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Research Article

How does disease location affect acute phase reactants in ulcerative colitis?

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ABSTRACT

Background: We aimed to evaluate erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), platelet (PLT) counts and albumin levels according to disease location in ulcerative colitis.
Methods: The ESR, CRP, WBC, PLT counts and albumin levels of 206 ulcerative colitis patients with endoscopic activity were retrospectively evaluated. Endoscopic activity had been assessed using Rachmilewitz endoscopic activity index. Patients were grouped according to the extent of disease by Montreal classification, and they were evaluated regarding the location and severity of disease according to the laboratory test results.
Results: Among 206 patients, 88 (42.7%) had extensive colitis, 89 (43.2%) of them had left sided colitis and 29 (14%) patients had proctitis. According to the endoscopic activity index, 32.04% of the patients had mild activity, 39.32% moderate activity and 28.64% had severe activity. As the disease extent progressed from the distal to the proximal intestine, CRP, ESR, WBC and PLT counts showed a significant increase while albumin levels showed a significant decrease. In our study, the test that yielded the best results in the assessment of disease activity was CRP, which was found to be high in 80% of patients with extensive colitis, followed by ESR, PLT and WBC counts. As the involved intestine shortened, the rate of patients with abnormal laboratory tests significantly decreased
Conclusion: CRP, ESR, WBC, PLT counts and albumin levels are of limited value in determining disease activity in ulcerative colitis patients, especially in those with proctitis

Keywords: Acute phase reactants; Ulcerative colitis; CRP

INTRODUCTION

The etiology of inflammatory bowel disease (IBD) is not fully known. It is characterized by chronic inflammation of the gastrointestinal tract. The disease typically progresses with relapses and remissions.[1] There are still some problems for the physicians regarding many aspects of IBD. These include the assessment of diagnosis, prognosis, disease activity, severity and treatment response. There is not only one single gold standard test for each of them. Instead, a combination of symptoms, clinical examination, laboratory findings, radiology and endoscopy with biopsy is used in making the diagnosis, in the assessment of disease severity and in predicting the outcome of the disease.[2]

An ideal marker that can be used in the assessment of disease activity in IBD should have multiple properties. It should be easily and rapidly performed, and should be cost-effective. In addition, the ideal laboratory marker should identify individuals at risk of disease, should be specific to the disease, should assess the activity of disease and should indicate the efficacy of treatment. Finally, it should have a prognostic value to predict relapse. However, there is no one single marker with all these properties.[1,2]

Active bowel inflammation in IBD patients is associated with the migration of leukocytes to the bowel and acute phase reaction. Serum white blood cell (WBC) count platelet (PLT) count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and albumin levels may alter during inflammatory conditions.[3] We, in this present study, aimed to evaluate ESR, CRP, WBC and PLT counts and albumin levels in ulcerative colitis patients according to disease location.

METHODS

Ulcerative colitis patients, who had been admitted to the Gastroenterology outpatient clinic of Izmir Katip Celebi University Ataturk Training and Research Hospital between January 2009 and December 2011, were retrospectively evaluated. From 735 patients, 206 ulcerative colitis patients who had been evaluated regarding ESR, CRP, WBC, PLT counts and albumin levels and had undergone colonoscopy within 3 days and had had endoscopic activity, were included in the study. Endoscopic activity had been assessed using Rachmilewitz activity index. According to this index, patients with an activity index between 4 and 6 were considered to have mild activity, those with an activity index between 7 and 9 were considered to have moderate activity and those with an activity index between 10 and 12 were considered to have severe endoscopic activity. Besides, patients with ulcerative colitis were grouped according to the extent of disease using Montreal classification. According to this classification, disease limited to the rectum was defined as proctitis, disease limited to the distal of splenic flexure was defined as left sided colitis, and disease that extends to the proximal of splenic flexure was defined as extensive colitis. The local hospital ethics committee approved the study.

After an overnight fasting, blood samples had been drawn from the patients in the morning. CRP levels were determined Architect C16000 (Abbott Diagnostics, Chicago, USA) biochemistry analyzer by immunoturbidimetric method. Serum albumin levels were measured using Architect C16000 (Abbott Diagnostics, Chicago, USA) biochemistry analyzer by colorimetric method. Beckman Coulter LH750 (Beckman Coulter, Miami, IL, USA) was used for leukocyte and PLT counts, in samples taken into 2 ml hemogram tubes with EDTA. Vacuplus ESR-120 (Len-med, Ankara, Turkey) automated device was used for the assessment of ESR, the rate at which red blood cells sediment in one hour, as millimeters per hour.

A CRP>0.8 mg/dL, a WBC count>10500 K/µL, a PLT count>450000 K/µL, and an albumin level<3.5 g/dL were interpreted as abnormal. In interpreting ESR results, an ESR> 15 mm/h and an ESR>20 mm/h for male and female patients<50 years of age, respectively, and an ESR>20 mm/h and an ESR>30 mm/h for 50 male and female patients>50 years of age, respectively were considered as abnormal. The patients were evaluated according to these laboratory test results regarding the location and severity of disease.

Statistical Package for the Social Sciences (SPSS) for Windows (version 17.0; SPSS Inc., Chicago, IL, USA) was used in the statistical analysis of data. Categorical variables were presented as number and percentages, and continuous variables were presented as mean and standard deviation. ANOVA was used in comparing more than two groups in large samples and Kruskal-Wallis was used for small samples. The statistical significance level was set at 0.05 for all tests

RESULTS

Among 206 patients with active ulcerative colitis, 88 (42.7%) had extensive colitis, 89 (43.2%) had left sided colitis and 29 (14%) had proctitis. According to the endoscopic activity index, 32.04% had mild disease, 39.32% had moderate disease, and 28.64% had severe disease (Table 1).

Table 1: Endoscopic activity findings according to disease location in patients with ulcerative colitis.

Involvement Site	Disease Activity			Total
	Mild n %	Moderate n %	Severe n %	
Extensive colitis	14 (15.9)	36 (40.9)	38 (43.1)	88
Left sided colitis	39 (43.8)	32 (35.9)	18 (20.2)	89
Proctitis	13 (44.8)	13 (44.8)	3 (10.3)	29
Total	66 (32.0)	81 (39.3)	59 (28.6)	206

When the laboratory findings were evaluated according to disease location (site of involvement), a significant difference was detected between the means of three involvement sites. As the disease extent progressed from the distal to the proximal intestine, CRP, ESR, WBC and PLT counts showed a significant increase, while the albumin levels showed a significant decrease (Table 2).

Table 2: Laboratory parameters according to the site of involvement in patients with ulcerative colitis.

	Extensive colitis n= 88	Left sided colitis n=89	Proctitis n=29	p
CRP (mg/dl)	12.2± 20.2[a] 70 (80)	4.1± 11.1[b] 51 (57)	1.3±3[c] 6 (21)	<0.001
ESR (mm/h)	52.4±28[a] 69 (78)	32.9± 26.3[b] 46 (52)	12.2±8.7[c] 2 (7)	<0.001
WBC (K/µL)	10578± 3757[b] 37 (42)	9598± 3094[b] 25 (28)	8001±2244[a] 2 (7)	0.001
PLT (K/µL)	431±154[a] 42 (48)	376±140[b] 28 (31)	290±62[c] 2 (7)	<0.001

Albumin (g/dl)	3.7±0.8[a] 29 (33)	4.2±0.5[b] 10 (11)	4.5±0.3[c] 0 (0)	<0.001

Mean ± SD All such values

n (%) All such values, Percentage of values above upper reference limit

Values in the same row not sharing the same superscript were significantly different

CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell count; PLT: Platelet count

When the abnormalities in the laboratory tests were evaluated according to the location of disease regarding the number of patients, CRP was found to be at high levels in 80% of the patients with extensive colitis, 57% of the patients with left sided colitis and only in 21% of patients with proctitis. The second best laboratory test for determining disease activity was ESR; high levels of ESR was determined in 78% of the patients with extensive colitis, 52% of patients with left sided colitis and 7% of patients with proctitis. CRP and ESR were followed by PLT and WBC counts, respectively. The worst results in determining disease activity were obtained from albumin; albumin levels were low in 33% of extensive colitis patients, 11% of left sided colitis patients and in none of the patients with proctitis. The efficacy of laboratory tests in assessing disease activity was significantly different between three involvement sites. As the involved intestinal segment shortened, the rate of patients with abnormal laboratory tests results significantly decreased. The laboratory test yielding the highest rate of abnormal results, CRP, was found to be high in only 21% of patients with proctitis. While ESR, WBC and PLT counts were found to be at high levels in 7% of patients with proctitis, albumin levels were within the normal range in all patients with proctitis (Table 2).

The numbers and percentages of patients according to disease severity and involvement site are presented in Table 3. According to this, for instance, when patients with mild disease were evaluated according to CRP levels, 79% of extensive colitis patients, 54% of left sided colitis patients and 15% of proctitis patients with mild disease had high CRP levels. There was a significant difference between the three groups (p=0.004).

Table 3: The numbers and percentages of patients with abnormal laboratory test results according to disease severity and involvement site.

	CRP Disease Severity			ESR Disease Severity			WBC Disease Severity			PLT Disease Severity		
	Mild n %	Moderate n %	Severe n %	Mild n %	Moderate n %	Severe n %	Mild n %	Moderate n %	Severe n %	Mild n %	Moderate n %	Severe n %
Extensive	11 (79)	29 (81)	30 (79)	9 (64)	27 (75)	33 (87)	4 (29)	15 (42)	18 (47)	3 (21)	19 (53)	20 (53)
Left sided	21 (54)	11 (56)	12 (67)	19 (48)	14 (44)	13 (72)	8 (21)	10 (31)	7 (39)	11 (28)	10 (31)	7 (39)
Proctitis	2 (15)	4 (31)	0 (0)	1 (8)	1 (8)	0 (0)	1 (8)	1 (8)	0 (0)	0 (0)	2 (15)	0 (0)
P	0.004	0.004	NA	0.008	<0.001	NA	NA	0.034	NA	NA	0.079	NA

CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; WBC: White blood cell count; PLT: Platelet count; NA: Not available

DISCUSSION

The assessment of intestinal inflammation in IBD remains to be problematic. Currently, the most reliable method is endoscopy with biopsy.[4] However, the fact that the endoscopic procedures are invasive and frequently disturbing, and the symptoms are usually subjective, has led to the use of laboratory markers in the assessment of disease activity in IBD.[2,5] Among these, acute phase reactants and ESR are the most frequently used laboratory markers.

While some acute phase reactants show an increase in inflammatory conditions, some of them decrease. These are termed as positive and negative acute phase reactants.[6] CRP is among the most commonly used acute phase reactants. When compared with the other acute phase proteins, CRP has a shorter half-life (19 hours). Therefore, the level of CRP increases in the early period of inflammation, and rapidly decreases by the regression of inflammation. When compared with CRP, ESR increases much more slowly and even if the inflammation clears up, its regression may take several days. The other frequently used laboratory markers are leukocyte and PLT counts and albumin levels. The number of leukocytes (WBC) increases as a part of the acute phase response. WBC count is also affected by some treatments used in IBD; while WBC counts may increase by the use of glucocorticoids, it may decrease by the use of azathioprine and 6-mercaptopurine. Like leukocytes, the number of PLTs may also increase in inflammatory conditions. When the wide normal range of PLTs is taken into consideration, its use as a laboratory marker is thought to be less beneficial.[2] Serum albumin levels may decrease in acute inflammation. However, albumin levels may be affected by nutritional factors.[7] As the changes in

ESR and acute phase reactants do not always accompany mucosal inflammation, these parameters may not reliably reflect the severity and extent of mucosal inflammation.[8]

Ricanek and colleagues, in their study, found a significant difference in CRP levels only between ulcerative colitis patients with mild and severe disease determined endoscopically. In the same study leukocyte and PLT counts were also evaluated and while there was a significant relation between leukocyte count and endoscopic activity in ulcerative colitis patients, no relation was determined between PLT count and endoscopic activity.[9] In a study of Schoepfer et al.,[10] CRP levels and WBC counts were significantly higher in patients with moderate ulcerative colitis compared to those with mild disease. However, no significant difference was found between patients with moderate and severe disease. Linskens et al.[11] in a study, found a significant difference between patients with active ulcerative colitis and those who showed remission 3 months after treatment in terms of ESR, CRP, WBC, and PLT counts and albumin levels. Solem et al.,[12] reported that the increase in CRP levels was significantly associated with active disease determined by ileocolonoscopy and increased ESR, trombocitosis and hypoalbuminemia in ulcerative colitis patients.

In the literature, there are a few studies evaluating acute phase reactants according to disease location in ulcerative colitis patients. Henriksen et al.,[13] in their study, in which they evaluated CRP, observed a significant increase in CRP levels with an increase in the extent of disease in ulcerative colitis patients. Furthermore, they determined normal CRP levels in 71% of patients at the time of diagnosis. Karoui and colleagues, in a study evaluating CRP levels in ulcerative colitis patients, found no relationship between high CRP levels and disease location. No significant association was found between CRP levels and disease severity, and normal CRP levels were determined in 32.8% of active patients.[14] Lok et al.,[15] in their study, found that ESR, CRP, WBC, PLT and albumin levels were significantly different between patients with and without extensive colitis. In the same study, when the patients were grouped according to disease activity as mild, moderate and severe, these five parameters were found to be significantly different between the groups.[15]

In our study, when mean levels of CRP, ESR, WBC, PLT and albumin were evaluated, there was a significant difference between ulcerative colitis patients with three different involvement sites. As the disease extent progressed from the distal to the proximal intestine, CRP, ESR, WBC and PLT counts significantly increased while albumin levels showed a significant decrease.

In our study, the laboratory test that yielded the best results in determining disease activity was CRP. CRP levels were found to be high in 80% of patients with extensive colitis. With regard to extensive colitis patients, CRP was followed by ESR (78%), PLT count (48%), WBC count (42%) and albumin levels (33%). Particularly the value of albumin was quite low in determining disease activity in patients with extensive colitis, left sided colitis, and proctitis. The worst laboratory test results were found in proctitis patients. The test that yielded the best results in proctitis patients was CRP levels, which was found to be high in 21% of the patients. While high ESR, WBC and PLT counts were identified in 7% of proctitis patients, none of the patients showed decreased albumin levels.

None of the tests evaluated in this present study was 100% efficient in determining disease activity in ulcerative colitis. Even CRP, yielding the best results was found to be high in 80% of extensive colitis patients. It was observed that these laboratory parameters yielded normal results in most of the patients with proctitis.

In conclusion, CRP, ESR, WBC and PLT counts and albumin levels are of limited value in determining disease activity in patients with ulcerative colitis, especially in those with proctitis. Therefore, these tests are not sufficient for determining disease activity in these patients. This fact has led to the increasing use of additional diagnostic tests like fecal markers for determining disease activity in the recent years. Further studies are needed to identify more reliable and easily applicable markers for determining disease activity in ulcerative colitis patients.

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REFERENCES

1. Vilela EG, Torres HO, Martins FP, Ferrari Mde L, Andrade MM, Cunha AS. Evaluation of inflammatory activity in Crohn's disease and ulcerative colitis. World J Gastroenterol. 2012;18:872-81.
2. Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? Gut. 2006;55:426–31.
3. Langhorst J, Elsenbruch S, Koelzer J, Rueffer A, Michalsen A, Dobos GJ. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. Am J Gastroenterol. 2008;103: 162–69.
4. Costa F, Mumolo MG, Ceccarelli L, Bellini M, Romano MR, Sterpi C, et al. Calprotectin is a stronger predictive marker of relapse in ulcerative colitis than in Crohn's disease. Gut. 2005;54:364–8.
5. Desai D, Faubion WA, Sandborn WJ. Review article: biological activity markers in inflammatory bowel disease. Aliment Pharmacol Ther. 2007;25:247–55.

6. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. N Engl J Med. 1999;340:448–54.
7. Iskandar HN, Ciorba MA. Biomarkers in inflammatory bowel disease: current practices and recent advances. Transl Res. 2012;159:313-25.
8. Minderhoud IM, Samsom M, Oldenburg B. What predicts mucosal inflammation in Crohn's disease patients? Inflamm Bowel Dis. 2007;13:1567–72.
9. Ricanek P, Brackmann S, Perminow G, Lyckander LG, Sponheim J, Holme O, et al. IBSEN II Study Group. Evaluation of disease activity in IBD at the time of diagnosis by the use of clinical, biochemical, and fecal markers. Scand J Gastroenterol. 2011;46:1081–91.
10. Schoepfer AM, Beglinger C, Straumann A, Trummler M, Renzulli P, Seibold F. Ulcerative colitis: correlation of the Rachmilewitz endoscopic activity index with fecal calprotectin, clinical activity, C-reactive protein, and blood leukocytes. Inflamm Bowel Dis. 2009;15:1851–8.
11. Linskens RK, van Bodegraven AA, Schoorl M, Tuynman HA, Bartels P. Predictive value of inflammatory and coagulation parameters in the course of severe ulcerative colitis. Dig Dis Sci. 2001;46:644-8.
12. Solem CA, Loftus EV, Tremaine WJ, Harmsen WS, Zinsmeister AR, Sandborn WJ. Correlation of C-reactive protein with clinical, endoscopic, histologic and radiographic activity in inflammatory bowel disease. Inflamm Bowel Dis. 2005;11:707–12.
13. Henriksen M, Jahnsen J, Lygren I, Stray N, Sauar J, Vatn MH, et al. IBSEN Study Group. C-reactive protein: a predictive factor and marker of inflammation in inflammatory bowel disease. Results from a prospective population-based study. Gut. 2008;57:1518–23.
14. Karoui S, Laz S, Serghini M, Bibani N, Boubaker J, Filali A. Correlation of C-reactive protein with clinical and endoscopic activity in patients with ulcerative colitis. Dig Dis Sci. 2011;56:1801–5.
15. Lok KH, Ng CH, Hung HG, Li KF, Li KK, Szeto ML. Correlation of serum biomarkers with clinical severity and mucosal inflammation in Chinese ulcerative colitis patients. J Dig Dis. 2008;9:219-24.

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