



# Determination of compliance with anti-TNF alpha treatment and quality of life in inflammatory bowel disease patients

Inflamatuvar bağırsak hastalarının anti-TNF alfa tedavisine uyum ve yaşam kalitelerinin belirlenmesi

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**ABSTRACT • Background and Aims:** This study aims to determine the relationship between compliance with anti-tumor necrosis factor alpha treatment and quality of life in inflammatory bowel patients. **Materials and Method:** The study was conducted at Gazi University Gastroenterology Department, Inflammatory Bowel Diseases Outpatient Clinic between 15 November 2023 and 1 March 2024. The study was completed with 123 patients. Study data were collected using the "Patient Information Form", "Ulcerative Colitis Simple Clinical Colitis Activity Index", "Harvey Bradshaw Activity Index", and "Inflammatory Bowel Diseases Quality of Life Scale", "Anti-Tumor Necrosis Factor Alpha Treatment Compliance Scale". **Results:** The total score the patients received from the Inflammatory Bowel Diseases Quality of Life Scale was  $159.40 \pm 32.56$ . The total mean score of the patients on the Anti-Tumor Necrosis Factor Alpha Treatment Compliance Scale was  $2.36 \pm 0.70$ . A moderate, negative relationship was found between the mean scores of the patients from the "Personal Factors" sub-dimension of the Anti-Tumor Necrosis Factor Alpha Treatment Compliance Scale and the total and all sub-dimensions of Inflammatory Bowel Diseases Quality of Life Scale ( $p < 0.001$ ). **Conclusion:** The patients who participated in the study were found to have moderate levels of adherence to anti-tumor necrosis factor alpha treatment and quality of life. Further studies are needed to enable the generalization of these findings.

**Key words:** Compliance, inflammatory bowel, nursing, quality of life

**ÖZET • Giriş ve Amaç:** Bu çalışmanın amacı, inflamatuvar bağırsak hastalarında anti-tümör nekrozis faktör alfa tedavisine uyum ile yaşam kalitesi arasındaki ilişkiyi belirlemektir. **Gereç ve Yöntem:** Çalışma, 15 Kasım 2023 ile 1 Mart 2024 tarihleri arasında Gazi Üniversitesi Gastroenteroloji Bölümü İnflamatuvar Bağırsak Hastalığı Polikliniği'nde yürütülmüştür. Çalışma 123 hasta ile tamamlanmıştır. Çalışma verileri "Hasta Bilgi Formu", "Ülseratif Kolit Basit Klinik Kolit Aktivite İndeksi", "Harvey Bradshaw Aktivite İndeksi" ve "İnflamatuvar Bağırsak Hastalığı Yaşam Kalitesi Ölçeği", "Anti-Tümör Nekrozis Faktör Alfa Tedavi Uyum Ölçeği" kullanılarak toplanmıştır. **Bulgular:** Hastaların İnflamatuvar Bağırsak Hastalığı Yaşam Kalitesi Ölçeği'nden aldıkları toplam puan ortalaması  $159.40 \pm 32.56$ 'dir. Hastaların Anti-Tümör Nekrozis Faktör Alfa Tedavi Uyum Ölçeği toplam puan ortalaması ise  $2.36 \pm 0.70$ 'dir. Hastaların Anti-Tümör Nekrozis Faktör Alfa Tedavi Uyum Ölçeği "Kişisel Etkenler" alt boyutundan aldıkları puan ortalamaları ile İnflamatuvar Bağırsak Hastalığı Yaşam Kalitesi Ölçeği toplam ve tüm alt boyutları arasında orta düzeyde negatif ilişki bulundu ( $p < 0.001$ ). Anti-Tümör Nekrozis Faktör Alfa Tedavi Uyum Ölçeği "Endişe ve Başetme" alt boyutunun toplam puan ortalamaları ile İnflamatuvar Bağırsak Hastalığı Yaşam Kalitesi Ölçeği tüm alt boyutlarının toplam puan ortalamaları arasında orta düzeyde negatif ilişki bulundu ( $p < 0.001$ ). **Sonuç:** Çalışmaya katılan hastaların anti-tümör nekrozis faktör alfa tedavisine uyumlarının ve yaşam kalitesi düzeylerinin orta seviyede olduğu belirlenmiştir. Sonuçların genellenebilmesi için bu konuda daha fazla araştırmaya ihtiyaç duyulmaktadır.

**Anahtar kelimeler:** Uyum, inflamatuvar bağırsak, hemşirelik, yaşam kalitesi.

## INTRODUCTION

Inflammatory bowel disease (IBD) is the uncontrolled inflammation of the intestinal mucosa that develops also in the absence of an infectious eti-

ology. The disease includes ulcerative colitis and Crohn's disease and progresses with idiopathic, chronic, relapse, and remission periods (1,2).

IBD is a chronic disease that seriously affects the quality of life progressing with attacks and remissions, and requires multiple drug use and constant monitoring (3). The symptoms that patients frequently experience due to the disease are diarrhea, abdominal pain, weight loss, anemia, and arthralgia. While treatment generally includes corticosteroids and biological drugs, the decision for surgical intervention is made specifically depending on the course of the disease. During the disease process, patients also struggle with a lot of psychological burdens. The unpredictability of the course of the disease, difficulties in bowel control and feelings caused by this such as shame, and the effects of the symptoms (social isolation, fatigue, and fear of catching cancer, etc.) are just a few of these psychological burdens (4). All these negativities experienced by patients cause a decrease in their quality of life. In a study conducted in Greece regarding IBD, the decrease in the quality of life of patients was found to be associated with their stress, anxiety, and depression levels (5).

Today, the aims of IBD treatment are listed as steroid-free remission, endoscopic recovery, reducing intestinal damage, and prevention of complications (stricture, fistula, abscess, etc.). To achieve these aims, it is necessary to prevent various stages of the immune process that develops in IBD. These include, for example, inhibition of proinflammatory cytokines, use of anti-inflammatory cytokines, inhibition of adhesion molecules, T cell inhibitors, signal transduction inhibitors. Anti-tumor necrosis factor (TNF) agents began to take part in treatment to block TNF- $\alpha$ , one of the pro-inflammatory cytokines (6). With the introduction of tumor necrosis factor alpha (TNF- $\alpha$ ) antagonists, the era of biological treatment in IBD began. The biological treatment era, which started with anti-TNF- $\alpha$  treatments, was a precursor of a safer and more successful period in the induction and maintenance of clinical response and remis-

sion. Although anti-TNF- $\alpha$  treatments are generally well tolerated, they may cause concerns due to infection, malignancy, and other side effects they give rise to. Therefore, compliance of patients with the treatment becomes important. No studies were found in the literature that evaluated compliance of IBD patients with anti-TNF alpha treatment and their quality of life together. This study aims to determine the relationship between compliance with anti-TNF alpha treatment and quality of life of IBD patients.

## **MATERIALS and METHOD**

### **Study Design**

The study is of descriptive-correlational type.

### **Research Questions**

- What is the quality of life of IBD patients?
- To what extent are IBD patients compliant with anti-TNF alfa treatment?
- Is there a relationship between the quality of life of and compliance with anti-TNF alfa treatment of IBD patients?

### **Population and Sample of the Study**

The study was conducted at Gazi University Gastroenterology Department IBD Outpatient Clinic between 15 November 2023 and 1 March 2024. All patients who met the inclusion criteria were tried to be reached in the study and the study was completed with 123 patients. As a result of the study, in the post-hoc power analysis made by taking into account the correlation test, the power of the sample size of 123 people was found to be 96.5% with a medium effect size and a significance level of 0.05.

### **Study Sample**

Patients diagnosed with IBD, who met the inclusion criteria of the study, volunteered to partici-

pate in the study, and gave written and verbal consent, constituted the study sample. Patients who were over 18 years of age, literate, had no communication difficulties, volunteered to participate in the study, and received anti-TNF alpha treatment were determined as inclusion criteria in the study sample. Patients with mental and physical health problems that could hinder communication were excluded from the sample.

### Data Collection Tools

Study data were collected using the “Patient Information Form”, “Ulcerative Colitis Simple Clinical Colitis Activity Index”, “Harvey Bradshaw Activity Index”, and “Inflammatory Bowel Diseases Quality of Life Scale”, “Anti-TNF Alpha Treatment Compliance Scale”.

### Patient Information Form

This form was created by researchers in line with the literature. It consists of questions regarding socio-demographic data, data regarding health and disease, and data regarding drug use (4,7-10).

### Inflammatory Bowel Disease Quality of Life Questionnaire (IBD-QOL)

The scale was developed to evaluate the quality of life of patients regarding inflammatory bowel diseases. The scale developed by Guyatt et al. (11) was adapted into Turkish by Akçura et al. (12). The scale consists of 32 items and has 4 sub-dimensions. 10 items constitute bowel symptoms, 5 items constitute systemic symptoms, 12 items constitute emotional function, and 5 items constitute social impairment in the scale. Each question is scored between 1 point “worst case” and 7 points “best case”, and the highest score to be obtained from the scale is calculated as 224 and the lowest score is 32. As the score increases, the quality of life of the patients increases. The Cronbach alpha value of the scale was found to be 0.95 (12). In this

study, the Cronbach’s alpha value of the scale was found to be 0.937.

### Ulcerative Colitis Simple Clinical Colitis Activity Index

It is a diagnostic tool and questionnaire used to assess the degree of symptoms in people with ulcerative colitis. The index was created in 1998 and is still used to evaluate the severity of symptoms. A score of 5 or higher indicates active disease (13).

### Harvey Bradshaw Activity Index

It consists of questions that enable categorizing the severity of Crohn’s disease quickly and detect remission. Harvey and Bradshaw was first published as a shorter and simpler alternative to the standard classification technique called the Crohn’s Disease Activity Index in The Lancet in 1980. Patients answer five questions and are given points based on the severity of their symptoms. Below 5 indicates remission (14).

### Anti-TNF Alpha Treatment Compliance Scale

The scale was developed by Başak et al. The scale consisting of 12 items and 4 sub-dimensions was determined to be valid and reliable. The scale includes positive and negative expressions. As a result of coding positive and negative expressions in the scale, if the score obtained from the scale is high, this indicates non-compliance of patients with the treatment. In the score distribution, scores between 0 and 2 were considered good compliance, values greater than 2 and less than 3 were considered medium compliance, and values of 3 and above were considered poor compliance. In the study in which the scale was developed, Cronbach’s alpha value was calculated as 0.892 (15). In this study, the Cronbach alpha value of the scale was found to be 0.765.

### Study Implementation Process

The data of the study was collected between November 15, 2023 and March 1, 2024. Before con-

ducting the study, the patients were interviewed face to face and informed about the purpose of the study. The application of the questionnaire and scales took approximately 20 minutes.

### Ethics Statement

Ethics committee approval for this study was obtained at the meeting of the Gazi University Ethics Commission dated 07.11.2023 and numbered 19. The study was complied with The World Medical Association Declaration of Helsinki. Written and verbal informed consent was obtained from all patients who volunteered to participate in the study.

### Data Analysis

SPSS Package program was used to evaluate the data obtained from the study. Number, percentage, mean, standard deviation, skewness and kurtosis coefficients, and Pearson Correlation test were used to evaluate the data. Skewness and kurtosis coefficients were accepted as normal distribution between values of -1.5 and + 1.5. Statistical significance value was accepted as  $p < 0.05$ .

## RESULTS

The descriptive characteristics of the patients are given in Table 1. The average age of the patients is  $39.21 \pm 13.52$ . 56.9% of the patients are women, 58.5% are married and have children. 60.2% of the patients are working and 34.1% are high school graduates. Regarding income levels of the patients, the income of 57.7% is equal to the expenses. The medical diagnosis of 67.5% of the patients is Crohn's disease. The rate of the patients diagnosed with IBD for 3-5 years is 29.3%. 22.8% of the patients had surgery due to IBD, and 45.5% were hospitalized due to IBD. 42.3% of the patients have chronic diseases other than IBD, and 38.2% constantly use drugs due to these chronic diseases. While the rate of current smokers is 22.8%, the rate of current alcohol users is 11.4%. The mean of Ulcerative

Colitis Simple Clinical Colitis Activity Index of the patients is  $1.7 \pm 1.7$ , and the mean of Harvey Bradshaw Activity Index is  $1.6 \pm 1.6$  (Table 1).

The total score the patients received from the Inflammatory Bowel Diseases Quality of Life Scale was  $159.40 \pm 32.56$ . Inflammatory Bowel Diseases Quality of Life Scale sub-dimensions and the mean scores they received were found as "Bowel Symptoms" to be  $52.10 \pm 10.19$ , "Systemic Symptoms" to be  $24.25 \pm 6.53$ , "Emotional Function" to be  $55.63 \pm 12.64$ , and "Social Impairment" to be  $27.17 \pm 7.46$ . The total mean score of the patients on the Anti-TNF Alpha Treatment Compliance Scale was  $2.36 \pm 0.70$ . Anti-TNF Alpha Treatment Compliance Scale sub-dimensions and the mean scores they received were found as "Personal Factors" to be  $3.07 \pm 1.14$ , "Awareness" to be  $1.59 \pm 1.00$ , "Quitting Treatment" to be  $2.10 \pm 1.10$ , and "Worrying and Coping" to be  $2.69 \pm 1.14$  (Table 2).

A moderate, negative relationship was found between the mean scores of the patients from the "Personal Factors" sub-dimension of the Anti-TNF Alpha Treatment Compliance Scale and the total and all sub-dimensions of IBD-QOL ( $p < 0.001$ ). A low-level, positive, and significant relationship was found between the "awareness" sub-dimension of the Anti-TNF Alpha Treatment Compliance Scale and the IBD-QOL "Emotional Function" mean scores ( $p < 0.05$ ). A low-level, negative, and significant relationship was determined between the mean scores of the patients from the "Quitting Treatment" sub-dimension of the Anti-TNF Alpha Treatment Compliance Scale and the total mean scores of the "Bowel Symptoms", "Systemic Symptoms", "Emotional Function" sub-dimensions of IBD-QOL ( $p < 0.05$ ). A moderate negative relationship was found between total mean scores of "Worrying and Coping" sub-dimension of Anti-TNF Alpha Treatment Compliance Scale and total mean scores of all sub-dimensions of IBD-QOL ( $p < 0.001$ ) (Table 3).

**Table 1** Descriptive characteristics of the patients (n = 123)

Characteristics	Number	Percentage
<b>Age (mean ± standard deviation)</b>	39.21 ± 13.52	
<b>Gender</b>		
Female	53	43.1
Male	70	56.9
<b>Marital status</b>		
Single	51	41.5
Married	72	58.5
<b>Presence of children</b>		
Yes	51	41.5
No	72	58.5
<b>Educational status</b>		
Primary school	24	19.5
High school	42	34.1
University and above	57	46.3
<b>Working status</b>		
Working	74	60.2
Not working	49	39.8
<b>Level of income</b>		
Income is less than expenses	26	21.1
Income equals expenses	71	57.7
Income exceeds expenses	26	21.1
<b>Diagnosis</b>		
Ulcerative colitis	40	32.5
Crohn's	83	67.5
<b>IBD diagnosis time</b>		
0-2 years	32	26.0
3-5 years	36	29.3
6-10 years	32	26.0
11 years and above	23	18.7
<b>Having surgery due to IBD</b>		
Yes	28	22.8
No	95	77.2
<b>Hospitalization due to IBD</b>		
Yes	56	45.5
No	67	54.5
<b>Anti-TNF alpha therapy received</b>		
Infliximab	80	65.1
Adalimumab	43	34.9
<b>Presence of chronic disease</b>		
Yes	52	42.3
No	71	57.7
<b>Continuous use of drug for chronic disease</b>		
Yes	47	38.2
No	76	61.8
<b>Smoking status</b>		
I smoke	28	22.8
I do not smoke	74	60.2
I quit smoking	21	17.1
<b>Alcohol drinking status</b>		
I drink alcohol	14	11.4
I do not drink alcohol	101	82.1
I quit drinking alcohol	8	6.5
<b>Ulcerative Colitis Simple Clinical Colitis Activity Index (mean ± standard deviation)</b>	1.7 ± 1.7	
<b>Harvey Bradshaw Activity Index (mean ± standard deviation)</b>	1.6 ± 1.6	

IBD: Inflammatory bowel disease, TNF: Tumor necrosis factor.

**Table 2** The mean score of the patients on Inflammatory Bowel Diseases Quality of Life Scale and Anti-TNF Alpha Treatment Compliance Scale (n = 123)

Scale and Scale Sub-dimensions	Mean ± Standard Deviation	Minimum - Maximum
<b>Inflammatory Bowel Diseases Quality of Life Scale</b>		
Bowel symptoms	52.10 ± 10.19	28.00 - 70.00
Systemic symptoms	24.25 ± 6.53	10.00 - 53.00
Emotional function	55.63 ± 12.64	20.00 - 84.00
Social impairment	27.17 ± 7.46	7.00 - 35.00
Total	159.40 ± 32.56	88.00 - 224.00
<b>Anti-TNF Alpha Treatment Compliance Scale</b>		
Personal factors	3.07 ± 1.14	1.00 - 5.00
Awareness	1.59 ± 1.00	1.00 - 5.00
Quitting treatment	2.10 ± 1.10	1.00 - 5.00
Worrying and coping	2.69 ± 1.14	1.00 - 5.00
Total	2.36 ± 0.70	1.00 - 4.58

TNF: Tumor necrosis factor.

**Table 3** The relationship between Inflammatory Bowel Diseases Quality of Life Scale and Anti-TNF Alpha Treatment Compliance Scale Scores of the patients (n = 123)

		Inflammatory Bowel Disease Quality of Life Questionnaire					
		Bowel Symptoms	Systemic Symptoms	Emotional Function	Social Impairment	Total	
Anti-TNF Alpha Treatment Compliance Scale	Personal factors	r	-0.578	-0.425	-0.544	-0.549	-0.605
		p	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>
	Awareness	r	0.073	0.124	0.191	0.080	0.142
		p	0.424	0.173	<b>0.034**</b>	0.379	0.116
	Quitting treatment	r	-0.218	-0.257	-0.240	-0.166	-0.251
		p	<b>0.015**</b>	<b>0.004**</b>	<b>0.007**</b>	0.066	<b>0.005**</b>
	Worrying and coping	r	-0.354	-0.347	-0.513	-0.333	-0.455
		p	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>
	Total	r	-0.437	-0.365	-0.454	-0.394	-0.478
		p	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>	<b>0.000*</b>

r = Pearson correlation test.

## DISCUSSION

Crohn's and ulcerative colitis diseases are called inflammatory bowel diseases and they affect the quality of life of patients. It was stated that biological treatments, which are now frequently used in the treatment of patients, have positive effects

on the quality of life of patients and should be investigated (10). In this study, findings regarding the quality of life of the patients, their compliance levels with anti-TNF alpha treatment, and the relationship between them are discussed below.

In this study, it was determined that the quality of life of patients was at a moderate level. In Brazil, it was found that the quality of life of IBD patients admitted to an outpatient treatment center in Brazil was at a good level (16). In a systematic review and meta-analysis study evaluating the quality of life of IBD patients, it was stated that there were strong study results that the quality of life of individuals with IBD was poorer than that of healthy individuals for both adults and children (4). The determinants of quality of life of patients are systemic symptoms, bowel symptoms, and effects on emotional and social impairment. In this study, the mean scores obtained from all sub-dimensions are at medium level. In the study by Mitropoulou et al. (2022), it was found that depressive, anxiety, and stress symptoms of the patients were negatively related to their quality of life (5). It is thought that there are many factors that affect quality of life of IBD patients and level of quality of life may be affected depending on many factors such as individual characteristics, health systems, and culture.

In this study, the compliance level of the patients with anti-TNF alpha treatment was determined to be moderate. In the study in which the Anti-TNF Alpha Treatment Compliance Scale was developed, compliance was found to be good in 71, to be moderate in 72, and to be poor in 22 of 165 people evaluated (15). In the literature, the number of studies evaluating compliance levels of IBD patients to anti-TNF alpha treatment is limited. It is thought that many factors may affect compliance level of patients. In a study conducted in multiple centers in Argentina, the researchers evaluated patients' compliance with treatment with 5-point Likert questions, and 50.3% of the patients reported that their compliance with oral drugs was insufficient. The patients stated the reasons for not complying with the treatment as forgetting the treatment, not finding the treatment necessary because they felt well, and the treatment being expensive etc.

(7). In a study conducted with IBD patients in China, the mean score of the patients on the Morisky Medication Adherence Scale was found to be  $6.11 \pm 1.93$ . This data showed that patients' compliance was low. In the same study, it was emphasized that in order to reduce the recurrence of symptoms and control the disease, healthcare personnel should pay attention to individual patient factors, simplify drug regimens, and formulate effective coping strategies to support drug treatment (8). In our study, it was determined that the patients showed the worst compliance with the "Personal Factors" sub-dimension of the Anti-TNF Alpha Treatment Compliance Scale. Therefore, in order for patients to adapt to treatment, their individual characteristics must be taken into consideration and planning must be made in line with expectations of patients.

In this study, a negative relationship was found at different levels between the total and most sub-dimensions of "Anti-TNF Alpha Treatment Compliance Scale" and "Inflammatory Bowel Disease Quality of Life Questionnaire" of the patients. The fact that Anti-TNF Alpha Treatment Compliance Scale scores of the patients increase (means worsening of compliance) means a decrease in quality of life scores. The study stated that using some biological treatments is effective in improving health-related quality of life (10). In a different study conducted with 251 IBD patients in Türkiye, it was similarly determined that the patients with high drug compliance had a better quality of life (9). The literature on the relationship between treatment compliance and quality of life of IBD patients is limited. More studies are needed, especially with patients receiving anti-TNF alpha treatment.

This study is strengthened by the use of validated, disease-specific instruments and the inclusion of patients receiving anti-TNF alpha therapy in a specialized gastroenterology outpatient clinic, enhancing the clinical relevance of the findings. However, the cross-sectional and single-center design

limits causal inference and generalizability. In addition, the reliance on self-reported measures and the relatively small sample size should be considered when interpreting the results.

In conclusion anti-TNF alpha treatment compliance and quality of life levels of the patients participating in the study were found to be moderate. It can also be said that their compliance with this treatment affects their quality of life. More study is needed in this area before the results can be generalized. Additionally, there is a need for intervention studies aimed at increasing patients' compliance and studies evaluating compliance and quality of life together.

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