J Surg Med. 2020;4(8):654-659.
DOI: 10.28982/josam.769877

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN=2602-2079

The value of adenosine deaminase level in assessing activation of inflammatory bowel disease

İnflamatuar bağırsak hastalığının aktivasyonunun değerlendirilmesinde adenosin deaminaz düzeyinin kullanımı

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Ethics Committee Approval: This study was approved by the Ethics Committee of Health Science University İstanbul Haydarpaşa Training and Research Hospital (HNEAH-KAEK 2013/KK/62). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Bu çalışma, Sağlık Bilimleri Üniversitesi İstanbul Haydarpaşa Eğitim ve Araştırma Hastanesi Etik Kurulu tarafından onaylanmıştır (HNEAH-KAEK 2013/KK/62). İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 8/30/2020
Yayın Tarihi: 30.08.2020

Abstract

Aim: There is still a need for an ideal laboratory test that can determine the type of disease, the degree of its activity, predict its course, and monitor treatment response in patients with inflammatory bowel disease (IBD). This study aims to investigate the relationship between disease types and activity with Adenosine deaminase (ADA) levels in patients with IBD.

Methods: A total of 92 patients with IBD [43 with Crohn's disease (CD) and 49 with ulcerative colitis (UC)] and 31 healthy control (HC) volunteers were included in this case-control study. Patients' age, gender, body mass index, location and severity of the disease, medication, endoscopic examination, hemogram, C-reactive Protein (CRP), and ADA results were evaluated.

Results: The mean ADA level was 24.87 (9.6 - 74.9) IU/L in the IBD group and 20.8 (13.7 - 38.9) IU/L in the HC group. The difference between the IBD and HC groups was statistically significant (P<0.013), while that between UC and CD groups was not (P=0.76). Mean ADA level was significantly higher in active UC patients than in inactive ones (P<0.001). To distinguish active UC patients from those in remission, a cut-off level of 21.64 U/L was determined for ADA with 77.6% confidence interval, 89% sensitivity and 60% specificity. Mean ADA level was significantly higher in the CD group compared to the HC group.

Conclusion: ADA level may be used as an alternative marker to distinguish active UC patients from those in remission, regardless of the disease location and the extent of the affected area.

Keywords: Ulcerative colitis, Crohn's disease, Adenosine deaminase

Öz

Amaç: Günümüzde, inflamatuar barsak hastalığı (İBH) hastalarda hastalığın türünü, aktivitesinin derecesini belirleyebilen, seyrini tahmin edebilen ve tedavi yanıtını izleyebilen ideal bir laboratuvar testine hala ihtiyaç vardır. Bu çalışmada İBH olan hastalarda hastalık aktivitesi ile adenozin deaminaz ADA düzeyleri arasındaki ilişki araştırıldı.

Yöntemler: Bu vaka-kontrol çalışmasına toplam olarak 92 IBH hastası [43 Crohn hastalığı (CD) ve 49 ülseratif kolit (UC)] ve 31 sağlıklı kontrol (HC) gönüllüsü dahil edildi. Hastaların yaşı, cinsiyeti, vücut kitle indeksi, hastalığın yeri ve şiddeti, ilaç tedavisi, endoskopik muayene, hemogram, C-reaktif Protein (CRP) ve ADA sonuçları retrospektif olarak değerlendirildi.

Bulgular: Ortalama ADA seviyesi IBH grubunda 24,87 (9,6 - 74,9) IU/L ve HC grubunda 20,8 (13,7 - 38,9) IU/L idi. IBH ve HC grubu arasındaki fark istatistiksel olarak anlamlıydı (P<0,013), ancak UC ve CD grubu arasındaki fark istatistiksel olarak anlamlı değildi (P=0,76). Ortalama ADA düzeyi aktif UC hastalarında inaktif olanlardan anlamlı olarak yüksekti (P<0,001). Aktif UC hastalarını remisyonda UC hastalarından ayırt etmek için, eğer ADA düzeyinin eşik değeri 77,6 güven aralığında 21,64 U/L olarak kabul edilirse, duyarlılık %89 ve özgüllük %60 olarak hesaplandı. Ortalama ADA düzeyi CD grubunda HC grubuna göre anlamlı derecede yüksekti.

Sonuç: ADA seviyesi, hastalığın bulunduğu yere ve etkilenen alanın boyutuna bakılmaksızın, aktif UC hastalarını remisyondaki UC hastalarından ayırmak için alternatif bir belirteç olarak kullanılabilir.

Anahtar kelimeler: Ülseratif kolit, Crohn hastalığı, Adenozin deaminaz

How to cite/Atıf için: Gökden Y, Hot S, Gönen C, Kalyon S, Çetinkaya ZA. The value of adenosine deaminase level in assessing activation of inflammatory bowel disease. J Surg Med. 2020;4(8):654-659.

Introduction

Inflammatory bowel diseases (IBD) are chronic inflammatory pathologies without any curative medical treatment, which develop due to recurrent immune system activation and inflammation, and course with gastrointestinal tract remission and exacerbations. Crohn's disease (CD) and ulcerative colitis (UC) are two types of IBD with similar epidemiology, etiology, and clinical features [1-3]. Many clinical activity predictors and noninvasive markers have been used to identify disease activity and plan treatment for patients with IBD. However, none of them has yet provided a definitive finding in detecting inflammatory activity as much as histopathological and endoscopic examinations [4]. An ideal laboratory test that would be able to identify the type of disease, determine the degree of disease activity, predict the course of the disease, and monitor the treatment response in patients with IBD would be beneficial for physicians. However, there is no laboratory marker with sufficient sensitivity and specificity to provide this convenience alone.

Adenosine deaminase (ADA) enzyme plays a role in the catabolism of purine nucleotides and catabolizes the conversion of adenosine and deoxyadenosine to inosine and deoxycinosine irreversibly [5]. It is widely available in body fluids and tissues. The most important biological activity of ADA is seen in lymphoid tissues: It plays an essential role, especially in the differentiation and proliferation of T lymphocytes [6]. ADA level is ten times higher in lymphocytic cells than in erythrocytes, and more common in T lymphocytes than B lymphocytes [7]. It is considered a non-specific marker of T cell activation and cellular immunity. ADA level increases in autoimmune diseases and inflammation and is used as an indicator of cellular immunity for tuberculosis, rheumatoid arthritis, Graves' disease, celiac disease, systemic lupus erythematosus, acute pancreatitis, acute appendicitis, and other infectious diseases [8-14]. However, studies regarding the level of ADA as an effective biomarker in the evaluation of intestinal inflammation and disease activity are ongoing [15].

The aim of this study is to investigate the relationship between ADA levels and diagnosis, as well as clinical and endoscopic activity of the disease in patients with UC and CD.

Materials and methods

A case-control study was conducted on patients with IBD followed in the gastroenterology clinic. All patients were definitively diagnosed with IBD by clinical, endoscopic, histopathologic, and radiologic examinations. Patients with abdominal abscess, intestinal obstruction, active gastrointestinal bleeding, chronic liver disease, other active infections, tuberculosis, malignant disease, chronic kidney failure, pregnancy, and those younger than 18 years of age were not included in the study. Thirty-one volunteer participants with similar characteristics in terms of age, gender, and body mass index included to constitute the healthy control (HC) group. These participants were selected from individuals who visited our hospital for routine health checks and without a history of any disease, malignancy, or chronic drug use.

The patients' ages, genders, body mass indexes, findings, durations, and severity of the disease, affected area of the intestine, medications, and previous operations were recorded. Endoscopic examination and laboratory blood tests of the patients were performed on the same day. The endoscopic examination of the patients was carried out by gastroenterologists with at least five years of experience. Smoking and alcohol use habits of the patients were recorded in detail.

In patients with UC, Truelove-Witts [16] and clinical colitis activity index (CCAI) criteria [17] were used to calculate clinical severity. Endoscopic Mayo Score [18] was used to categorize endoscopic severity. UC patients with CCAI index scores ≤4 were considered clinically inactive. Bloodless defecation 1-2 times a day, normal hemoglobin, and erythrocyte sedimentation rate, as well as the absence of fever and tachycardia, are characteristics of inactive disease according to the Truelove-Witts score.

UC patients with Mayo Scores between 0 and 1 considered to be in endoscopic remission. CD activity index (CDAI) [19] and a simple endoscopic score (SES-CD) [20] were used for patients with CD. CD patients with a CDAI value <150 were considered to have clinically inactive disease. Clinically active CD patients were divided into three subgroups as mildly active (CDAI was between 150-220), moderately active (CDAI was between 221-450), and severely active (CDAI> 450). Patients were also evaluated endoscopically according to SES-CD, and scores between 0-2 were considered as endoscopically inactive, and scores above 2 were considered as endoscopically active disease.

ADA level was determined in all patients for biochemical evaluation of disease activity. For laboratory tests, venous blood was collected from the patients and control groups after 10-12 hours of fasting (to eliminate possible lipemia) into tubes containing EDTA, sodium citrate, and gel (Becton Dickinson, USA). The gel tubes were centrifuged for 10 minutes in 3500 RPM (1300g) after resting for 30 minutes. Whole blood count (EDTA blood samples) and erythrocyte sedimentation rates (ESR) (performed using the Westergreen method from sodium citrate blood sample) were measured with the Sed Rate Screener 100 (SRS 100, Greiner Bio-one GmbH, Austria) device. CRP was measured from serum samples with the nephelometric method (Immage, Beckmann Coulter, USA).

The serum samples were kept at -70ºC for measuring ADA levels later, and frozen samples were thawed and studied just before the analysis. Repeated freezing and thawing were avoided. ADA levels of all patients were measured using the Enzymatic-spectrophotometric method. Total ADA levels were evaluated by the Giusti and Galanti method [21]. Samples incubated with adenosine and free ammonium ions were measured. The concentration of ammonium ions formed in 1 minute was expressed in U/L and defined as the ADA level.

Ethical considerations

This study was approved by the Ethics Committee of Health Science University İstanbul Haydarpaşa Training and Research Hospital (HNEAH-KAEK 2013/KK/62) and carried out according to the principles of the Helsinki Declaration.

Written informed consent was obtained from all patients and volunteer participants.

Statistical analysis

Nonparametric tests were used to evaluate non-normally distributed study data. Descriptive statistical methods (median) were used, and the nonparametric Kruskal Wallis test was utilized to compare quantitative data between groups. Mann Whitney U test was used to identify groups with differences. The mean rank values were considered in determining the source of group differences. Nonparametric Kendall's Taub relation test was made use of for the correlation analysis of parameters. Power analysis was performed using the computer-aided statistics program G-power. According to previous studies [22,23] in the literature, the smallest sample size to represent the population with 95% strength was calculated as 36 participants with 1.25 effect size and 5% alpha error margin. IBM SPSS (Statistical Package for Social Sciences) Statistics 20 program was used for statistical analysis in evaluating the study findings.

Results

Ninety-two IBD patients (43/49, CD/UC) and 31 healthy volunteers were included in this study. There were 19 female and 24 male patients in the CD group, 27 female, and 22 male patients in the UC group, and 15 female, 16 male patients in the control group. The median ages of the CD, UC and control groups were 39 years (24-66), 37 years (16-74), and 39 years (25-55), respectively. IBD group patients and healthy volunteers, as well as UC and CD subgroup patients were similar in terms of mean age and gender distribution (Table 1).

The mean ADA level was 24.87 (9.6 - 74.9) IU/L in the IBH group and 20.8 (13.7 - 38.9) IU/L in the healthy volunteer group. The mean ADA level of all IBD patients was significantly higher than that of the healthy volunteer group (P=0.013). Also, the mean ADA levels of CD [26.48 (13.8-74.9) IU/L] and UC [23.8 (9.6-43) IU/L] groups were statistically significantly higher (P=0.028, P=0.027 respectively) compared with the healthy volunteer control group. However, ADA levels of patients in the UC and CD groups were similar (P=0.76).

When ADA levels were compared in the CD subgroups according to disease localization (Normal: no active disease as diagnosed by endoscopy; Localization: Colonic, ileal, ileocolonic) and CDAI (<150; mild, 150-219; moderate and >220; severe), the results were similar (Table 2). When the patients with CD were classified into those with clinically active and inactive disease according to CDAI (<150; inactive, ≥150; active) and SES-CD (0-2; inactive, >2; active), there was no significant difference between ADA levels and disease activity (Table 3). However, in patients with CD, ESR, and CRP values were significantly higher in the active group than the inactive group with respect to the CDAI classification (P=0.002, P=0.035, respectively).

No significant differences were found between the disease types in the CD subgroups (stricting, penetrating, nonpenetrating-nonstricturing) and the ADA levels (Table 2). When the patients with UC were compared between subgroups according to CCAI (score between 0-4: subgroup 0, between 5-10: subgroup 1, 11-17: subgroup 2, 18 and above: subgroup 3), subgroup 0, which had the lowest disease activity, was found to significantly differ in terms of ADA levels, ESR, and CRP values from the other groups (P=0.002, P=0.001, P=0.010 respectively) (table 2).

Table 1: The characteristics of study and control groups

Characteristic	HC	IBD	CD	UC	*P*-value
Patients, n	31	92	43	49	
Gender / Male Female	15/16	46/46	19/24	27/22	0.30
Median Age (Range, Years)	39 (24-55)	36.8 (16-74)	36 (19-63)	37.2 (16-74)	0.29
Median BMI (Range kg/m2)	24.2 (18.4-37.9)	22.82 (13.7-37.5)	22.4 (16.2-35.2)	23.15 (13.7-37.5)	0.38
Smoke (+/-)	10 /21	28 / 64	11 / 32	17 / 32	0.28
Years of Disease (Median)	---	5.5 (1-16)	6.1 (1-15)	5.0 (1-16)	---

HC: healthy controls, IBD: inflammatory bowel disease, CD: crohn's disease, UC: ulcerative colitis, BMI: body mass index

Table 2: Serum ADA, CRP and ESR levels in IBD classified by potential categorical coverable

Variable	n	ADA (IU/L)	*P*-value	CRP (mg/dl)	*P*-value	ESR (mm/h)	*P*-value
Crohn's disease							
Disease location							
Normal	5	17.98(13.8-23.4)		1.03(0.13-2.13)		22.8(10-45)	0.53
Colonic	6	33.25(15-74.9)	0.093	5.5(0.13-14)	0.142	45.6(19-64)	
Ileal	16	22.43(14.9-47.6)		2.71(0.1-12)		22.8(21-71)	
Ileocolonic	16	28.6(14.5-48.7)		3.07(0.16-14)		39.06(21-14.9)	
CDAI							
<150	24	23.5(13.8-74.9)		1(0.1-14)		19(0.21-58)	<0.001
150-219	11	23(15-38.4)	0.832	2(0.13-14)	0.009	46(20-79)	
>220	8	22.1(14.9-34.9)		3.51(2-10)		55(35-90)	
Disease behavior							
B1	21	24.3(13.8-74.9)		1.65(0.1-14)		3510-90)	0.724
B2	12	23(14.9-47.6)	0.606	1.94(011-14)	0.980	29(0.21-71)	
B3	10	21.65(14.5-41)		1.64(0.13-6.44)		35(14-54)	
Ulcerative colitis							
Disease location							
Proctitis	4	19.95(9.6-28)		0.5(0.26-1.3)		26(16-34)	0.946
Left side	27	22(12.2-42.9)		1.2(0.1-6)		28(6-70)	
Pancolitis	18	23.8(11-43)	0.615	1.17(0.1-7.3)	0.522	29(10-83)	
CCAI							.
<4	21	20.9(11-28.7)		0.31(0.1-7.3)		19(6-54)	0.010
5-10	14	28.95(20-43)		0.94(0.11-2.28)	0.001	42(12-70)	
11-17	14	23.4(9.6-36.3)	0.002	4.4(0,4-6)		34(28-83)	
>18	7	24.9(20.9-42.9)		1.54(0.4-5.3)		25(10-83)	
Truleove-Wits index							
0	4	28.35(17-29.4)		0.28(0.26-0.31)		21.5(12-32)	0.031
1	12	21.35(11-42.7)		0.29(0.1-3.59)		18.5(6-61)	
2	22	22(9.6-43)	0.757	1.25(0.11-6)	<0.001	34(12-70)	
3	11	24.7(12.4-42.9)		4.4(0.4-7.3)		28(10-83)	
Mayo score							
0	5	28(17-29.4)		0.26(0.1-0.31)		14(12-32)	0.110
1	4	29.95(18.5-29.9)	.596	0.44(0.28-0.63)	.001	12(6-61)	
2	23	22(11-43)		0.98(0.11-6)		28(12-70)	
3	17	22.7(9.6-36.3)		2.2(0.4-7.3)		30(10-83)	

Data presented as median (IQR), ADA: Adenosine deaminase, IBD: Inflammatory bowel disease, CDAI: Crohn's disease activity index, CCAI: Clinical colitis activity index

Table 3: Serum ADA, CRP and ESR levels in inactive-active IBD

Variable	n	ADA (IU/ml)	*P*-value	CRP (mg/dl)	*P*-value	ESR (mm/h)	*P*-value
Crohn's disease							
CDAI							
Inactive	26	24.25(13.8-74.9)	0.032	1.05(0.1-14)	0.035	20(0.21-67)	0.002
Active	12	21.70(14.9-38.4)		2(0.13-14)		45(20-90)	
SES-CD							
Inactive	31	21.90(13.8-74.9)	0.832	0.47(0.11-14)	0.003	18.5(10-57)	<0.001
Active	8	23(14.5-47.6)		1.65(0.1-14)		35(0.21-90)	
Ulcerative Colitis							
CCAI							
Inactive	28	20.9(11-28.7)	0.001	0.31 (0.1-7.30)	0.005	19(6-54)	0.002
Active	21	25.65(9.6-43)		1.53(0.11-6)		34(10-83)	

Data are presented as median (IQR), ADA: Adenosin deaminase, IBD: Inflammatory bowel disease, CDAI: Crohn disease activity index, CCAI: Clinical colitis activity index, SES-CD: Simple Endoscopic Score for Crohn's Disease

The patients with CD were divided into six subgroups regarding the medicine they used. ADA levels were compared between the medicine subgroups (mesalazine (n:3), azathioprine (n:23), budesonide (n:2), azathioprine + budesonide (n:3), anti-

TNF (n:8), and azathioprine + steroid (n:4)), and no differences found (P>0.05).

As the UC group was classified into active and inactive subgroups according to CCAI, ADA levels, CRP, and ESR values were higher in the active UC subgroup than the inactive subgroup (P=0.001, P=0.005, P=0.002, respectively), but ADA levels were comparable (Table 2). The cut-off level for the value of ADA in differentiating active UC patients from inactive ones was determined as 21.64 IU/L, with 76.8% power of discernment, 89% sensitivity, and 60% specificity by the ROC curve. The cut-off for CRP was 0.80, with 74% power of discernment, 68% sensitivity, and 42% specificity, and for ESR, it was 18mm/s, with 85% discrimination power, sensitivity 85.6%, and specificity 30% (Figure 1).

There was no significant difference in ADA levels between UC patients according to endoscopic Mayo score and Truelove-Witts clinical activity index (P=0.596, P=0.757, respectively).

ADA levels of UC patients did not differ according to the drugs they used, which were as follows: 5-ASA (n=30), steroid (n=1), 5-ASA+azathioprine (n=6), 5-ASA+azathioprine+steroid (n=3), 5-ASA+steroid (n=8), anti-TNF+azathioprine (n=1). In addition, the ADA levels of the smokers and non-smokers among CD and UC patients were similar (P=0.29, P=0.27 respectively).

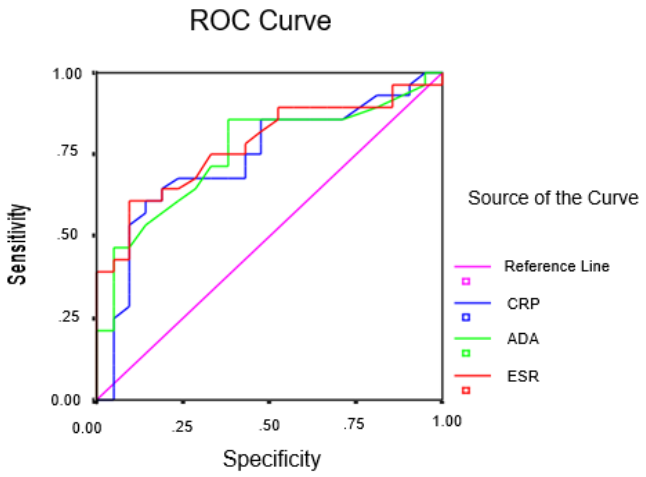

Figure 1: ROC curve of CRP, ESR, and ADA levels in Ulcerative Colitis patients

Discussion

IBD is a chronic inflammatory pathology of the gastrointestinal tract without curative medical treatment and is triggered by environmental, genetic, microbial, or immunoregulatory factors. IBD has remission and exacerbation periods. CD and UC are two main forms of IBD, and the underlying causes are similar in terms of epidemiological and clinical features [1]. Diagnosis, activity, and treatment results in patients with IBD are evaluated by the combination of clinical examination, laboratory tests, radiology, endoscopic and histological findings. Although clinical, endoscopic, and histopathological methods are one step ahead in terms of diagnostic importance, the benefits of laboratory findings should not be overlooked.

In the recent years, many noninvasive tests have been studied in the evaluation of intestinal inflammation, but a simple, widely available, and successful one is yet to be found. CRP, ESR, white blood cell (WBC) count, fecal calprotectin, and polymorphonuclear neutrophil elastase were noninvasive tests used for this purpose. While CRP value correlates with disease activity, especially in patients with CD, this correlation is weaker in patients with UC [4]. Fecal calprotectin has been used in recent years as a noninvasive sensitive stool test to detect intestinal inflammation in both UC and CD patients. It has proven to be a better predictor, especially in patients with UC. On the other hand, ESR is less used in clinical practice because it has a longer half-life, and its relationship with inflammation is weaker compared to that of CRP. Due to the limitations of the current noninvasive tests, the search for the optimal test, which can be used in both diagnosis and activity determination of patients with IBD will likely continue.

ADA plays a role in the maturation and function of monocytes and macrophages. It is the main enzyme involved in lymphoid cell differentiation, and the highest ADA activity is detected in lymphocytes, especially T lymphocytes and monocytes. ADA activity is higher in CD + 4 lymphocytes than in CD + 8 lymphocytes [24-27]. As a non-specific marker of T cell activation and cellular immunity, ADA levels increase in a variety of autoimmune and inflammatory diseases that cause cell-mediated immune response [8-14].

It seems rational to use inflammatory markers for diagnosis and activity determination in IBD, the main pathogenetic mechanism of which is T-cell activation and chronic intestinal inflammation. In our study investigating the diagnostic benefit of ADA level as a marker of T cell activation and cellular immunity in patients with IBD, it was significantly higher in patients with IBD compared to the control group. ADA levels were also higher in patients with active disease compared to the HC group and patients with inactive disease in the UC group. However, there was no significant difference in ADA levels between patients with clinically active and inactive disease in the CD group.

Although it is known that ADA level increases in IBD, few studies have evaluated its relationship with disease activity in the literature. The relationship between ADA levels and clinical and endoscopic disease activation was investigated in patients with CD by Maor et al. [22] and in patients with UC by Beyazıt et al. [23]. In both studies, akin to the results in our study, ADA level was higher in patients with UC and CD compared to the HC group. WBC, CRP, and ESR values were frequently used inflammatory markers to determine IBD activity in clinical practice. These parameters may vary with the severity of inflammation. However, they are not sufficient to reflect disease activity, as they have low sensitivity and specificity for intestinal inflammation [4,28].

In our study, ADA level was significantly higher in the UC group compared to the CD group, in which CRP and ESR values were also higher. When patients with active and inactive UC were compared, CRP, ESR, and ADA levels were significantly higher in the active disease group. In their study, Beyazıt et al. [23] evaluated ADA level as a marker of disease activity in patients with UC and found it to be significantly higher in patients with active UC compared to those with inactive disease. In that study, ADA cut-off value was 9.45 U/L, and its predictive accuracy of active disease was 83.7%

(sensitivity 83.3%, specificity 84.2%). In our study, the results were similar, and ADA level was higher in patients with UC compared to the HC group. ADA was significantly higher in the active disease group than the inactive disease group. According to our calculations, the diagnostic value of ADA was similar to other non-invasive laboratory parameters such as CRP and ESR.

In our study, there was no correlation between ADA levels, CRP, and WBC values in the UC patient group. Contrary to our study, Beyazıt et al. [23] found a correlation between ADA level, WBC, and CRP values in patients with UC. However, in their study, ADA cut off value was lower than ours. Differences in the kits used, the time of blood drawing, and in the process of handling and processing serum samples may play a role in the formation of divergent results. As a result of their study, Maor et al. [22] found that ADA and CRP values were higher in patients with active CD compared to HC participants. Additionally, they reported a significantly lower ADA level and CRP value in patients with inactive CD (CDAI <150). They also reported a significantly positive correlation between ADA and CRP values in patients with CD. They claimed that ADA levels could distinguish between active and nonactive CD. However, in our study, while ADA level was higher in the CD group compared to the HC group, there were no significant differences between active and inactive patients with CD. Additionally, we did not observe any correlation between ADA levels and other inflammatory parameters (CRP, ESR, WBC) in the CD group. The results of ADA levels in patients with CD by Sajjadi M et al. [29] were similar to our results. They also could not demonstrate that ADA level was associated with disease activity and other inflammatory markers (CRP, ESR, and fecal calprotectin) in patients with CD.

The effects of drugs used by patients on inflammation may alter ADA levels. Therefore, patient groups were also compared in terms of the drugs they used in our study. There was no difference in ADA levels between patient groups using different pharmacological agents. Additionally, in patients with active UC, although ADA level was high, no relationship was demonstrated between the degree of severity and endoscopic and clinical activity. ADA levels were negatively correlated with drugs used in patients with UC. Evaluation of all these data suggest that with the use of more potent immunoregulatory drugs in patients with higher inflammation and clinical activity, ADA levels are expected to be relatively lower.

Limitation

Possible limitations of ADA level measurement and its use in clinical practice should be considered. Because tuberculosis patients are prominent in our country, the use of ADA levels in determining IBD activity is limited, especially in patients with suspected intestinal tuberculosis. In these patients, the diagnosis of intestinal tuberculosis should be ruled out first. Undoubtedly, easily applicable, and reproducible noninvasive tests will be preferred more. This feature should also be provided for ADA measurement. The cut-off values used in studies conducted with ADA levels differ from each other, and even its mean value in one study may be the same as that of healthy controls in another study. For this reason, ADA level measurements should be standardized before common use recommendations. As inflammatory markers, ADA levels, which are elevated in patients with IBD and appear to be associated with high inflammatory response, especially in patients with active UC, seem to be usable in determination of the clinical activity.

In our study, the potential of ADA levels to distinguish the active disease from inactive disease was similar to that of commonly used CRP since it is cheaper, reproducible, and easier in routine. However, an elevated serum CRP level is not a specific finding and may vary due to several inflammatory and non-inflammatory responses. It has been shown that serum CRP levels are independently related with serum albumin level and cardiovascular diseases [30]. Many factors such as age, gender, smoking addiction, body mass index, liver failure, lipid levels, and blood pressure can affect baseline CRP levels. In addition, it has been shown that healthy postmenopausal women receiving hormone replacement therapy have high CRP levels and, in these cases, CRP is the most affected inflammatory marker. Also, some drugs used for other diseases, such as HMG CoA-reductase inhibitors, have also been shown to reduce high CRP levels [31].

Conclusion

ADA level was higher in patients with IBD than HC volunteers, reflecting inflammation in the gastrointestinal tract. It was found effective in distinguishing active disease from inactive disease in UC patients. However, its effectiveness was similar that of CRP, which is widely used in daily practice. Especially considering the low sensitivity of CRP in the determination of activity in the UC patient group, ADA level measurement may be beneficial for patients in which a definitive decision regarding disease activity cannot be made, despite evaluation of the CRP value. Although its routine use is not yet recommended, ADA level is useful in determining the clinical activity of IBD and can be preferred in selected cases. Additionally, before the widespread use of ADA levels is recommended, it should be ensured that it is easily applicable in larger populations.

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