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Study of serum neutrophil gelatinase-associated lipocalin level in inflammatory bowel disease patients

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Objective
This study aimed to evaluate the role of neutrophil gelatinase-associated lipocalin (NGAL) in the determination of disease activity and response to treatment in inflammatory bowel disease (IBD) patients.

Background
IBDs are among the most important gastrointestinal diseases. Confirmation of the diagnosis and detection of disease activity mostly entails utilization of invasive procedures. NGAL is a protein mainly secreted by neutrophils. Previously, in IBD, overexpression of NGAL in colon epithelium has been shown.

Patients and methods
This study was conducted on 35 naive patients with clinical, laboratory, endoscopic, and histopathological findings of active IBD, including active ulcerative colitis (UC) and active Crohn's disease (CD), and the same patients of the first group while on remission by medical therapy. In addition, 20 non-IBD patients were enrolled as the control group. Patients and controls were subjected to laboratory investigations, abdominal ultrasound, lower gastrointestinal endoscopy, and biopsy taking for histopathology and quantitative measurement of serum NGAL using enzyme-linked immunosorbent assay kits.

Results
There was a highly significant elevation of serum NGAL in active IBD patients (active UC and active CD) ($P < 0.001$) compared with inactive IBD patients (inactive UC and inactive CD) and the control group. In addition, there was a highly significant elevation of serum NGAL in inactive IBD patients ($P < 0.001$) when compared with the control group. Serum NGAL correlated positively with inflammatory markers, UC activity index, histopathological activity, and clinical CD activity index.

Conclusion
Serum NGAL is valuable noninvasive marker in the assessment of IBD patients regarding disease activity and response to treatment.

Keywords:
Crohn's disease, inflammatory bowel disease, neutrophil gelatinase-associated lipocalin, ulcerative colitis

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Introduction

Inflammatory bowel disease (IBD) is an idiopathic disease including Crohn's disease (CD) and ulcerative colitis (UC) and is characterized by chronic relapsing intestinal inflammation. It is thought that IBD results from an aberrant and continuing immune response to the microbes in the gut, catalyzed by the genetic susceptibility of the individual. Although the etiology of IBD remains largely unknown, it involves a complex interaction between the genetic, environmental, or microbial factors and the immune responses [1].

Endoscopy is used to make an initial diagnosis of IBD, distinguish CD from UC, assess the disease extent and activity, monitor response to therapy, allow for surveillance of dysplasia or neoplasia, and provide endoscopic treatment such as stricture dilation [2]. Unless contraindicated because of severe colitis or possible toxic megacolon, a full colonoscopy with intubation of the terminal ileum should be carried out during the initial evaluation of patients with a clinical presentation suggestive of IBD [3].

Neutrophil granulocytes, in particular, are responsible for the destructive process and symptoms seen in inflammatory disease by releasing proteolytic enzymes and proteins as lipocalins [4]. Neutrophil gelatinase-associated lipocalin (NGAL), known as lipocalin-2, a protein secreted by neutrophils, exerts

bacteriostatic effects in infection by its ability to capture and decrease siderophores secreted by certain bacteria, thus inhibiting bacterial growth [5]. There is an overexpression of NGAL in the colon epithelium, suggesting that NGAL evaluation may help in studying the pathophysiology of IBD and assessment of the disease activity [6].

Patients, methods, and aim

The present study aimed to evaluate the role of serum NGAL in the assessment of IBD patients (UC and CD) as regards disease activity, correlation with inflammatory markers, and IBD activity indices, as well as the assessment of response of these patients to treatment. This study was conducted on 35 patients with IBD who were referred to the endoscopy unit of the Tropical Medicine Department, Menoufia University Hospital, in the period between March 2013 and February 2015. There were 26 (74.3%) men and nine (25.7%) women, their ages ranging between 28 and 59 years with a mean value of 38.23 ± 8.75 years. In addition, 20 non-IBD patients of matched age and sex were selected as the disease control group (Figs. 1 and 2).

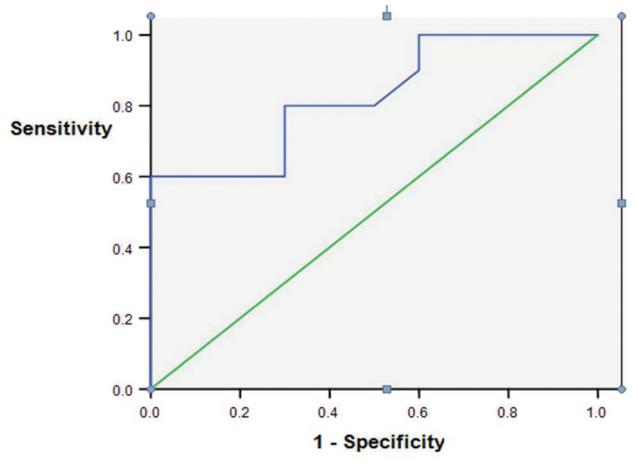
Patients and controls were classified into the following groups:

- Group I (active IBD group): it included 35 naive patients with clinical, laboratory, endoscopic, and histopathological findings of active IBD. These patients were classified into two subgroups:
  - Group Ia (active UC group), which included 25 naive patients with evidence of active UC. This subgroup included 18 (72%) men and seven (28%) women, their ages ranging between 28 and 59 years with a mean value of 39.28 ± 9.33 years
  - Group Ib (active CD group), which included 10 naive patients with evidence of active CD; there were eight (80%) men and two (20%) women, their ages ranging between 28 and 48 years with a mean value of 36.5 ± 6.8 years
- Group II (inactive IBD group): it included the same patients as in group I while on remission induced by medical therapy. They were classified into two subgroups:
  - Group IIa (inactive UC group), which included the same patients as in group Ia (UC patients) but on remission [induction of remission in active UC was achieved by using a full dosage of aminosalicylates (5-ASAs) (oral or per rectal forms) with or without steroids (oral or parental or per rectal) and azathioprine] regarding severity and extend of the disease
  - Group IIb (inactive CD group), which included the same patients as in group Ib (CD patients) but on remission (remission in active CD was induced by using mesalazine, ciprofloxacin, metronidazol with or without steroids, and azathioprine) regarding severity and extend of the disease
- Group III (control group): it included 20 patients of matched age and sex complaining of lower gastrointestinal (GI) symptoms but without laboratory, colonoscopic, and histopathological evidence of IBD [11 patients diagnosed with irritable bowel syndrome (IBS) based on the Rome 3 criteria, seven patients with piles, and two patients with anal fissure].

Exclusion criteria

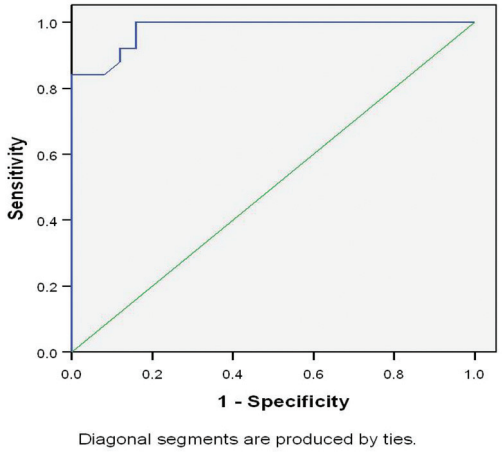
Patients with a past history of any malignant condition, especially colorectal carcinoma, and history of operation, especially GI surgery, and patients with lever cell failure and chronic renal failure (as the lipocalin is expressed in a very low level in the hepatocytes

Figure 1



Receiver operating characteristic curve to predict exacerbation in Crohn's disease.

Figure 2



Receiver operating characteristic curve to predict exacerbation in ulcerative colitis.

endothelial cells, and tubular cells of the kidneys) were excluded from the study.

The study was conducted in accordance with the Declaration of Helsinki. All participants signed a written informed consent, and the Ethics Committee of the Faculty of Medicine, Menoufia University, approved the study protocol.

All patients and controls were subjected to the following:

Full detailed history taking and complete clinical examination to determine clinical activity in IBD patients.

An imaging study in the form of abdominal ultrasonography was performed for all patients to exclude evidence of chronic liver disease or kidney disease.

Total colonoscopy with illioscopy and biopsy taking

Olympus Evis CV 100 videoscope (Shinjuku-ku, Tokyo, Japan) (Olympus, Japan) was used for histopathological examination to confirm the diagnosis. Bowel preparation was done using polyethylene glycol (MoviPrep, Westerville, Ohio, USA). Endoscopy was carried out after sedation using midazolam (Medathetic 5 mg/ml). Colonoscopic extend and disease severity and complications were reported.

Colonoscopic biopsies were taken as every 10 cm from four quadrants, from stricture, mass lesion, or polyps with adjacent flat mucosa. The sample was preserved in formalin and sent for a histopathological study [7]. Assessment of disease severity (activity indices) was based on ulcerative colitis activity index (UCAI) (Mayo score) [8] and histopathological UC grading [9] in UC groups, and on Crohn's disease activity index (CDAI) [10], endoscopic CDAI [11], and CD histopathological grading in CD patients [12].

Laboratory investigations

All laboratory investigations were carried out in the Medical Biochemistry Department, Faculty of Medicine, Menoufia University.

Five ml of venous blood samples were drawn from each patient, 2 ml of blood were used on EDTA tubes for measuring complete blood count and erythrocyte sedimentation rate (ESR), whereas the remaining 3 ml in serum separator tube was allowed to clot for 10–20 min at room temperature before centrifugation for 20 min at the speed of 2000–3000 rpm. Serum was removed and used for measuring C-reactive protein (CRP), renal function tests (serum creatinine and blood urea nitrogen), and liver function tests [serum albumin, aspartate transaminase, alanine transaminase, bilirubin (total and direct), and international normalized ratio]. Stool analysis was performed for each patient and a quantitative measurement of serum NGAL by enzyme-linked immunosorbent assay technique was carried out (Wkea Med Supplies Corp., Changchun, China).

The kit assay of human NGAL level in the sample used purified human NGAL antibody to coat microtiter plate wells and make solid-phase antibody, then NGAL was added to the wells. Combined NGAL with enzyme-labeled, become antibody–antigen enzyme complex, after washing completely, adding substrate. The substrate becomes blue and the color change is measured spectrophotometrically at a wavelength of 450 nm. The concentration of NGAL in the samples is then determined by comparing the measurements of the samples to the standard curve.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using statistical package for the social sciences 19.0 for Windows (SPSS; SPSS Inc., Chicago, Illinois, USA) and MedCalc 13 for Windows (MedCalc Software bvba, Ostend, Belgium). A P value less than 0.05 was considered statistically significant.

Results

There was no significant difference between the studied groups as regards age distribution (t = 0.53; P = 0.66) and sex (χ^2 = 0.12; P = 0.73).

Clinical evidences of activity of IBD (body built, diarrhea, rectal bleeding, abdominal tenderness, abdominal masses, fever, and pallor) were present in various proportions in active IBD groups, whereas they were absent in IBD groups on remission leucocytosis, and anemia was present in various proportions in active IBD groups.

There was a highly significant increase in ESR (first hour) and CRP of active UC (72.12 ± 13.76 mm/h and 44.20 ± 19.61 mg/l, respectively) and of active CD(79.80±11.56mm/hand34.40±6.82mg/l,respectively) when compared with inactive UC (18.60 ± 3.0 mm/h and 5.74 ± 1.25 mg/l, respectively) and inactive CD (37.40 ± 11.02 mm/h and 11.10 ± 10.44 mg/l, respectively) and control groups (16.35 ± 2.94 mm/h and 4.05 ± 1.50 mg/l, respectively).

The scoring of activity indices denoted disease activity ranging from mild to severe in active IBD

groups (UC and CD), whereas these scoring systems confirmed disease remission in inactive IBD groups (UC and CD) (Table 1).

Histopathological evidences of activity were present in the active UC group (lamina properia neutrophils and eosinophils, neutrophils in epithelium, crypt destruction, erosion or ulceration) and the active CD group (epithelial damage, polymorphnuclear cells infiltrate in Lichen Planus (LP) and/or in epithelium, erosions or ulcers, active granuloma), whereas they were absent in the IBD groups on remission (Table 2).

Table 1 Activity indices in inflammatory bowel disease groups

UCAI	UC groups	
	Active UC (*n* (%))	Inactive UC (*n* (%))
0-2 (remission)	0 (0)	25 (100)
3-6 (mild)	3 (12)	0 (0)
7-9 (moderate)	8 (32)	0 (0)
>10 (sever)	14 (56)	0 (0)
CD activity index	**CD groups**	
	Active CD (*n* (%))	Inactive CD (*n* (%))
Clinical CD activity index		
<5 (remission)	0 (0)	10 (100)
≥5 (active disease)		
6-10 (mild)	3 (30)	0 (0)
11-15 (moderate)	3 (30)	0 (0)
>15 (sever)	4 (40)	0 (0)
Endoscopic CD activity index (E-CDI)		
<6 (range: 0.2-3.6) (inactive CD)	0 (0)	10 (100)
≥6 (range: 8.8-13.2) (active CD)	10 (100)	0 (0)

CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis; UCAI, ulcerative colitis activity index.

Table 2 Histopathological findings in inflammatory bowel disease groups (active and inactive)

UC histopathological grade	UC groups (*N*=25)	
	Active (*n* (%))	Inactive (*n* (%))
Grade 0: architectural changes	25 (100)	25 (100)
Grade 1: chronic inflammatory infiltrate	25 (100)	0 (0)
Grade 2: lamina properia neutrophils and eosinophils	25 (100)	0 (0)
Grade 3: neutrophils in epithelium	25 (100)	0 (0)
Grade 4: crypt destruction	11 (44)	2 (8)
Grade 5: erosion or ulceration	8 (32)	0 (0)
	CD groups (*N*=10)	
	Active (*n* (%))	Inactive (*n* (%))
CD histopathological findings		
Architural changes	10 (100)	10 (100)
Epithelial damage	10 (100)	0 (0)
Mononuclear cells infiltration in LP	10 (100)	10 (100)
PMN infiltrate in LP	10 (100)	0 (0)
PMN in epithelium	10 (100)	0 (0)
Erosions or ulcers	10 (100)	0 (0)
Granuloma	10 (100)[a]	10 (100)[b]

CD, Crohn's disease; PMN, polymorphnuclear cells; UC, ulcerative colitis. [a]Active granuloma (neutrophils are present). [b]Inactive granuloma (neutrophils are absent).

There was a highly significant elevation of serum NGAL in active IBD patients [active UC (90.62 ± 67.87 ng/ml) and active CD (41.12 ± 8.99 ng/ml)] when compared with inactive IBD patients [(inactive UC (25.68 ± 6.10 ng/ml) and inactive CD (30.02 ± 6.32 ng/ml)] and the control group (9.12 ± 3.30 ng/ml). In addition, there was a significant elevation of serum NGAL in active UC when compared with active CD and a highly significant elevation of serum NGAL in inactive IBD (UC and CD) when compared with the control group (Table 3).

Analysis of data obtained from the ROC curve revealed that serum NGAL at cut-off point 33.7 ng/ml could detect disease activity in UC patients [sensitivity (100%), specificity (84%), accuracy (92.0%), positive predictive value (PPV) (86.2%), negative predictive value (NPV) (100%)]. Whereas at this cut-off point, serum NGAL could detect disease activity in CD patients with lower values (sensitivity of 80.0%, specificity of 70.0%, accuracy of 75.0%, PPV of 72.7%, NPV of 77.8%) (Table 4).

In UC patients, serum NGAL was correlated highly significantly with ESR (r = +0.70, P < 0.001), CRP (r = +0.82, P < 0.001), UCAI (r = +0.72, P < 0.001), and UC histopathological grading (r = +0.47, P = 0.04). In CD patients serum NGAL was correlated significantly with CRP (r = +0.543, P = 0.016), ESR (r = +0.49, P = 0.03), clinical CDAI (r = +0.47, P = 0.04), and CD histopathological grading (r = +0.47, P = 0.04); however, there was no significant correlation of serum NGAL with endoscopic CDAI (r = +0.33, P = 0.15) (Table 5).

Discussion

The present study revealed a highly significant elevation of serum NGAL in active IBD patients [active UC (90.62 ± 67.87 ng/ml) and active CD (41.12 ± 8.99 ng/ml)] when compared with inactive IBD patients [(inactive UC (25.68 ± 6.10 ng/ml) and inactive CD (30.02 ± 6.32 ng/ml)] and the control group (9.12 ± 3.30 ng/ml). The elevation of serum NGAL in the active UC group was significant when compared with the active CD group. Moreover, serum NGAL was positively correlated with inflammatory markers (CRP and ESR) in UC and CD patients, UCAI and UC histopathological grading in UC patients, and clinical CDAI and CD histopathological grading in CD patients. These results were in agreement with the results of previous studies in some respects and in contrast to them in some other respects.

Oikonomou *et al.* [13] reported that serum NGAL levels were elevated in IBD patients compared with either HC or IBS patients (in agreement with our

Table 3 Serum neutrophil gelatinase-associated lipocalin in the studied groups

Variables	Studied groups				Controls (*N*=20)
	IBD groups (*N*=35)				
	Active IBD		Inactive IBD		
	Active UC (*N*=25)	Active CD (*N*=10)	Inactive UC (*N*=25)	Inactive CD (*N*=10)	
Serum NGAL (ng/l)					
Mean±SD	90.62±67.87	41.12±8.99	25.68±6.10	30.02±6.32	9.12±3.30
Range	34.8-253.2	30.6-54.4	16.5-36.6	16.8-36.2	5.7-19.6
			U		*P*
Active vs. inactive UC groups			5.80		0.001
Active vs. inactive CD groups.			2.46		0.01
Active UC vs. active CD groups			2.26		0.02
Inactive UC vs. inactive CD groups			1.70		0.09
Active UC vs. control groups			5.71		<0.001
Active CD vs. control groups			4.40		<0.001
Inactive UC vs. control groups			5.62		<0.001
Inactive CD vs. control groups			4.36		<0.001
Active UC vs. inactive CD			5.62		<0.001
Active CD vs. inactive UC			4.36		<0.001

CD, Crohn's disease; IBD, inflammatory bowel disease; NGAL, neutrophil gelatinase-associated lipocalin; UC, ulcerative colitis.

Table 4 Validity of serum neutrophil gelatinase-associated lipocalin for prediction of activity of Crohn's disease and ulcerative colitis

Serum NGAL at cut-off point (33.7 ng/l)	Sensitivity (%)	Specificity (%)	Positive predictive value (PPV) (%)	Negative predictive value (NPV) (%)	Accuracy
In UC	100	84.0	86.2	100	92.0
In CD	80.0	70.0	72.7	77.8	75.0

Sensitivity, specificity, PPV, NPV, and accuracy of serum NGAL at cut-off point 33.7 ng/l for prediction of activity in UC patients were higher when compared with those in CD patients. CD, Crohn's disease; NGAL, neutrophil gelatinase-associated lipocalin; UC, ulcerative colitis.

Table 5 Correlation between serum neutrophil gelatinase-associated lipocalin and various factors in inflammatory bowel disease patients

Variables	Serum NGAL	
	Correlation coefficient	*P*
CRP		
UC	+0.82	<0.001 (HS)
CD	+0.543	0.016 (S)
ESR		
UC	+0.70	<0.001 (HS)
CD	+0.49	0.03 (S)
UCAI	+0.72	<0.001 (HS)
Clinical CD activity index	+0.47	0.04 (S)
E-CDAI	+0.33	0.15 (NS)
UC histopathological grading	+0.74	0.001 (HS)
CD histopathological grading	+0.47	0.04 (S)

CD, Crohn's disease; CRP, c-reactive protein; E-CDAI, endoscopic Crohn's disease activity index; HS, highly significant; ESR, erythrocyte sedimentation rate; S, significant; UC, ulcerative colitis.

results) and no significant difference was shown between UC and CD (in contrast to our results). The authors suggested that their results strongly implicating NGAL involvement in bowel inflammation and in the pathophysiology of IBD could reflect the degree of IBD activity. However, these results cannot yet established NGAL assessment as a single blood test in IBD patients [13].

Mowat *et al.* [14] reported that IBD patients treated with 5-ASAs monotherapy had lower levels of NGAL compared with other treatments. The authors suggested that monotherapy with 5-ASAs, chiefly utilized in quiescent and mild UC, is correlated with relatively lower grade of inflammation, compared with co-administration with other drugs warranted to control moderate and severe disease [14].

Bolignano *et al.* [15] reported that CD patients exhibited increased serum NGAL values compared with controls and the infusion of a single high dose of infliximab induced an impressive reduction in these levels. These findings suggest the role of serum NGAL in the systemic adaptations to CD, also confirming the values of serum NGAL measurement in the evaluation of early responses to therapy or in predicting different clinical outcomes [15].

Yeşil *et al.* [16] reported that serum NGAL levels were elevated in the IBD group compared with the HC group, and in UC patients compared with CD patients (in agreement with our results). Moreover, the levels were significantly higher in UC pancolitis than in the left-sided colitis, in colonic CD than in ileal CD, and also in ileocolonic CD than in ileal CD. However, the serum NGAL concentration did not differ between quiescent and active stages (in contrast to our results). The authors suggested that the increased serum NGAL level in IBD patients could be related to colonic inflammatory load; however, before

serum NGAL can be used for diagnostic proposes, it is important to establish a normal range in healthy population, standard method for its measuring and its diagnostic cut-off value [16].

As regards correlation of serum NGAL with activity indices in IBD patients, it was reported that serum NGAL shows a highly significant correlation with CRP and ESR among both UC and CD patients. Furthermore, the serum NGAL levels demonstrated a significant ability in discriminating inactive from mild, mild from moderate, and moderate from severe disease, as defined by UCAI and clinical CDAI, endoscopic CDAI, respectively. However, did not performed in that study correlations between serum NGAL and histopathological grading in both CD and UC patients [13]. On the other hand, Yeşil *et al.* [16] reported that no significant difference could be detected between serum NGAL levels when compared with activity indices (UCAI in UC patients and clinical as well as endoscopic CD activity indices in CD patients). In addition, Janas *et al.* [17] reported that serum NGAL levels in children with IBD were higher than that in healthy and non-IBD children. Moreover, serum NGAL levels in UC and CD children did not correlate with disease activity and markers of inflammation [17]. Vucelic [18] explained that the reason for the absence or presence of significance between serum NGAL and activity indices is that the indices such as UCAI and CDAI used to document disease activity show various limitations in monitoring IBD and the inability of these clinical indices to accurately reflect disease activity in all IBD patients.

The present study revealed that serum NGAL at cut-off point 33.7 ng/ml could detect disease activity in UC patients [sensitivity (100%), specificity (84%), accuracy (92.0%), PPV (86.2%), NPV (100%)]. Whereas at this cut-off point, serum NGAL could detect disease activity in CD patients with lower values [sensitivity (80.0%), specificity (70.0%), accuracy (75.0%), PPV (72.7%), NPV (77.8%)]. When comparing the reported cut-off point in the present study with the previous studies, higher and lower cut-off points were reported.

Oikonomou *et al.* [13] reported different cut-off points to distinguish between different IBD groups and other groups (all these cut-off points were higher than that of the present study). Serum NGAL at cut-off point 60 ng/ml could distinguish IBD from healthy controls and IBS with moderate performance, almost equal to CRP and superior to ESR. However, at a cut-off point of 75 ng/ml, serum NGAL could distinguish active IBD from HC and IBS with a sensitivity of 95% and specificity of 85%, active UC and active CD from HC with a sensitivity of 97% and specificity of 83%, and active IBD from IBS with a sensitivity of 97% and specificity of 81% in active UC and sensitivity of 93% and specificity of 73% in CD. Moreover, at cut-off point 96 ng/ml, serum NGAL was superior to ESR and CRP in differentiating active from inactive IBD [13].

Yeşil *et al.* [16] reported that serum NGAL at cut-off point 29 ng/ml (closer to our result) was the most suitable cut-off point for distinguishing IBD from the control group with sensitivity and specificity of 76.1 and 60.9%, respectively.

In IBD studies, the marked differences in the mean values and cut-off points of serum NGAL prevent the determination of one global cut-off value that can be used around the world. These differences could be attributed to the use of different kits to measure serum NGAL levels, different groups performing the tests, racial factors and differences in blood collection times, transport and processing of serum samples, interobserver variability in endoscopy, and different gut microbiota in people from different regions [19]. Moreover, Yeoh *et al.* [20] suggested that the age of the population is an important factor as serum NGAL level increases with age.

The explanation of the elevated serum NGAL concentrations in IBD could be attributed to different inflammatory mechanisms activating local or distant neutrophils, macrophages, and other immune cells, reflecting the magnitude of inflammatory response. Apart from the amount of NGAL sourced from pre-formed, pre-packaged neutrophil granule proteins at the site of inflammation, a major mechanism of de-novo upregulation involves fundamental upstream inflammatory pathways, including signalling through toll/interleukin (IL)-1 receptor activated by lipopolysaccharide (LPS) and IL-1b release, leading to nuclear factor-jB induction. In addition, in-vitro studies have demonstrated that NGAL transcription is markedly increased in macrophages stimulated with LPS, Pam3CSK4 lipopeptide, and flagellin, detected by toll like receptors-4 (TLR4), TLR2/1, and TLR5, respectively [21]. It was reported that LPS *in vivo* induces a 200-fold increase in NGAL messenger RNA transcription and a 20-fold increase in protein concentration in a TLR4-dependent manner. TLR4, in particular, is significantly increased in intestinal epithelial cells and lamina propria mononuclear cells throughout the lower GI tract in active IBD [22]. Moreover, Karlsen *et al.* [23] stated that the established importance of nuclear factor-jB networks within the intestinal epithelium in sustaining normal mucosal homeostasis and in mediating pathogen-specific responses appears to be finally responsible for activation of NGAL genes transcription, leading to upregulation of serum NGAL

in IBD. Activation of the aforementioned mechanisms appears to be rather independent of disease location, although disease extent seems to play a role, as shown in UC; this could explain the better performance of NGAL in UC compared with CD colitis, where a hypothesis of limited colon epithelial cells affection in CD colitis may be the cause of limited NGAL upregulation. However, the small number of patients with isolated colon disease in the CD subgroup cannot provide sufficient data to assume that NGAL levels could discriminate UC from CD colitis [21]. Furthermore, Carlson *et al.* [4] reported increased levels of NGAL in colorectal perfusion fluids in UC patients, indicating neutrophil involvement in the local inflammatory process. The authors suggested that NGAL may serve as a specific marker of intestinal neutrophil activation in UC. Granulocyte macrophage–colony stimulating factor, and to some extent IL-8, may play a role in neutrophil accumulation and priming in this disease [4].

Conclusion

Serum NGAL is a valuable noninvasive marker in the assessment of IBD patients (disease activity and response to treatment) as it is elevated in active IBD patients (particularly active UC), correlated positively with inflammatory markers (CRP and ESR) and markers of disease activity (UCAI and UC histopathology grading in UC patients and clinical CDAI in CD patients), decreased in IBD patients on remission induced by medical therapy (the decrease was highly significant in inactive UC patients and significant in inactive CD patients).

Serum NGAL at cut-off point 33.7 ng/ml could detect UC disease activity [sensitivity (100%), specificity (84%), PPV (86.2), NPV (100%), and accuracy (92%)], whereas in CD patients this cut-off point could detect disease activity with lower values [(sensitivity (80%), specificity (70%), PPV (72.7), NPV (77.8), and accuracy (75%)].

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Conflicts of interest

There are no conflicts of interest.

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