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Value of Fecal Galectin-3 in Assessment of Activity and Remission of Ulcerative Colitis

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Abstract:

Background: Inflammatory bowel diseases (IBD), which primarily include Crohn's disease (CD), affecting any part of the gastrointestinal tract, and ulcerative colitis (UC), confined to the colon- are characterized by diverse factors influencing disease activity and treatment evaluation. This research aimed to assess the Value of fecal Gal-3 in assessment of activity and remission of ulcerative colitis. **Methods:** This prospective research was conducted on 60 subjects who were divided into two groups; group 1 (including 40 UC cases) and reassessed after 3 months of treatment and group 2 (20 control cases) who attended to hospital for endoscopy as an investigation for diarrhea, crampy abdominal pain, urgency, tenesmus and their colonoscopy reveal no abnormality. What was investigated for both groups? **Results:** Fecal calprotectin (FC) and Gal-3 were significantly increased in UC cases. FC decreased after 3 months of treatment but was did not reach statistical significance, while there was a significant decrease in fecal Gal-3 in cases after treatment. According to the ROC curve, the best cut off point of fecal Gal-3 level to identify cases with active UC was 0.447 (ng/ml) with 87.5% sensitivity and 85% specificity. And the best cut off point of fecal Gal-3 level to identify cases with remission UC was 0.3165 (ng/ml) with 90% sensitivity and 50% specificity. **Conclusion:** Fecal Gal-3 could be used as a biomarker for UC disease activity and treatment assessment. What about FC?

Keywords: Fecal Gal-3; Ulcerative Colitis; Inflammatory bowel diseases; Fecal calprotectin.

Introduction

Inflammatory bowel diseases (IBD) represent a group of chronic, immune-mediated inflammatory disorders primarily affecting the gastrointestinal tract. The two principal subtypes of IBD are Crohn's disease (CD), which may involve any portion of the digestive system from mouth to anus, and ulcerative colitis (UC), which is confined exclusively to the colon. Cases with either CD or UC frequently present with hallmark symptoms such as persistent diarrhea, abdominal discomfort, fatigue, and unintended weight loss [(1)].

Establishing a diagnosis of IBD generally necessitates a multifaceted approach that integrates clinical symptomatology with laboratory investigations, such as measurements of C-reactive protein (CRP) and fecal calprotectin (FC), as well as direct visualization via endoscopy. Among these modalities, endoscopic assessment remains the gold standard for diagnosis, as no single blood-based biomarker has yet demonstrated sufficient sensitivity or specificity for reliable identification of IBD [(2)].

The clinical course of IBD is typically characterized by a relapsing-remitting pattern, whereby periods of active inflammation alternate with phases of remission or minimal disease activity. In routine clinical practice, assessment of IBD activity often involves a composite evaluation comprising: (i) symptom-based scoring systems such as the Crohn's Disease Activity Index (CDAI) and the Harvey-Bradshaw Index (HBI) for CD, and the Simple Clinical Colitis Activity Index for UC; (ii) quantification of inflammatory biomarkers, particularly CRP and FC; and (iii) endoscopic examination of the intestinal mucosa [(2)].

Despite its diagnostic accuracy, repeated endoscopic evaluation poses significant limitations; it is invasive, costly, burdensome for cases, and carries procedural risks. Among non-invasive serum markers, CRP is the most commonly utilized in clinical settings. However, its utility is compromised by limitations in both sensitivity and specificity: (i) CRP levels can be elevated in a wide range of inflammatory conditions beyond CD and UC, and (ii) up to one-quarter of cases with active mucosal inflammation confirmed by endoscopy may present with normal CRP levels [(3)].

In contrast, FC has shown superior accuracy in identifying intestinal inflammation as opposed to CRP, making it a more reliable non-invasive biomarker for disease monitoring [(4)]. Nonetheless, there remains an unmet need for additional accurate, non-invasive markers capable of reliably reflecting disease activity in IBD.

Galectins constitute a family of 15 mammalian proteins with an affinity for galactoside residues, unified by a conserved carbohydrate recognition domain (CRD) within their amino acid sequences [(5)]. Structurally, they are classified into three distinct types: proto-type, chimeric-type, and tandem-repeat-type. These proteins are widely distributed in human tissues, with predominant expression observed in epithelial and immune cells. Among them, galectins-1, -2, -3, -4, and -8 have been specifically identified in the epithelial lining of the gastrointestinal tract [(6)].

Biologically, galectins interact with galactose-terminated glycans on the surface of cells, and such interactions have been implicated in the immunopathogenesis of IBD. In particular, their involvement in mediating T-cell apoptosis and modulating NF-κB signaling pathways suggests a pivotal role in driving mucosal inflammation in IBD [(7)].

Given these properties, the present research was undertaken to evaluate the clinical relevance of fecal Galectin-3 (Gal-3) as a potential biomarker for distinguishing between active disease and remission in cases with UC.

Patients and methods:

Patients:

This prospective research included 40 naïve cases attended from outcase IBD Clinic of Hepatology, Gastroenterology and infectious diseases Department, Mahalla Hepatology Teaching Hospital, El-Mahalla Elkobra and Benha University, Egypt and 20 controls, from May 2022 to August 2022.

Written informed consent was obtained from all participants prior to their inclusion in the research. Ethical approval was secured from the Scientific Research Ethics Committee of the Faculty of Medicine, Benha University- Approval code: MD 12-10-2021- before commencement of the research.

Eligibility criteria included adult cases of either sex, aged over 18 years, with a confirmed diagnosis of ulcerative colitis established through clinical assessment, endoscopic findings, and histopathological examination. Participants were required to be both willing and capable of complying with the research protocol, including the provision of blood and stool samples and undergoing colonoscopic evaluation.

Exclusion criteria encompassed pregnancy; current use of medications such as non-steroidal anti-inflammatory drugs (NSAIDs); presence of autoimmune disorders; and significant comorbid conditions including arrhythmias, heart failure, renal or respiratory insufficiency, and colorectal malignancy.

Grouping: Studied cases: 40 naïve UC cases in the research fullfiled criteria of active ulcerative colitis (endoscopically and clinically). **Control cases:** 20 cases-cross matched with age and sex- were added as control group presented with crampy abdominal pain, diarrhea, urgency and tenesmus with normal colonoscopy. The cases group will be reassessed after 3 months of medical treatment clinically, laboratory and endoscopically.

Methods:

All studied cases were subjected to the following: Full history taking, including; [demographic data (age, sex, history of present illness.), history of disease manifestations and other relevant medical and surgical history]. **Full clinical examination:** with special prominence on abdominal pain, significant weight loss, rectal bleeding, bloody diarrhea, constipation, nausea, tenesmus, abdominal distension, passage of mucus, vomiting and low-grade fever. **Routine laboratory investigations; [**Complete blood count, CRP, ESR, serum creatinine, stool analysis, radiological investigations (including; abdominal ultrasound to exclude the presence of associated diseases or complications), FC level by ELISA, measurements of fecal Galactin -3 by enzyme linked sorbent assay (ELISA)].

Stool samples were collected from all research participants for assessment of fecal Galactin -3

Prior to biochemical analysis, all cellular samples were thoroughly lysed to ensure efficient release of intracellular contents. For adherent cell lines, cells were first detached using trypsin and subsequently collected by centrifugation. In contrast, suspension cells were directly harvested by centrifugation without the need for enzymatic detachment. Once collected, the cell pellets were washed three times with ice-cold phosphate-buffered saline (PBS) to eliminate residual culture medium and serum-derived proteins. The washed cells were then resuspended in 1× PBS and subjected to lysis by one of two standardized methods. In the first method, samples were exposed to four cycles of ultrasonication to mechanically disrupt the cell membranes. Alternatively, a freeze–thaw approach was employed, wherein cells were frozen at –20°C or below and then thawed at room temperature with gentle mixing; this cycle was repeated three times to achieve effective lysis. Following cell disruption, all samples were centrifuged at 1500×g for 10 minutes at 2–8°C to remove insoluble cellular debris. The resulting supernatant, clear of particulate matter, was collected and used for downstream assay procedures.

Reagent preparation

To maintain uniform assay conditions and ensure reproducibility, all reagents and biological samples were brought to room temperature (18–25°C) prior to use. This equilibration step was critical for preserving reagent activity and minimizing variability in assay performance.

Standard: The standard was reconstituted by adding 1.0 mL of Diluent Buffer to the lyophilized vial, followed by gentle mixing to avoid foaming, and allowed to stand at room temperature for 10 minutes to ensure complete dissolution. This produced a stock concentration of 10 ng/mL. A seven-point two-fold serial dilution was then prepared by transferring 0.5 mL of Diluent Buffer into each of seven labeled tubes, sequentially diluting the stock to achieve concentrations of 10, 5, 2.5, 1.25, 0.625, 0.312, and 0.156 ng/mL. An eighth tube containing only Diluent Buffer served as the blank (0 ng/mL). Each dilution was thoroughly mixed before proceeding to the next to ensure consistency across the calibration range.

Detection reagents A and B were briefly centrifuged to ensure homogeneity, then diluted 1:100 with Diluent Buffer to obtain their respective working concentrations.

The wash buffer was freshly prepared by diluting 20 mL of the 30× concentrate with 580 mL of deionized water, resulting in 600 mL of 1× solution, mixed well to ensure uniform composition.

The TMB substrate was carefully handled using sterile pipette tips to prevent contamination. Only the required volume was aspirated, and no excess was returned to the original container, preserving the reagent's stability and ensuring consistent chromogenic development during the final detection step.

What about FC testing?

Approval code: MD 12-10-2021

Statistical analysis

Statistical analysis was done by SPSS 20.0. (Armonk, NY: IBM Corp). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test and ANOVA (F) test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test or Fisher's exact test when appropriate & ROC curve to predict validity of Gal-3 in detection of cases. A two tailed P value < 0.05 was considered statistically significant.

Results:

The studied cases and the control group exhibited comparability regarding sex, occupation, residence, smoking, operation history, HTN, DM, and other chronic conditions, with no statistically significant differences observed. However, a significant difference was detected in relation to age and marital status, as the case group showed a predominance of older and married individuals as opposed to the control group ($p \leq 0.05$). Clinically, bleeding per rectum, urgency, tenesmus, and weight loss- were significantly more frequent among cases, p value?. Laboratory findings revealed significant differences in Hb and WBC, with a marked increase in both anemia and leukocytosis in the case group p value?. Additionally, FC and Gal-3 levels were significantly elevated in UC cases, reflecting enhanced inflammatory activity, **Table (1).**

Regarding extraintestinal manifestations, there were 17.5% of studied cases had extraintestinal manifestations (peripheral arthropathy). Regarding to medical treatment, 22.5% received 5-ASA therapy, 50% received corticosteroids and 27.5% received biological therapy (infliximab). Response to treatment was seen in 75% of 40 cases, **Table (2).**

Regarding to clinical finding at baseline-according to Truelove and Witts- there were 42.5% of the studied cases had moderate to severe active and 57.5% severe active. However, colonoscopic finding at baseline, there were 100% of the studied cases had mucosal erythema,

82.5% severe friability, 80% loss of vascular marking, 80% erosions, 77.5% ulcers and 32.5% spontaneous bleeding. 77.5%(in letters) of the studied cases had a Mayo score 3 at baseline which is the highest score**.** Histopathological finding at baseline in the studied cases, there were100% had acute cryptitis, 90% had crypt abscess, 25% pseudopolyps and no dysplastic change, **Table (3).**

Regarding Truelove and Witts, after 3 months of treatment, mild and moderate to severe activity were 77.5% and 22.5%, respectively. Regarding to colonoscopic finding after 3 months of treatment, 57.5% of studied cases had normal mucosa, 75% had normal vascular marking, 80% had no friability, 97.5% had no erosions, 90% had no ulcers and 100% had no spontaneous bleeding. About histological finding, 62.5% of studied cases had acute cryptitis, 77.5% had no cryptal abscess, 87.5% had no pseudopolyps and no dysplasia after 3 months of treatment, **Table (4).**

Table 1: Demographic data, Lower GIT symptoms, Laboratory finding, Fecal Gal-3 and fecal calprotectin finding in the studied cases and control cases

Variable		**Studied cases (n=40)**		**Control cases (n=20)**		**p-value**
		n.	%	n.	%	
Sex	Male	14	35.0%	10	50.0%	0.264
	Female	26	65.0%	10	50.0%	
Age		33.3±7.47		26.9±5.33		0.001*
Occupation		12	30.0%	10	50.0%	0.130
Residence	Rural	16	40.0%	8	40.0%	1.000
	Urban	24	60.0%	12	60.0%	
Marital state		35	87.5%	13	65.0%	0.040*
Smoking		13	32.5%	5	25.0%	0.550
Operations		5	12.5%	0	0.0%	0.159
HTN		0	0.0%	0	0.0%	-
DM		0	0.0%	0	0.0%	-
Other diseases		0	0.0%	0	0.0%	-
Lower GIT symptoms						
Bloody diarrhea		40	100%	20	100%	-
Crampy abdominal pain		37	92.5%	20	100%	0.544
Bleeding per rectum		10	25%	0	0%	0.023*
Urgency		35	87.5%	10	50%	0.002*
Tenesmus		33	82.5%	10	50%	0.008*
Constipation		0	0.0%	0	0.0%	-
Loss of weight		30	75%	0	0%	<0.001*
Laboratory finding						
Creatinine (mg/dl)		0.898±0.13		0.935±0.1		0.253
Hb (g/dl)		9.89±1.00		11.59±0.47		<0.001*
WBC (thouthands/cmm)		9.45±2.86		5.67±0.98		<0.001*
Platelet (thouthands/cmm)		340.48±105.13		294.50±64.85		0.084
Gal-3 (ng/ml)		1.79±0.59		0.05±0.02		<0.001*
Fecal calprotectin (mg/kg)		543.63±389.79		29.25±10.76		<0.001*

Data arte presented as Mean±SD or frequency (%), *: statistically significant as P value <0.05.

Table 2: Extraintestinal manifestations and ulcerative colitis treatment regimens in the studied cases

Variable		Cases (n=40)	
		n.	%
Extraintestinal manifestations (peripheral arthropathy)		7	17.5%
Variable		**Studied cases(n=40)**	**Response to treatment**
Medical treatment regimens	5 ASA	9 (22.5%)	6 (66.6%)
	Corticosteroids	20 (50%)	15 (75%)
	Biological therapy (Infliximab)	11 (27.5%)	9 (81.8%)

Table 3: Clinical finding and laboratory invetigations according to Truelove and Witts, Colonoscopic, Mayo score and histopathological finding in the studied cases at baseline

Variable			Studied cases (n=40)	
			n.	%
Clinical finding and laboratory invetigations				
Bowel movement <4/day			0	0%
Bowel movement 4-6/day			14	35%
Bowel movement >6/day			26	65%
Small amount of blood in stool			10	25%
Mild to moderate amount of blood in stool			18	45%
Visible blood in stool			13	32.5%
Pyrexia>37.8			0	0%
Pulse >90 (b/m)			0	0%
Anemia Hb <10.5 (gm/dl)			17	42.5%
ESR<20 (mm)			2	5%
ESR<30 (mm)			17	42.5%
ESR>30 (mm)			21	52.5%
CRP normal			17	42.5%
CRP<30 (mg/l)			15	37.5%
CRP >30 (mg/l)			9	22.5%
Truelove and Witts	Mild		0	0%
	Moderate		17	42.5%
	Severe		23	57.5%
Colonoscopic finding				
Mucosal erythema			40	100%
Vascular marking		Normal	0	0%
		Decreased	8	20%
		Absent	32	80%
Friability		No	0	0%
		Mild	7	17.5%
		Severe	33	82.5%
Erosions			32	80%
Ulcers			31	77.5%
Spontaneous bleeding			13	32.5%
Mayo score		0	0	0%
		1	0	0%
		2	9	22.5%
		3	31	77.5%
Histopathological finding				
Acute cryptitis			40	100%
Cryptal abscess			36	90%
Pseudopolyps			10	25%
Dysplasia			0	0%

Table 4: Comparison regarding colonoscopic finding, Mayo score, histopathological finding, clinical finding, fecal calprotectin and Gal-3 at baseline and after 3 months of treatment studied cases (follow up)

Variable		At baseline of studied cases (n=40)		Studied cases after 3 months of treatment (n=40)		p-value
		n.	%	n.	%	
Mucosal erythema		40	100%	17	42.5%	<0.001*
Vascular marking	Normal	0	0%	30	75%	<0.001*
	Decreased	8	20%	7	17.5%	
	Absent	32	80%	3	7.5%	
Friability	Mild	7	17.5%	6	5%	<0.001*
	Severe	33	82.5%	2	15%	
Erosions		32	80%	1	2.5%	<0.001*
Ulcers		31	77.5%	4	10%	<0.001*
Spontaneous bleeding		13	32.5%	0	0%	<0.001*
Mayo score	0	0	0%	22	55%	<0.001*
	1	0	0%	8	20%	
	2	9	22.5%	7	17.5%	
	3	31	77.5%	3	7.5%	
Hstopathological finding						
Acute cryptitis		40	100%	15	37.5%	<0.001*
Cryptal abscess		36	90%	9	22.5%	<0.001*
Pseudopolyps		10	25%	5	12.5%	0.227
Dysplasia		0	0%	0	0.0%	-
Clinical finding						
Bowel movement <4/day		0	0%	34	85%	<0.001*
Bowel movement 4-6/day		14	35%	5	12.5%	0.388
Bowel movement >6/day		26	65%	0	0%	<0.001*
Small amount of blood in stool		10	25%	3	7.5%	0.065
Mild to moderate amount of blood in stool		18	45%	0	0%	<0.001*
Visible blood in stool		13	32.5%	0	0%	<0.001*
Pyrexia>37.8		0	0%	0	0%	<0.001*
Pulse >90 b/m		0	0%	0	0%	<0.001*
Anemia Hb <10.5 (gm/dl)		17	42.5%	0	0%	<0.001*
ESR<20 (mm)		2	5%	35	87.5%	<0.001*
ESR<30 (mm)		17	42.5%	4	10.0%	0.004*
ESR>30 (mm)		21	52.5%	1	2.5%	<0.001*
CRP normal		17	42.5%	32	80.0%	<0.001*
CRP<30 (mg/dl)		15	37.5%	8	20.0%	0.143
CRP >30 (mg/dl)		9	22.5%	0	0.0%	0.004*
Truelove and Witts	Mild	0	0%	31	77.5%	<0.001*
	Moderate	17	42.5%	9	22.5%	
	Severe	23	57.5%	0	0.0%	
Fecal calprotectin (mg/kg)		543.63±389.79		75.70±27.90		0.127
Gal-3 (ng/ml)		0.75±0.290		0.65±0.283		<0.001*

*: statistically significant as P value <0.05

Fecal calprotectin (FC) was decreased after 3 months of treatment but was not reach statistical significance. While, there was significantly decreased in fecal Gal-3 in cases after treatment p value?, **Table (5).**

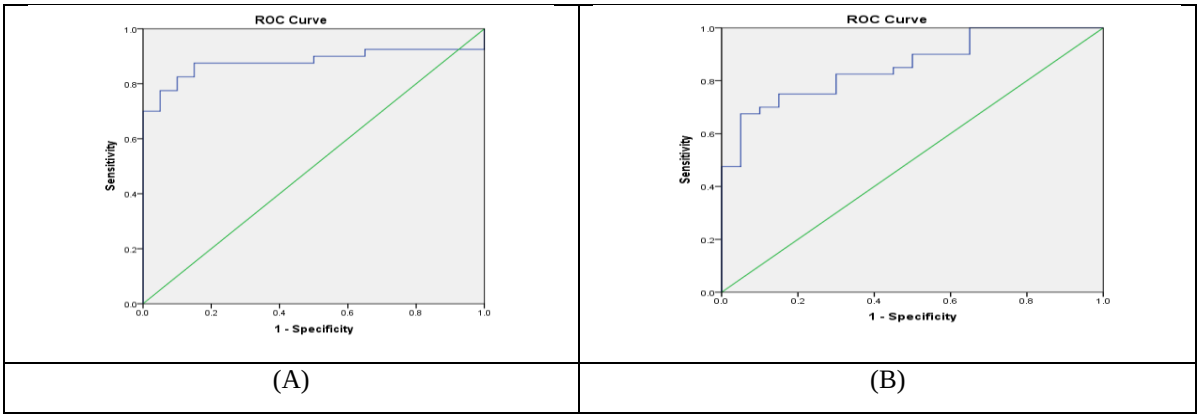
According to the ROC curve, the best cut off point of fecal Gal-3 level to identify cases with active UC was 0.447 (ng/ml) with 87.5% sensitivity and 85% specificity, **Figure 1 (A).**

And, the best cut off point of fecal Gal-3 level to identify cases with remission UC was 0.3165 (ng/ml) with 90% sensitivity and 50% specificity, **Figure 1 (B).**

Table 5: Comparison between fecal calprotectin and Gal-3 at baseline and after 3 month of treatment

Variable	Studied cases at baseline (n=40)	After 3 months treatment (n=40)	p-value
Fecal calprotectin (mg/kg)	543.63±389.79	75.70±27.90	0.127
Gal-3 (ng/ml)	0.75±0.290	0.65±0.283	<0.001*

*: Statistically significant at p ≤ 0.05, Data are presented as Mean±SD



(A) (B)

Figure 1: Validity of fecal Gal-3 in assessment of studied cases (A) before treatment and (B) after 3 months treatment

Discussion:

In the current research, there were 40 UC cases and 20 control cases with the mean age (33.3±7.47) years and (26.9±5.33) years respectively.

This result agreed with Elwakila and co-authors, who found that the mean age of the cases was 36.64 years, also, in correlation with Cosnes and co-authors, who reported that although there has been an increased incidence of UC in different age groups, yet the majority of cases with UC in recent decades are in the age group of 30–40 years at diagnosis [8, 9].

In this present research, there was predominance of females in the studied cases (60%) but it didn't reach a statistically significant difference between the studied cases and control. This agrees with Amer and co-authors., who showed that the percentage of females among UC group was significantly high [10].

Regarding the clinical symptoms, our research showed that bloody diarrhea was the main presenting symptom in studied cases (100%) and crampy abdominal pain (92.5%) with no a significantly difference compared with control. Other symptoms, urgency (87.5%), tenesmus (82.5%), bleeding per rectum (75%), weight loss (75.0%) were significantly higher in the

studied cases than control, p value? Table (2).

This agrees with Elnagdy and co-authors., who also found that (80%) UC cases presented with abdominal pain, (100%) tenesmus, (60%) weight Loss and (36%) rectal bleeding [(11)].

Also, these results agree with Elwakila and co-authors who reported that 78.6% of the UC cases had more than six motions per day, 82.1% of the cases had bloody motions, 100% of the cases had mucoid motions, 26% of the cases had bleeding per rectum, 51.8% of the cases had abdominal pain, 58.9% had tenesmus while 23.2% reported constitutional symptoms [(8)].

In the current research, 7 (17.5%) cases showed extraintestinal manifestations (peripheral arthropathy). While, Moussa and co-authors., who showed that 7.5% of the UC cases had arthralgia [(12)].

On the other hand, our result was higher than Elwakila and co-authors., reported (3.6%) cases showed extraintestinal manifestations (Joint and skin manifestations) [(8)].

Regarding the laboratory findings in the present research, anemia and leukocytosis- were significantly higher in studied cases than in control ($P < 0.001$, < 0.001 respectively). This agrees with Elwakila and co-authors., who repoted that the mean hemoglobin content in their research cases was 10 gm% (anemic level) [(8)].

In this research, the assessment of the mucosa by colonoscopy showed a Mayo score for endoscopic severity calculated for the studied cases of the present research to determine the activity of the disease had 77.5% Mayo score 3 and 22.5% Mayo score 2.

These results align with the findings of Min and Kang-Moon, who described the characteristic endoscopic appearance of UC as involving edematous and erythematous mucosa, diminished or absent vascular markings, and increased mucosal fragility. In advanced cases, the mucosal surface may exhibit erosions, ulcerations, and episodes of spontaneous bleeding [(13)].

After 3 months of treatment, cases were reassessed by colonoscopy to identify the endoscopic remission using the Mayo score. The most of the cases of the research 55% of studied cases had Mayo score 0, 20% had Mayo score 1, 17.5% had Mayo score 2 and 7.5% had Mayo score 3.

In the present research, we found that the most frequent histological findings in between cases; acute cryptitis (100%), crypt abscess (90%), but the least frequent findings were pseudopolyps (25%) with no dysplastic change. Also, 62.5% of studied cases had acute cryptitis, 77.5% had no cryptal abscess, 87.5% had no pseudopolyps and no dysplasia after 3 months of treatment.

In the current research- regarding Truelove and Witts score- consider UC cases were moderate to severe active in (42.5%) and severe in (57.5%). However, Truelove and Witts score shows that mild and moderate to severe activity were (77.5% and 22.5%), respectively after 3 months of treatment.

In the present research, FC levels were found to be significantly elevated in the case group as opposed to controls ($P < 0.001$), with a notable decline observed following treatment. These findings are in concordance with the systematic review conducted by D'Amico and co-authors, which encompassed twelve studies involving a total of 1,168 UC cases. Their analysis demonstrated a strong and consistent association between FC concentrations and the histologic activity of disease in adults with UC. Importantly, FC levels were markedly reduced in cases of histologic remission, while significantly elevated values were observed in the presence of microscopic inflammation, independent of the histologic scoring system, FC assay used, or the cut-off values applied. As such, FC emerges as a valuable, non-invasive biomarker for detecting and monitoring histologic disease activity in UC, offering clinicians a

reliable tool to assess inflammatory status without the need for repeated invasive procedures [14].

Emerging research has increasingly highlighted the pathogenic significance of various galectin isoforms in experimental models of colitis [15] among them; Gal-3 has garnered particular attention for its role in modulating the immune response. In dextran sodium sulfate (DSS)-induced models of colitis, Gal-3 has been shown to facilitate macrophage activation during the early (induction) phase of inflammation, thereby contributing to the initiation and amplification of the colonic inflammatory cascade [16].

In the current research, fecal Gal-3 levels were significantly elevated in UC cases as opposed to the control group ($P < 0.001$), and a marked reduction was observed following treatment, also with a statistically significant difference ($P < 0.001$). These findings are in concordance with the research by Volarević and co-authors, who explored the molecular mechanisms underlying Gal-3–mediated regulation of colonic inflammation and examined its potential utility as a biomarker for tracking the progression of UC. Their results demonstrated that Galectin-3 concentrations in both serum and fecal samples showed a negative correlation with clinical, endoscopic, and histopathological indices of disease activity, further supporting its value as a non-invasive marker for disease monitoring in UC [17].

Volarevic and colleagues conducted a compelling research in which they observed a marked elevation in fecal Gal-3 concentrations among cases with UC as opposed to healthy controls. Notably, Gal-3 levels were significantly higher in individuals with mild UC relative to those with moderate or severe disease activity ($p < 0.05$), suggesting a potential inverse relationship between Gal-3 and disease severity. This negative correlation ($r = –0.294$, $p = 0.049$) points to the possible role of Gal-3 as a biomarker indicative of early-stage inflammation rather than advanced disease [17]. Moreover, the authors identified a significant inverse correlation between fecal Gal-3 and FC levels ($r = –0.250$, $p = 0.047$), a well-established marker used to monitor disease activity in UC [19].

These observations align with findings from other research groups who have underscored the diagnostic and prognostic significance of Gal-3 in UC [20,21,22].

Frolova and co-authors observed elevated concentrations of Gal-3 in serum samples from UC cases during active disease phases, suggesting its potential link to inflammatory activity [20]. Similarly, Papa Gobbi and colleagues reported dysregulated expression of Gal-1, -3, -4, and -9 in inflamed colonic tissues of IBD cases as opposed to non-inflamed tissues from individuals with non-inflammatory conditions, indicating that a galectin-based tissue signature may aid in the diagnosis of CD and UC [21].

Although their use of linear discriminant integrative analysis successfully differentiated IBD from other intestinal inflammatory disorders, galectin profiling did not enable discrimination between CD- and UC-specific pathological changes [21].

Further, Block and co-authors demonstrated through immunohistochemical analysis that Gal-3 was prominently expressed on immune cells infiltrating the colon in UC, whereas its expression on epithelial cells did not correlate with disease severity, limiting its utility for monitoring progression [22].

Conversely, our findings diverge from those reported by Yu and co-authors, who conducted a comprehensive evaluation of serum Gal-1, -2, -3, -4, -7, and -8 levels in cases with IBD and in healthy controls, aiming to determine their relevance in assessing disease activity. Their results demonstrated that both Gal-1 and Gal-3 were significantly elevated in the serum of UC and CD cases relative to healthy individuals. Nevertheless, despite this elevation, neither Gal-1 nor Gal-3 proved

effective in distinguishing between active and quiescent phases of UC or CD [18].

Regarding the predictive value of fecal Gal-3, we found that cut off point of fecal Gal-3 to identify cases with active UC was (0.447 ng/ml), the sensitivity and specificity were (87.5 and 85% respectively) and the best cut off point to identify response after treatment was (0.3165 ng/ml) with 90% sensitivity and 50% specificity.

Volarevic and co-authors employed ROC analysis to assess the diagnostic performance of serum Gal-3 levels in stratifying UC cases based on disease severity, mild, moderate, or severe colitis. The analysis revealed that serum Gal-3 serves as a highly reliable biomarker for tracking UC progression, demonstrating a sensitivity of 95% and a specificity of 91.7%. The identified serum cutoff values enabling differentiation between mild and moderate, and moderate and severe UC, were 954 pg/mL (0.954 ng/mL) and 580 pg/mL (0.580 ng/mL), respectively. Additionally, fecal Gal-3 concentrations exceeding 553.44 pg/mL (0.553 ng/mL) were indicative of disease attenuation, with a sensitivity of 72.7% and specificity of 60.9%. [17]

Limitations of research

This research has some limitations; like, small number of cases and the research used fecal Gal-3. So, we need to do a large scale research on a large number of subjects and do both fecal and serum Gal-3 to the cases.

Conclusion:

Fecal Gal-3 was a significant marker that increased in ulcerative colitis cases, also significantly associated with increased disease activity.

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Author Contributions

All authors contributed equally to the conception, design, data collection, analysis, and interpretation of this research. The manuscript was collaboratively written and critically reviewed by all co-authors, each of whom has approved the final version and takes full responsibility for the integrity and accuracy of the work.

Conflicts of Interest

The authors declare that there are no conflicts of interest, financial or otherwise, that could have influenced the outcome or presentation of this research. The research was conducted with complete academic transparency and objectivity.

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