Fecal B-cell-activating factor as a new noninvasive marker in the evaluation of ulcerative colitis Egyptian patients: a comparative cross-sectional study

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Background and aim
Diagnosis of ulcerative colitis (UC) is suspected clinically and confirmed through endoscopic biopsy. It can be followed-up and assessed by noninvasive biomarkers such as fecal calprotectin. Recently, B-cell-activating factor (BAFF) has been proposed to be a regulator of B-cell and T-cell immune responses and to be associated with inflammatory processes in autoimmunity. The aim of our study was to clarify the role of fecal BAFF as a simple predictor for disease activity and severity in patients with UC.

Patients and methods
Fifty Egyptian patients with UC were divided into two groups: group I including 40 patients with active UC (newly diagnosed) and group II including 10 patients with inactive UC (previously diagnosed); disease activity was assessed according to the Mayo activity scoring index; fecal BAFF and fecal calprotectin were measured for all patients using enzyme-linked immunosorbent assay.

Results
Significantly higher levels of Fecal BAFF and fecal calprotectin were found among patients with active UC, as compared with inactive UC patients. Fecal BAFF more than or equal to 50 μg/g had 97.5% sensitivity and 100% specificity in predicting disease activity in comparison with fecal calprotectin, which had a sensitivity and specificity of 90% at a cut off value more than or equal to 47 μg/g. In predicting disease severity, fecal BAFF more than or equal to 340 μg/g had a sensitivity of 95% and specificity of 100%, while fecal calprotectin more than or equal to 170 μg/g had a sensitivity of 80% and specificity of 95%.

Conclusion
Fecal BAFF is more sensitive and specific in predicting UC activity and severity than fecal calprotectin.

Keywords:
biomarker, fecal b-cell-activating factor, fecal calprotectin, inflammatory bowel disease, ulcerative colitis

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Introduction

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by attacks of remissions and exacerbations. Although endoscopic modalities with biopsy sampling seem to be the most reliable method for estimating disease severity, they are invasive and costly [1].

Many serum markers are in common use in reflecting UC disease activity; however, they have only modest accuracy. Therefore, adjunctive use of other serum markers that will be more sensitive and specific for determination of disease activity and severity is strongly needed in daily clinical practice [2].

B-cell-activating factor (BAFF), a member of the tumor necrosis factor (TNF) superfamily predominantly produced by myeloid cells and neutrophils, is critical for the maintenance of normal B-cell development and homeostasis [3]. Dysregulated expression and/or function of BAFF has been demonstrated to be associated with several autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus, primary Sjogren's syndrome, and B-cell malignancies [4].

However, limited data are present on the role of BAFF in UC; hence, the aim of our study was to investigate the role of fecal BAFF in evaluating the activity and severity of UC.

Patients and methods

Patients

Over a period of 8 months, this comparative cross-sectional study was performed on 50 Egyptian patients who were more than or equal to 18 years old and diagnosed as UC patients by colonoscopy and tissue histopathology. This study was performed according to the ethical standards for human experimentation approved by the human research committee of Ain Shams University Hospitals and informed written consents were obtained from all participants. They were recruited from the Gastroenterology outpatients' clinic and department of Ain Shams University hospitals.

(1) They were divided into two groups:
Group I: 40 patients with active UC (newly diagnosed).
Group II: 10 patients with inactive UC (previously diagnosed and are being followed-up in the gastroenterology outpatients' clinic)
(2) The activity of UC was assessed according to Mayo activity scoring index, which is a combined endoscopic and clinical scale; it was first proposed by Schroeder *et al.* [5]. It is a composite of subscores from four categories: stool frequency, rectal bleeding, findings of colonoscopy, and physician's global assessment (Fig. 1). It ranges from 0 to 12, with higher scores indicating more severe disease [6].

Exclusion criteria

(1) Patients with rheumatoid arthritis, systemic lupus erythematosus, primary Sjogren's syndrome, and B-cell malignancies.
(2) Patients having infectious colitis within 1 month or microscopic colitis.
(3) Patients with a history of colorectal surgery or colorectal cancer.
(4) Patients who were regularly taking NSAIDs before their enrollment.

Methods

After obtaining informed written consent, the included patients were subjected to the following:

(1) Full history taking and clinical examination with special emphasis on abdominal pain, weight loss, rectal bleeding, diarrhea, malaise, lethargy, anorexia, nausea, tenesmus, abdominal distension, the passage of mucous, vomiting and low-grade fever. Past history of appendectomy or other operations and positive family history of IBD were also recorded, along with full clinical examination. The frequency of bowel movements and amount of rectal bleeding were scored as 0, 1, 2, 3, according to the Mayo score of activity index [5].
(2) Laboratory investigations:
(a) Complete blood picture.

Figure 1

Frequency of bowel movements
0 = Normal for the patient
1 = 1-2 stools/day in addition to the usual
2 = 3-4 stools/day in addition to the usual
3 = >5 stools/day beyond the usual

Rectal Bleeding
0 = No blood
1 = Blood streaks in less than half of evacuations
2 = Evidence of fresh blood in most of the evacuations
3 = Bowel movements with fresh blood

Endoscopic findings
0 = Normal mucosa or inactive disease
1 = Mild disease (enanthema, loss of vascular pattern, mild friability)
2 = Moderate disease (obvious enanthema, loss of vascular pattern, friability, erosions)
3 = Severe disease (spontaneous bleeding, ulceration)

Global Medical Assessment[a]
0 = Normal
1 = Mild disease
2 = Moderate disease
3 = Severe disease

Scores (Points)	Disease severity
≤ 2 and no subscore >1	Clinical remission
3-5	Mild activity
6-10	Moderate activity
11-12	Severe activity

[a]The global medical evaluation takes into account the daily complaint of the patient with regard to abdominal discomfort, pain, a feeling of well-being (normal, above or below the average), physical examination findings and the patient's performance of daily activities.

Mayo score of activity index [5].

(b) Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) titer.
(c) Rheumatoid factor titer, antinuclear antibody, anti-Ro and anti-La antibodies.
(d) Liver function tests: alanine transaminase, aspartate transaminase, total bilirubin, serum albumin and prothrombin time.
(e) Kidney function tests: serum creatinine, blood urea nitrogen, sodium (Na) and potassium (K).
(f) Complete stool analysis, culture and sensitivity to exclude the presence of infection (whenever needed).
(g) Fecal calprotectin titer:

Calprotectin assay was measured in fecal extracts by enzyme-linked immunosorbent assay using the PhiCal Calprotectin kit (Immundiagnostik AG, Bensheim, Germany) according to the manufacturer's instructions.

(a) Fecal BAFF titer:

BAFF contained in fecal extracts was measured using the enzyme-linked immunosorbent assay kit (Quantikine Human BAFF/BLyS/TNFSF13B Immunoassay by R&D Systems Inc., Boston: 1 Broadway, Floor 14 Cambridge, MA, USA and Canada) according to the manufacturer's instructions.

Reference values for stool:

Less than or equal to 50.0 μg/g was considered normal, from 50.1 to 120.0 μg/g was borderline, more than or equal to 120.1 μg/g was abnormal [7].

(3) Endoscopic assessment:

Magnesium citrate, an osmotic laxative (FDA approved), was used for bowel preparation before endoscopic workup [8]. Colonoscopy (CF-Q260; Olympus, Tokyo, Japan) was performed, and multiple biopsies were taken by experienced endoscopists who scored the intestinal inflammation activity according to Mayo activity scoring index [5], blinded to the fecal markers' results. Biopsies were examined by an expert histopathologist to confirm the diagnosis of UC.

Statistical analysis

The collected data were revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 19.0.1 for Windows, 2001; SPSS Inc., Chicago, Illinois). Statistical presentation and analysis of the present study was conducted, using the mean ±SD, χ^2, linear correlation coefficient (r), analysis of variance test and receiver operating characteristic curve analysis. P value less than 0.05 was considered statistically significant.

Results

Descriptive data

Our study included 50 Egyptian patients diagnosed as having UC; there were 24 (48%) male individuals and 26 (52%) female individuals, aged 17–47 years old (mean age, 33.8±7.8 years), as shown in Table 1 with their laboratory data.

According to the Mayo score of activity index, they were classified into the following groups: group I: 40 patients with active UC (their score range, 3–12) and group II: 10 patients with inactive UC (their score ≤2 and no subscore > 2). Active UC patients (n=40) were further classified according to their scores into those having mild disease (50%) (n=20), moderate disease (32.5%) (n=13), and severe disease (17.5%) (n=7), as shown in Fig. 2.

Comparative data

Comparison between active (group I) and inactive UC (group II) patients with regard to their demographic data revealed no statistical significance as regards their age, sex, and family history of IBD.

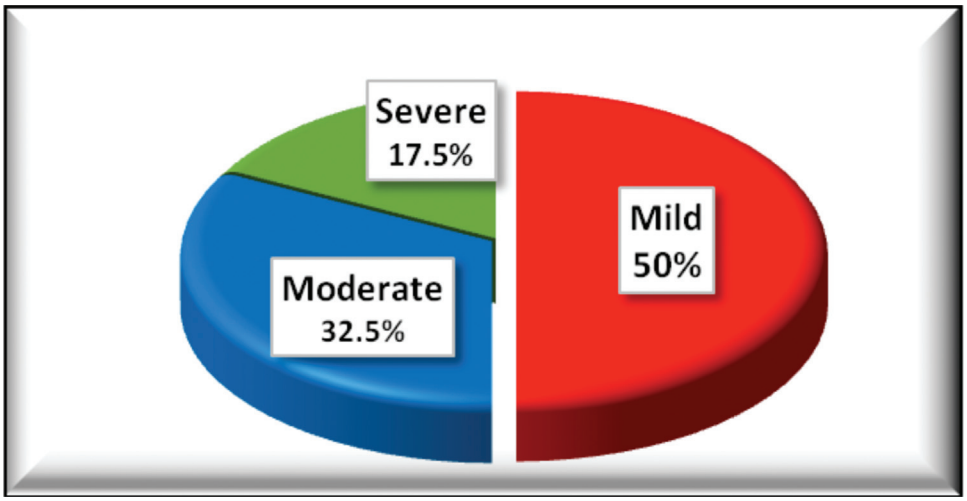
While comparing the laboratory data between group I and group II, there was significant difference between

Table 1 Descriptive data statistics of studied patients (n=50)

Descriptive statistics (N=50)		
	Range	Mean±SD
Age (years)	17–47	33.760±7.771
Hemoglobin (g/dl)	7.9–16.2	12.188±1.944
WBCs (×10^3)	3.9–11.6	7.048±2.176
Platelets (×10^3)	178–413	305.880±69.497
ESR (mm/h)	2–120	31.520±26.602
CRP (mg/l)	0–96	22.840±22.719
Serum albumin (g/dl)	2.9–3.8	3.318±0.229
ALT (U/l)	23–45	36.800±5.714
AST (U/l)	17–64	31.700±8.003
ALP (U/l)	57–98	81.540±11.341
Serum creatinine (mg/dl)	0.7–1.3	0.942±0.142
BUN (mg/dl)	4–24	8.800±4.760
Na (mEq/l)	132–144	139.180±2.953
K (mEq/l)	3.8–5.1	4.400±0.341
Ca (mg/dl)	8.5–9.5	8.982±0.177
PT (s)	11–14	12.540±0.885
INR	1–1.2	1.022±0.055
Mayo score of activity index (0–12)	0–12	5.460±3.553
Fecal calprotectin (μg/g)	10–1200	218.440±266.322
BAFF (μg/g)	10–1640	403.340±409.425

ALP, alkaline phosphate; ALT, alanine transaminase; AST, aspartate transaminase; BAFF, B-cell-activating factor; BUN, blood urea nitrogen; Ca, calcium; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; K, potassium; Na, sodium; PT, prothrombin time; WBC, white blood cell.

Figure 2



Distribution of active UC patients according to disease severity. UC, ulcerative colitis.

them concerning hemoglobin concentration, as it was lower in active UC patients than in the inactive group (with a mean of 11.7 and 14.2, respectively) ($P>0.05$). As regards ESR and CRP, there were statistically significant differences between the two groups, as both titers were higher in patients with active UC ($P<0.05$). Concerning fecal calprotectin titer, there was significant difference between both groups, as titer was higher in patients with active UC ($P<0.05$). As regards fecal BAFF titer, there was a statistically significant difference between the two groups, as shown in Table 2.

On comparing different disease severity groups of active UC ($n=40$) as regards fecal markers (fecal calprotectin titer and fecal BAFF titer), there was a significant difference between the three groups with highest mean titer in patients with severe UC (778.57 ±244.71 and 1248.57±330.93, respectively, with $P<0.05$), as shown in Tables 3 and 4. Moreover, there was a positive significant correlation between fecal markers and disease severity, as fecal calprotectin titer and fecal BAFF titer increase with severity of UC ($r=0.75$ and $r=0.897$, respectively, with $P<0.05$) (Figs 3 and 4). Correlation between fecal markers and studied parameters in all patients ($n=50$) revealed positive significant correlation between them and ESR, CRP and Mayo activity score, with negative significant correlation with hemoglobin ($P<0.05$), as shown in Tables 5 and 6.

At the best cut-off value of more than or equal to 50 µg/g, fecal calprotectin had a sensitivity of 90% and a specificity of 90%, for detection of active UC patients over inactive ones using receiver operating characteristic curve analysis with an overall accuracy of 95.5% (Table 7, Fig. 5), whereas fecal BAFF can predict active UC patients from inactive ones at the cutoff point of more than or equal to 47 µg/g with a sensitivity of 97.5% and specificity of 100%, with an overall accuracy of 99.8% (Table 7, Fig. 5).

With further subdivision of the first group according to the severity of the disease, the following was revealed: fecal calprotectin at a cut-off value more than or equal to 170 µg/g had 80% sensitivity and 95% specificity in predicting severe UC among active UC cases, with an overall accuracy of 88% (Table 8, Fig. 6). In contrast, and at a cut off value more than or equal to 340 µg/g, fecal BAFF had 95% sensitivity and 100% specificity in predicting severe UC among active UC cases, with an overall accuracy of 98.7% (Table 8, Fig. 6).

Discussion

Diagnosis of UC is based on a combination of history and examination, blood parameters, endoscopy and tissue histopathology [9]. In order to avoid invasive investigations, several noninvasive markers have been evaluated for their capacity to distinguish between functional and organic inflammatory gastrointestinal disease [10]. However, they still have limited capacity for prediction of disease activity and severity [11]. It is evident that a simple, rapid, sensitive, specific, noninvasive marker to evaluate colonic inflammation in UC is needed [12].

Therefore the focus of this study was to evaluate the utility of fecal BAFF as a simple, easy and available predictor for disease activity and severity in patients with UC.

Table 2 Comparison between the two groups as regards laboratory investigations

Laboratory investigations	Groups		*t* test	
	Active UC (*N*=40)	Inactive UC (*N*=10)	*t*	*P* value
Hemoglobin (g/dl)				
Range	7.9–14.1	12.9–16.2	–4.191	<0.001*
Mean±SD	11.690±1.789	14.180±1.090		
WBCs ($\times10^3$)				
Range	4–11.6	3.9–9.2	1.580	0.121
Mean±SD	7.288±2.185	6.090±1.952		
Platelets ($\times10^3$)				
Range	178–413	187–387	–0.415	0.680
Mean±SD	303.825±72.065	314.100±60.807		
Serum albumin (g/dl)				
Range	2.9–3.8	3–3.6	0.275	0.784
Mean±SD	3.323±0.236	3.300±0.211		
ALT (U/l)				
Range	23–45	26–45	–0.061	0.951
Mean±SD	36.775±5.824	36.900±5.547		
AST (U/l)				
Range	17–64	23–43	0.394	0.695
Mean±SD	31.925±8.365	30.800±6.663		
ALP (U/l)				
Range	57–98	57–96	0.383	0.703
Mean±SD	81.850±11.405	80.300±11.595		
Serum creatinine (mg/dl)				
Range	0.7–1.3	0.7–1.1	0.546	0.588
Mean±SD	0.948±0.141	0.920±0.148		
BUN (mg/dl)				
Range	4–24	6–24	–1.194	0.238
Mean±SD	8.400±4.500	10.400±5.661		
Na (mEq/l)				
Range	132–144	134–144	–0.261	0.795
Mean±SD	139.125±2.919	139.400±3.239		
K (mEq/l)				
Range	3.8–5.1	4–4.9	–0.514	0.609
Mean±SD	4.388±0.349	4.450±0.321		
Ca (mg/dl)				
Range	8.5–9.5	8.7–9.2	0.636	0.528
Mean±SD	8.990±0.182	8.950±0.158		
PT (s)				
Range	11–14	11–13	1.370	0.177
Mean±SD	12.625±0.925	12.200±0.632		
INR				
Range	1–1.2	1–1	1.442	0.156
Mean±SD	1.028±0.060	1.000±0.000		
ESR (mm/h)				
Range	10–120	2–22	2.914	0.005*
Mean±SD	36.625±27.312	11.100±6.420		
CRP (mg/l)				
Range	2–96	0–12	3.073	0.003*
Mean±SD	27.400±23.198	4.600±4.006		
BAFF (μg/g)				
Range	40–1640	10–42	3.644	0.001*
Mean±SD	497.675±406.139	26.000±10.499		
Fecal calprotectin (μg/g)				
Range	30–1200	10–90	2.579	0.013*
Mean±SD	264.425±279.553	34.500±22.785		

ALP, alkaline phosphate; ALT, alanine transaminase; AST, aspartate transaminase; BAFF, B-cell-activating factor; BUN, blood urea nitrogen; Ca, calcium; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; K, potassium; Na, sodium; PT, prothrombin time; WBC, white blood cell. *Significant *P* value.

Table 3 Comparison between fecal calprotectin titer and disease severity in active ulcerative colitis patients (group I) (*N*=40)

Disease severity	Fecal calprotectin (μg/g)		ANOVA	
	Range	Mean±SD	*F*	*P* value
Mild (*N*=20)	30–180	96.350±41.354	71.272	<0.001*
Moderate (*N*=13)	50–510	246.154±140.332		
Severe (*N*=7)	500–1200	778.571±244.706		
Tukey's test				
Mild and moderate	Mild and severe		Moderate and severe	
0.007*	<0.001*		<0.001*	

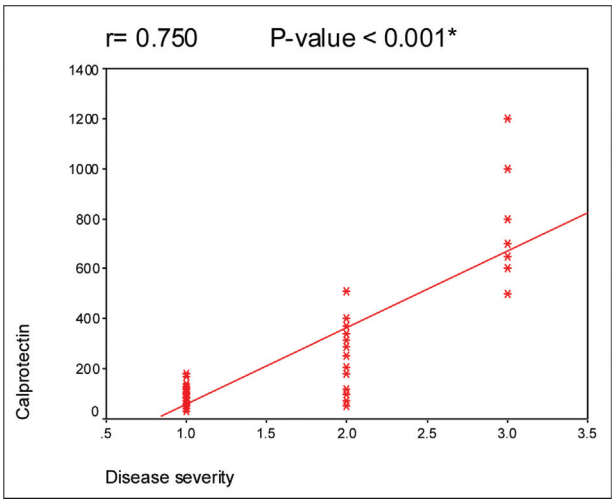
ANOVA, analysis of variance. *Significant *P* value.

Table 4 Comparison between fecal B-cell-activating factor titer and disease severity in group I patients (*N*=40)

Disease severity	Fecal BAFF (μg/g)		ANOVA	
	Range	Mean±SD	*F*	*P* value
Mild (*N*=20)	40–340	225.600±85.377	100.160	<0.001*
Moderate (*N*=13)	295–700	511.923±131.459		
Severe (*N*=7)	770–1640	1248.571±330.929		
Tukey's test				
Mild and moderate	Mild and severe		Moderate and severe	
<0.001*	<0.001*		<0.001*	

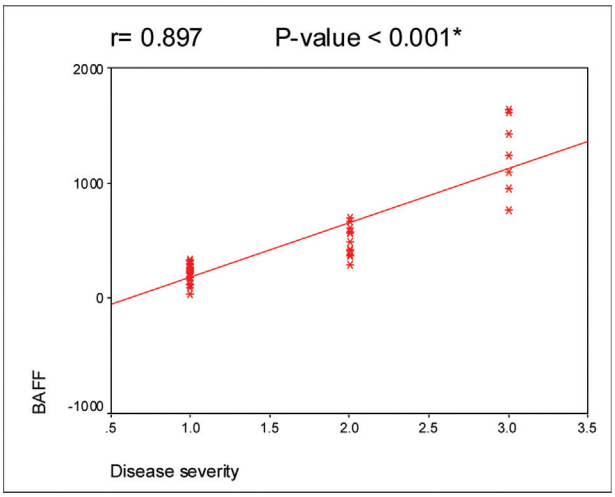
ANOVA, analysis of variance; BAFF, B-cell-activating factor. *Significant *P* value.

Figure 3



Correlation between fecal calprotectin titer and disease severity.

Figure 4



Correlation between fecal BAFF titer and disease severity. BAFF, B-cell-activating factor.

According to the Mayo activity scoring index [5], the studied patients were divided into two groups: 10 patients with inactive UC and 40 patients with active UC, subdivided into 20 patients with mild disease, 13 moderate and seven patients with severe UC.

As regards demographic data, the mean age of cases of UC was 33.8±7.8 years. This was in accordance with another study conducted by Zahedi *et al.* [13], who reported that the mean age of patients with UC was 39.4 years.

Under normal circumstances, CRP is produced by hepatocytes in low quantities (<1 mg/l). However, following an acute-phase stimulus such as inflammation, hepatocytes rapidly increase the production of CRP under the influence of interleukin-6 and TNF-α and may reach peak levels of 350–400 mg/l [14]. The ESR determination reflects the changes in the various acute-phase proteins [15]. Hence, as part of acute-phase reactants, both ESR and CRP are increased in active UC patients compared with inactive patients.

In our study, CRP was significantly elevated in patients with active UC compared with those with inactive UC, with mean values of 27.4±23.2 and 4.6±4, respectively.

ESR also was higher in group I patients than in group II patients, with mean values of 36.6±27.3 and 11.1 ±6.4, respectively. Our study was in line with Peyrin-Biroulet *et al.* [16], and Solem *et al.* [17], who found that ESR and CRP were helpful in differentiating active IBD from inactive IBD; hence, they might be used as markers of disease activity. However, ESR may be influenced by the size, shape, and number of erythrocytes and by other factors, including age, sex, anemia, blood dyscrasias, and pregnancy, which can account for the different results between the studies [18].

It is known that colonoscopy and taking biopsies for histopathological examination is essential for diagnosing IBD. It is used to make an initial diagnosis of IBD, distinguish CD from UC, assess disease extension and activity, and monitor response to treatment and survey for dysplasia [19].

Aiming to find noninvasive markers for diagnosis of IBD, fecal biomarkers are the most important markers, which comprise a group of substances that are produced by the inflamed neutrophils in intestinal mucosa. The main use of these markers is in diagnosing and assessing disease severity. They may also have a role in assessing treatment effect and prediction of relapse [20].

As regards fecal calprotectin titer, we found in our study that there was a significant difference between both groups, being higher in the active group with a mean value of 264.4±279.56 μg/g and a mean value of 34.5±22.79 μg/g in the inactive group (P=0.013). Concerning disease severity, there was also a statistically significant difference between different disease severity groups of active UC (P>0.001). Using Spearman's rho, there was a positive

Table 5 Correlation between fecal calprotectin titer and studied parameters in all patients (n=50)

Correlations		
	Fecal calprotectin	
	r	*P* value
Age (years)	–0.128	0.432
Hemoglobin (g/dl)	–0.477	0.002*
WBCs (×10^3)	0.135	0.406
Platelets (×10^3)	0.114	0.484
ESR (mm/h)	0.718	<0.001*
CRP (mg/l)	0.751	<0.001*
Serum albumin (g/dl)	0.104	0.523
ALT (U/l)	0.014	0.930
AST (U/l)	–0.042	0.798
ALP (U/l)	0.264	0.100
Serum creatinine (mg/dl)	–0.153	0.347
BUN (mg/dl)	0.079	0.627
Na (mEq/l)	–0.144	0.374
K (mEq/l)	0.063	0.701
Ca (mg/dl)	–0.177	0.276
PT (s)	–0.246	0.126
INR	–0.132	0.416
Mayo score of activity index (0–12)	0.858	<0.001*

ALP, alkaline phosphate; ALT, alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; Ca, calcium; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; K, potassium; Na, sodium; PT, prothrombin time; WBC, white blood cell. *Significant *P* value.

Table 6 Correlation between B-cell-activating factor and other parameters in all patients (N=50)

Correlations		
	Fecal BAFF	
	r	*P* value
Age (years)	–0.093	0.568
Hemoglobin (g/dl)	–0.580	<0.001*
WBCs (×10^3)	0.071	0.665
Platelets (×10^3)	0.109	0.503
ESR (mm/h)	0.680	<0.001*
CRP (mg/l)	0.696	<0.001*
Serum albumin (g/dl)	0.140	0.390
ALT (U/l)	–0.023	0.888
AST (U/l)	–0.013	0.938
ALP (U/l)	0.157	0.334
Serum creatinine (mg/dl)	0.029	0.860
BUN (mg/dl)	0.159	0.328
Na (mEq/l)	–0.044	0.790
K (mEq/l)	0.123	0.449
Ca (mg/dl)	–0.162	0.317
PT (s)	–0.285	0.075
INR	–0.184	0.255
Mayo Score of activity index (0–12)	0.899	<0.001*

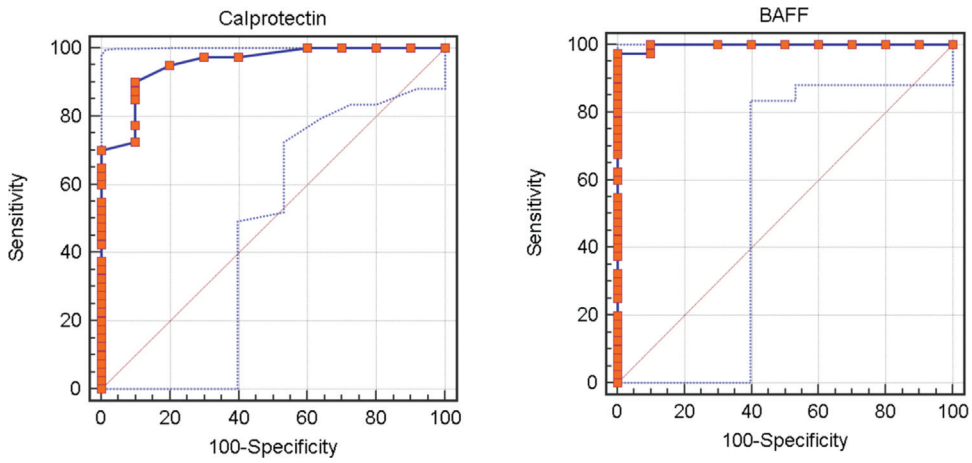
ALP, alkaline phosphate; ALT, alanine transaminase; AST, aspartate transaminase; BAFF, B-cell-activating factor; BUN, blood urea nitrogen; Ca, calcium; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; K, potassium; Na, sodium; PT, prothrombin time; WBC, white blood cell.

Table 7 Comparison between fecal B-cell-activating factor and fecal calprotectin titers as regards sensitivity and specificity to disease activity

	ROC curve for disease activity					
	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
Calprotectin	≥50	90.0	90.0	97.3	69.2	95.5%
BAFF	≥47	97.50	100.00	100.0	90.9	99.8%

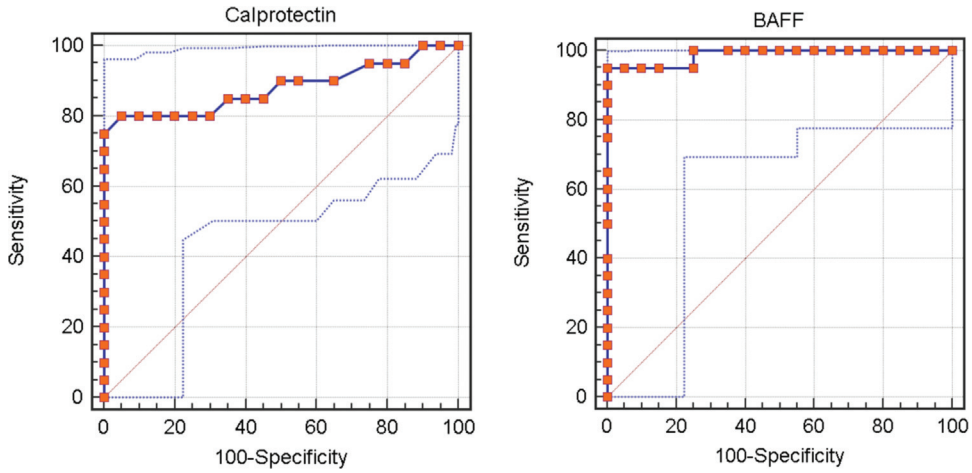
BAFF, B-cell-activating factor; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic.

Figure 5



ROC curve representing sensitivity and specificity of fecal BAFF and fecal calprotectin in disease activity. BAFF, B-cell-activating factor; ROC, receiver operating characteristic.

Figure 6



ROC curve representing sensitivity and specificity of fecal BAFF and fecal calprotectin in disease severity. BAFF, B-cell-activating factor; ROC, receiver operating characteristic.

Table 8 Comparison between fecal B-cell-activating factor and fecal calprotectin titers as regards sensitivity and specificity to disease severity

	ROC curve for disease severity					
	Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
Calprotectin	≥170	80.0	95.0	94.1	82.6	88%
BAFF	≥340	95.0	100.00	100.0	95.2	98.7%

BAFF, B-cell-activating factor; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic.

significant correlation between fecal calprotectin titer and disease severity, as its titer increases with severity of UC (r=0.75, P<0.001). This was in agreement with a study conducted by Silberer *et al.* [21], who found that fecal calprotectin correlates with the endoscopically assessed severity of intestinal inflammation. Moreover, Egea-Valenzuela *et al.* [22], have proposed fecal calprotectin as a biomarker of enteric inflammation, as its presence in the stool is directly proportional to neutrophil activity in the intestinal lumen. Our study was also in line with the study by Paduchova and Durackova [12], who proposed the role of fecal calprotectin to differentiate mild from moderate inflammation of the gastrointestinal tract.

Concerning fecal BAFF titer, our study found that there was a statistically significant difference between both groups, it being higher in the active group (P=0.001) with a mean value of 497.68±406.14 μg/g and a mean value of 26±10.5 μg/g in the inactive group.

Comparing the ratios as regards disease severity according to Mayo activity scoring index, there was a statistical significance of fecal BAFF titer for determining disease severity as mild, moderate and severe, with the mean for them being 225.6, 511.9 and 1248.6 μg/g, respectively, with *P* value less than 0.001. Using Spearman's rho, there was positive significant correlation between fecal BAFF titer and disease severity, as its titer increases with severity of UC (r=0.897, P<0.001). This study was in line with the study carried out by Zhang *et al.* [23], which demonstrated that BAFF expression is increased in serum, local colon, and feces of patients with IBD. Furthermore, a strong positive correlation was observed between BAFF and disease activity in patients with UC, and also with proinflammatory cytokines TNF-α and interleukin-1b. These results highlight an important role of elevated BAFF levels in the pathogenesis of IBD.

Comparing the two groups as regards disease activity, fecal calprotectin's sensitivity and specificity were 90% at a cut-off value of more than or equal to 47 μg/g with an accuracy of 95.5%, positive predictive value (PPV) of 97.3% and negative predictive value (NPV) of 69.2%; while fecal BAFF's sensitivity and specificity were 97.5 and 100%, respectively, at a cut-off value of more than or equal to 50 μg/g with an accuracy of 99.8%, PPV of 100% and NPV of 90.9%, which implies that fecal BAFF is more sensitive and specific than calprotectin for determining disease activity (according to Mayo activity scoring index). Furthermore, as regards the disease severity, fecal calprotectin's sensitivity and specificity were 80 and 95%, respectively, at a cut-off value of more than or equal to 170 μg/g, with an accuracy of 88%, 94.1% PPV, and 82.6% NPV, while fecal BAFF's sensitivity and specificity were 95 and 100% at a cut-off value of more than or equal to 340 μg/g, with an accuracy of 98.7%, 100% PPV, and 95.2% NPV; hence, fecal BAFF was also more sensitive and specific for determining disease severity than calprotectin.

This was in agreement with Fu *et al.* [24], who detected fecal BAFF and calprotectin levels in the same samples; they implied that fecal BAFF could be a good indicator for overall evaluation of mucosal inflammation and severity. As regards disease severity, BAFF more than or equal to 227.3 μg/g yielded 84% sensitivity, 100% specificity, 100% PPV, and 64% NPV, while calprotectin more than or equal to 50 μg/g yielded 76% sensitivity, 93% specificity, 97% PPV, and 53% NPV. Hence, fecal BAFF has a better performance as compared with fecal calprotectin in the evaluation of intestinal inflammation in UC.

The present study had a few limitations. First, the number of patients included in the present study is relatively small. Second, the underlying relations between fecal BAFF, calprotectin and extension of UC were not studied.

Conclusion

Our results revealed that fecal BAFF is a simple and noninvasive marker that can be helpful for differentiating active UC from inactive disease; it also correlates with grade of severity and with higher sensitivity and specificity than fecal calprotectin in determining disease activity and severity, implying that BAFF is a promising biomarker in UC and that it can be an additive to the other tools that clinicians use in practice. Future studies may be needed to evaluate the role of fecal BAAF as a biomarker for surveillance of colonic cancer in UC patients.

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Conflicts of interest

There are no conflicts of interest.

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