker for the diagnosis of IBD. However, evidence regarding its utility for disease activity assessment and treatment monitoring remains inconsistent. Further large-scale prospective studies using standardized assay methods and validated diagnostic thresholds are needed to establish its clinical utility.

DECLARATIONS

Acknowledgment: Not applicable.

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

Ethical Approval: Ethical approval was not required because this study was a systematic review and meta-analysis based on previously published studies and did not involve direct human or animal participation.

Financial Support and Sponsorship: This study received no specific funding from any public, commercial, or non-profit funding agency.

Data Availability Statement: All data supporting the findings of this study are available within the published articles included in this systematic review and meta-analysis.

Author Contributions: I Putu Bagus Andika Pratama: Conceptualization, methodology, literature search, data extraction, data analysis, and manuscript preparation. Budiono Raharjo and Anak Agung Sagung Amanda Achintya: Supervision, validation, and critical revision of the manuscript. All authors read and approved the final manuscript.

Declaration of the Use of Artificial Intelligence in Scientific Writing: Artificial intelligence tools were used to assist with language refinement and grammatical editing. All authors reviewed and take full responsibility for the accuracy and integrity of the manuscript.

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