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The Relationship Between Endoscopic Findings and Laboratory Results in Inflammatory Bowel Disease

İnflamatuvar Barsak Hastalıklarında Laboratuvar Sonuçları ile Endoskopik Bulgular Arasındaki İlişki

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The Relationship Between Endoscopic Findings and Laboratory Results in Inflammatory Bowel Diseases

ABSTRACT

Objective: The aim of this study was to determine the relationship between routine laboratory indicators [Including hemoglobin, white blood cells, platelets, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP)] and the extent of endoscopic involvement in individuals with inflammatory bowel disease (IBD).

Material and Method: The medical records of patients who were diagnosed with Ulcerative Colitis (UC) and Crohn's Disease (CD) between 2009 and 2015 were retrospectively examined. Endoscopic findings and hemoglobin, white blood cell, platelet, ESR, and CRP values at the time of colonoscopy were analyzed. An exploratory multinomial regression model was created to examine the association of laboratory parameters and endoscopic involvement localization.

Results: In UC, a significant decrease in hemoglobin levels was present in cases with extensive colitis/pancolitis compared to distal type colitis (*p=0.02*), while no significant difference was found between left-sided colitis and distal type colitis. Elevated ESR values were notably found in left-sided colitis (*p=0.007*) and extensive colitis/pancolitis (*p=0.043*) compared to distal type colitis. CRP levels were significantly higher in cases with extensive colitis/pancolitis (*p=0.015*). No relationship was identified between laboratory parameters and the endoscopic location of involvement in CD.

Conclusion: Although hemoglobin value, ESR and CRP levels are helpful in determining the location of involvement in UC, their effects have not been observed in CD. In addition to these basic laboratory values, other parameters should also be taken into consideration in the evaluation of patients.

Key words: C-reactive protein, Crohn's Disease, Erythrocyte sedimentation rate, Ulcerative Colitis.

ÖZET

Amaç: Bu çalışmanın amacı, inflamatuvar barsak hastalığı (İBH) olan olgularda rutin laboratuvar bulguları (hemoglobin, beyaz küre, trombosit, eritrosit sedimentasyon hızı (ESH), C-reaktif protein (CRP)) ile endoskopik tutulum alanları arasındaki ilişkiyi belirlemektir.

Gereç ve Yöntem: 2009-2015 yılları arasında Ülseratif Kolit (ÜK) ve Crohn Hastalığı (CH) tanısı alan hastaların tıbbi kayıtları geriye dönük olarak incelendi. Endoskopik bulgular ile kolonoskopi sırasındaki hemoglobin, beyaz kan hücresi, trombosit, ESR ve CRP değerleri kaydedildi. Laboratuvar parametreleri ile endoskopik tutulum lokalizasyonu arasındaki ilişkiyi incelemek için multinominal lojistik regresyon modeli oluşturuldu.

Bulgular: ÜK'de; ekstensif kolit/pankolit tutulumunda distal tip kolite göre hemoglobin değerinde anlamlı derecede düşüş saptanmışken (*p=0.02*), sol taraf kolitiyle distal tip kolit arasında anlamlı fark saptanmamıştır. Sol taraf koliti (*p=0,007*) ve ekstensif kolit/pankolit (*p=0.043*) tutulumunda distal tip kolite göre ESH değerleri belirgin yüksek bulunmuştur. CRP değeri sadece ekstensif kolit/pankolit tutulumunda anlamlı yüksek çıkmıştır (*p=0.015*). CH için laboratuvar parametreleri ile tutulum yerleri arasında herhangi bir ilişki bulunamamıştır.

Sonuç: ÜK›de hemoglobin değeri, ESR ve CRP düzeyleri tutulumun yerini belirlemede yardımcı olsa da CH'de etkileri görülmemiştir. Hastaların değerlendirilmesinde bu temel laboratuvar değerlerinin yanı sıra diğer parametrelerin de dikkate alınması gerekir.

Anahtar kelimeler: C-reaktif protein, Crohn Hastalığı, Eritrosit sedimentasyon hızı, Ülseratif Kolit.

Introduction

Inflammatory bowel diseases (IBD), encompassing Ulcerative Colitis (UC) and Crohn's Disease (CD), are persistent inflammatory conditions capable of affecting any segment of the gastrointestinal tract, often manifesting through periods of remission and exacerbation. The diagnosis of these diseases relies on a comprehensive evaluation involving clinical, endoscopic, and histopathological features. However, it's crucial to note no finding is definitively diagnostic (1,2).

The incidence and prevalence of IBD vary by geographical region, ethnic group and race. The prevalence of IBD generally ranges between 0.3% and 0.5%, with women being slightly more frequently affected. It exhibits a bimodal age distribution for disease onset diagnosis. The incidence increases in young people aged 15-25, with the second peak occurring between the ages of 40-60 (3).

In UC, inflammation persists in the bowel wall and is limited primarily to the mucosa. The rectum is always involved in the disease and may progress towards the proximal segments. Pseudopolyps, polypoid tags of the mucosa, may be present on endoscopy during periods of active disease and remission. These are not true adenomas containing granulation tissue poor in epithelium. Dysplastic changes can be observed in the long term, increasing the risk of colon cancer. Macroscopically, the affected segment in CD exhibits ulcers, stenosis, fistulas, and abscesses. CD involves both segmental and full-thickness complications. A distinguishing characteristic of CD is the identification of granulomas (4-5).

The length and severity of the affected colon segment determine the clinical presentation of UC (6). If colon involvement extends up to 10-12 cm from the distal end, it is defined as distal type colitis, if it involves up to the splenic flexure, it is defined as left-side colitis, and if it extends beyond the splenic flexure, it is defined as diffuse colitis (7). CD may be inflammatory, obstructive or fibrostenotic (8). Terminal ileum involvement is present in 45-47% of patients, colon involvement in 30%, ileocolic involvement in 20%, and upper gastrointestinal tract involvement in 3-5% (9-10).

The role of laboratory findings in IBD is to identify specific forms of the disease in a less-invasive way, determine the degree of disease activity, predict the course of the disease, and predict the response to treatment interventions. The main laboratory markers in IBD are acute phase reactants including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), hemogram, fecal and serological markers.

The purpose of our study is to determine the relationship between routine laboratory findings (hemogram, ESR, CRP) and endoscopic involvement sites in cases diagnosed with IBD.

Materials and Methods

The study received ethics committee approval on 02.06.2015, with the Clinical Research Ethics Committee Service number B.30.2.ATA.0.01.00/124, which determined that there was no scientific or ethical contravention.

The records of patients diagnosed with UC and CD who applied to the the Internal Medicine Clinic of Atatürk University Faculty of Medicine between 2009 and 2015 were retrospectively examined. Hemoglobin, white blood cell, platelet, ESH, and CRP values of the patients on the date of colonoscopy were obtained from laboratory records. Patients who underwent bowel surgery, had malignancy or were pregnant, those under the age of 18, and patients receiving treatment for IBD were not included in the study.

Patients were divided into subgroups based on endoscopic findings at the time of inclusion in the study as follows: UC patients 1) Distal type colitis, 2) Left-sided colitis, 3) Extensive colitis/Pancolitis and CD patients 1) Colitis, 2) Ileitis, 3) Ileocolitis.

Statistical analysis

Descriptive statistics were performed to summarize baseline characteristics. Firstly, the minimum, maximum, mean, and median laboratory values of UC and CD and their subgroups were determined. Afterwards, the Compatibility Test, Pearson and Deviance Test, Pseudo R2 Test, Multinominal Logistic Regression Test and Classification Test were performed for the statistical validity of the model. Analysis and interpretations were made using the (Statistical Package for the Social Sciences) SPSS 18 software package.

Table I. Demographic Data of the Cohort

		Crohn's Disease (n=42)			Ulcerative Colitis (n=156)		
		Colitis	Ileitis	Ileocolitis	Distal colitis	Left-sided colitis	Extensive colitis / Pancolitis
n		7	23	12	45	46	65
Mean age (year) (minimum-maximum)	44.9 (18-83)	42.04 (19-71)			46.01 (18-80)		
Male/Female (n)	104 / 94	3 / 4	13 /10	6 / 6	25/20	26/20	36/29

Results

This retrospective study was conducted with 198 cases. Forty-two (21.2%) of them had CD and 156 (78.8%) of them were diagnosed with UC. The demographic characteristics of the cohort are summarized in Table I.

Data Analysis of Patients with Ulcerative Colitis

Hemoglobin, ESR and CRP values had a significant effect on the model; however, age, platelet, and white blood cell counts had unremarkable impact. The reference point for regression analysis in the UC model was determined as distal type colitis. Multinominal logistic regression analysis revealed that a one-unit increase in ESR value increases the probability of the disease being left-sided colitis by 1.055 times; it increases the probability of having extensive colitis/pancolitis by 1.041 times. A one-unit decrease in hemoglobin value increases the probability of the extensive colitis/pancolitis by 0.731 times. A one-unit increase in the CRP value increases the probability of the disease being extensive colitis/pancolitis by 1.064 times compared to the probability of the disease being distal type colitis (Table II).

When the variables used in the study were classified, it was seen that 61.5% of the patients were correctly classified by the analysis using independent variables. According to subgroups, 77.8% of the

Table II. Multinominal logistic regression results of Ulcerative Colitis group using distal colitis as the reference category

		B	Standard deviation	Wald	Sig.	Exp(B)	95% Confidence Interval	
							Lower limit	Upper limit
Left-sided colitis	Constant	0.369	2.475	0.022	0.881			
	WBC (10^3/L)	0.000	0.000	0.879	0.348	1.000	1.000	1.000
	HGB (g/dl)	-0.085	0.139	0.377	0.539	.918	0.699	1.206
	Platelet (x10^3/µl)	0.000	0.000	2.519	0.113	1.000	1.000	1.000
	ESR (mm/h)	0.054	0.020	7.297	0.007*	1.055	1.015	1.098
	CRP (mg/L)	0.040	0.026	2.368	0.124	1.041	0.989	1.095
	Age	0.001	0.016	0.001	0.975	1.001	0.969	1.033
Extensive/ Pancolitis	Constant	2.229	2.359	0.893	0.345			
	WBC (10^3/L)	0.000	0.000	0.704	0.401	1.000	1.000	1.000
	HGB (g/dl)	-0.314	0.135	5.385	0.020*	0.731	0.561	0.952
	Platelet (x10^3/µl)	0.000	0.000	0.326	0.568	1.000	1.000	1.000
	ESR (mm/h)	0.040	0.020	4.106	0.043*	1.041	1.001	1.081
	CRP (mg/L)	0.062	0.026	5.864	0.015*	1.064	1.012	1.118
	Age	0.002	0.017	0.011	0.916	1.002	0.970	1.035

WBC, White blood cell; HGB,Hemoglobin; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein

Table III. Multinominal logistic regression results of Crohn's Disease group using colitis as the reference category

		B	Standard deviation	Wald	Sig.	Exp(B)	%95 Confidence Interval	
							Lower limit	Upper limit
Ileitis	Constant	0.409	3.875	0.006	0.939			
	WBC (10^3/L)	-0.064	0.48	0.018	0.894	0.938	0.366	2.402
	HGB (g/dl)	0.611	2.877	0	0.985	6.62	0	
	Platelet (x10^3/µl)	0	0.003	0.029	0.865	1	0.994	1.005
	ESR (mm/h)	-0.133	9.562	0.001	0.969	0.322	2.2	4.6
	CRP (mg/L)	0.638	3.14	0.019	0.89	1.65	3	1.2
	Age	**-0.333**	0.035	0.063	.000*	0.264	0.246	0.282
Ileocolitis	Constant	2.097	3.891	0.006	0.939			
	WBC (10^3/L)	-0.064	0.48	0.018	0.894	0.938	0.366	2.4
	HGB (g/dl)	0.749	2.877	0	0.985	7.57	0	
	Platelet (x10^3/µl)	0	0.003	0.028	0.866	1	0.994	1
	ESR (mm/h)	-0.144	2.562	0.001	0.969	0.319	2.1	4.6
	CRP (mg/L)	0.646	1.14	0.019	0.89	6.016	3	1.2
	Age	-0.305	0	.	.	0.271	0.271	.271

WBC, White blood cell; HGB,Hemoglobin; ESR, Erythrocyte sedimentation rate; CRP, C-reactive protein

patients classified as distal type colitis were correctly predicted by the analysis. For other categories, these rates were 28.3% and 73.8%, respectively.

Data Analysis of Patients with Crohn's Disease

The reference point for the CD group was determined to be colitis. According to the results, no relationship was present between laboratory results and the location of disease involvement in the CD cohort. Table III summarizes the multinominal logistic regression analysis of data from the CD group.

It was observed that 76.2% of the patients were correctly classified by the analysis using independent variables. While 54.8% of the patients whose disease type was classified as ileitis were correctly predicted by the analysis, these rates for the other categories were 16.7% and 28.6%, respectively.

According to the Nagalkerke R2 evaluation, 41.9% and 80.3% of the change in the probability of the disease subtype in the UC and CD models, respectively, can be explained by the values obtained as a result of the laboratory results.

Discussion

The objective of the present study was to estimate the relationship between laboratory findings and endoscopic diagnosis in patients with IBD. Our model, based on the evaluation of laboratory parameters for IBD, is statistically significant. However, for UC, 41.9% of the change in probability regarding the type of disease can be explained by the values obtained because of the laboratory results. This indicates that existing parameters alone are insufficient to diagnose the disease and that auxiliary methods are required in addition to these parameters.

In the literature, the relationship between acute phase reactants and endoscopic involvement areas in UC patients has been evaluated in various studies using validated indices (11-18). Koçhan et al. identified statistically significant variations in ESR, CRP, platelet, and hemoglobin levels based on the Truelove-Witts index, a clinical activity index, in UC patients. However, no significant difference in leukocyte levels was noted. Additionally, a significant

distinction was observed only in leukocyte levels (*p=0.041)* between the CD and UC groups based on the disease localization. Nevertheless, the small number of patients between the groups led to the interpretation of an insufficient statistical comparison (19). In the study conducted by Önal et al. using Truelove-Witts clinical and Rachmilewitz endoscopic indices in patients with UC, an increase in CRP, ESR and white blood cell counts was found in patients with active UC compared to inactive patients. However, only statistical significance was shown in CRP values (20). In 2013, Yeşil et al. investigated whether RDW is a marker of active disease in patients with IBD. Their results revealed that the CRP and ESR levels in patients with active CD were significantly higher than those in remission or in the controls. Similar results were observed in patients with active UC versus UC patients in remission. No statistically significant differences were found between the CRP and ESR levels of UC patients in remission and CD patients in remission (21). Although we did not evaluate active and inactive patients in the present study, a negative relationship was found with hemoglobin value and a positive relationship with ESR and CRP levels in extensive/pancolitis type of UC patients with extensive/pancolitis type involvement.

The most common hematological finding in IBD is anemia (22). There are mainly two types of anemia in IBD: iron deficiency and chronic disease anemia (23). According to the results of this study, the decrease in hemoglobin value increases the possibility of involvement as extensive colitis/pancolitis, which is the more serious form of the disease. Besides, in left-sided colitis, no significant decrease in hemoglobin value was detected compared to distal type colitis. This may be attributed to the higher amount of bleeding in extensive colitis/pancolitis compared to the other types. Consistent with the present study, Kalaycı et al. reported that a significant decrease in hemoglobin value was present in patients with extensive colitis in UC (24).

ESR is widely used as a biomarker of IBD activity (25,26). It is less consistent with changes in disease activity compared to CRP. However, in the study conducted by Costa et al. in both UC and CD, it was reported that neither ESR nor CRP differed significantly between the relapsing and non-relapsing groups (27). The present study does not provide information about relapse, however supports that there is a positive relationship between the progression of the disease's involvement and the increase in ESR value.

Although CRP is not specific for IBD, its advantageous properties as a biomarker are that it can be measured easily and reliably in diagnostic laboratories and has a short half-life. Elevated CRP levels show a modest correlation with endoscopic UC and are indicative of UC clinical activity. In 2008, Lok et al. undertook a study involving 49 Chinese UC patients. They explored the sensitivity and correlation of routine serum biomarkers, such as CRP, ESR, white blood cell count, hemoglobin, platelet count, and albumin, with clinical severity and mucosal inflammation (28). Their findings indicated a strong correlation between routine serum biomarkers and endoscopic extensive colitis, but not with proctitis or left-sided colitis. These biomarkers proved beneficial in identifying patients with extensive colitis or clinically severe disease. In a cohort study of 43 UC patients conducted according to the Mayo Clinic activity index, there was a significant relationship between high CRP values and disease activity among inflammatory biomarkers other than platelets (29). They observed a significant association between elevated CRP levels in CD patients with moderate to severe clinical activity, as well as with other studied biomarkers of inflammation, active disease during ileocolonoscopy, and severely active ileitis/colitis on biopsies. In a study conducted by Chouhan et al., it was reported that the CRP value is an easy method to determine the activity and extent of the disease (30). In the present study, CRP levels were found to be significantly higher in extensive colitis/pancolitis than in distal type colitis. This may be due to widespread mucosal damage occurring in extensive colitis/pancolitis or being normal in cases of unknown cause, as in the literature mentioned. The fact that this effect was not detected significantly in left-sided colitis can be thought to be due to less mucosal damage compared to extensive colitis/pancolitis.

In this study for CD, 80.3% of the change in probability regarding the type of disease can be explained by the values obtained because of the

laboratory results. This high rate supports that the parameters used are more helpful in the diagnosis of the disease compared to UC. In the study of Yeşil et al., it was shown that the sensitivity of CRP levels in cases diagnosed with CD was 93% and the specificity was 64%. It was also stated that the sensitivity of the ESR level in showing the activity of the disease was 86% and its specificity was 58%. (21). In Sarıtaş study, a significant change was found in hemoglobin, ESR and CRP values in ileal CD (31). In the study of Koçhan et al., no significant difference was present in leukocyte, hemoglobin, platelet, ESR and CRP levels according to CD subtype (19). In the study of Nogueira et al., it was stated that ESR, platelet and white blood cell values were insufficient to determine CD activity, and a significant decrease was observed in CRP levels after 32 weeks of treatment (32). In the study conducted by Marie et al. with 28 cases diagnosed with CD, they found that CRP levels were normal only in CD with soft mucosal lesions in cases with elevated CDAI. Although this normality is estimated to be due to genetic change in CRP levels, in the study conducted by Willot et al., no relationship was found between CRP levels and genotypes (33,34). In the study conducted by Solem et al. with CD, they found that CRP values were lower in ileal lesions than in colonic lesions (29). While CRP value is considered a valuable marker in evaluating relapse, remission and treatment response in CD, the results of this study concluded that it does not play a role in predicting localization.

The present study has some limitations. Major limitations were the retrospective nature of the study, along with an inadequate number of patients in the cohort and the absence of a control group. Furthermore, UC and CD activity indexes could not be determined because the complaints at the time of colonoscopy, the presence of extraintestinal involvement, physical examination findings, complications, accompanying the disease, and the disease pattern for CD were not recorded. Despite this, the fact that it was conducted in a large cohort makes this study valuable.

In conclusion, in addition to the parameters used in the follow-up of patients with IBD, other non-invasive, more reliable parameters may be needed, especially for CD. In addition, it was concluded that it would be more appropriate to record the complaints of the patients during admission, physical examination findings and colonoscopy records and determine the activity indexes to follow the patients and determine the treatment management more accurately.

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