

Celiac disease and COVID-19 pandemic : should we worry?

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Abstract

Background and study aims : The Coronavirus Disease 2019 (COVID-19) epidemic especially worries people with chronic diseases the entire world. In this study, the frequency, and clinical course of COVID-19 infection in patients with Celiac disease (CD) were investigated. CD patients' adherence to purchasing gluten free products (GFPs), the strict diet, and how patients' anxiety affects CD symptoms during the COVID-19 outbreak were also examined.

Patients and methods : A detailed-questionnaire was administered by telephone, and e-mail to the CD patients to determine the status of these patients in obtaining GFPs, and dietary compliance during the COVID-19 pandemic. State and trait anxiety levels of patients were evaluated using the State-trait Anxiety Inventory (STAI) scale. Additionally, whether patients with CD were diagnosed with COVID-19, and if diagnosed, their clinical course of the disease were investigated.

Results : One hundred and one patients were included in the study. The total number of patients who could obtain GFPs decreased significantly in the pandemic than before the pandemic. The patients' state anxiety index was 40.7 ± 7.9 , and the trait anxiety index was 44.5 ± 8.5 , and all patients were evaluated as mildly anxious. During the pandemic, two female patients were diagnosed with COVID-19.

Conclusion : CD patients did not have any additional risk compared to other individuals in terms of becoming infected with COVID-19 for patients under gluten free diet, and these patients will have a similar clinical course as individuals without CD. (*Acta gastroenterol. belg.*, 2020, 83, 517-525).

Keywords : Celiac disease : COVID-19, gluten free diet, anxiety.

Introduction

In December 2019, pneumonia that was caused by SARS-CoV-2 was identified in Wuhan City, China, and it was called Coronavirus disease 2019 (COVID-19) (1). Cases of pneumonia that are caused by this virus spread rapidly within a short time, and affected many countries with epidemics, and it was declared a global pandemic by the World Health Organization (WHO) on 11 March 2020. Although COVID-19 causes mild flu-like symptoms in most patients, this disease can also progress to fatal complications such as severe progressive pneumonia, acute respiratory distress syndrome, and organ failure caused by cytokine storm syndrome (2). The first patient in Turkey with COVID-19 infection was detected on 11 March 2020. The first death caused by COVID-19 infection occurred on 15 March 2020, and the infection was confirmed to have spread throughout Turkey on 1 April 2020. Thus, many Turkish people went to supermarkets, and pharmacies to stock up

on large amounts of food and supplies, similar to those in other countries. Mineral water, tonic drinks, medical masks, flour, pasta, cookies, rice, and other supplies with a long shelf life were exhausted within a short time. The government announced that restaurants could only provide takeaway and home delivery services, and markets could sell by paying attention to social distancing during limited working hours. Additionally, a curfew was imposed on those under 20 years of age and over 65 years of age. The most common reason for hospitalization was having an additional chronic disease, and the most common cause of mortality was being elderly for patients with COVID-19 infection (3,4). Under these conditions, it was inevitable that the elderly population with chronic diseases were fearful and anxious about the COVID-19 outbreak.

The first step in the infection is binding of SARS-CoV-2 to a host cell via its target receptor. Angiotensin converting enzyme 2 (ACE2) is the host target receptor for the SARS-CoV-2 virus (5,6). The gastrointestinal tract (GIT) is thought to be susceptible to SARS-CoV-2 infection because of ACE2 receptors, which are commonly expressed in the gut (7). Digestive system symptoms that are associated with SARS-CoV-2 infection may result from a direct viral effect, immunoactivation, or secondary organ damage during the course of the infection (8,9). Fever and respiratory symptoms are typically seen in patients with COVID-19. In addition, two studies reported that at least one gastrointestinal symptom was observed in these patients, with a frequency of 51%, and 61%, respectively. The most common GIT symptoms are anorexia, nausea, and diarrhea (10,11). There were also 16% of COVID-19 patients who presented with GIT symptoms alone, without respiratory symptoms (12). It is difficult for physicians to distinguish whether GIT symptoms are present in patients with chronic bowel disease, whether the symptoms are an exacerbation of existing bowel disease or associated with COVID-19. Additionally, viral nucleocapsid proteins were detected in gastric, duodenal, and rectal epithelial

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Submission date : 18/09/2020

Acceptance date : 28/10/2020

cell samples from COVID-19 patients (8). However, how this virus affects patients with chronic GIT disease remains unknown. Studies on COVID-19 in patients with inflammatory bowel disease (IBD) acknowledge that the presence of IBD poses no additional risk for COVID-19 infection, and the prevalence is the same as in the general population (13-16).

However, there is insufficient information about the coexistence of COVID-19 infection and other chronic GIT diseases such as celiac disease (CD). CD is a chronic immune-mediated enteropathy of the small intestine that is triggered by gluten exposure in individuals with a genetic predisposition (17). Although it is characterized by inflammation of the small intestine, it is also associated with increased morbidity and mortality due to comorbid causes such as osteoporosis, lymphoma, and pneumonia (18-21).

A strict lifelong gluten-free diet (GFD) is the only treatment for patients with CD. However, following a strict lifelong GFD is difficult, and creates serious social problems. Gluten-free products (GFPs) are more expensive than other foods, which makes the diet more difficult to follow. Celiac patients may worry about themselves because COVID-19 causes more morbidity and mortality in people with chronic disease, and therefore, they may have delayed going to the hospital for fear of becoming infected even if they had complaints during the pandemic. COVID-19 infection also caused radical changes in daily life on a global scale. Because of the curfew, millions of people were unable to complete their daily routines and were isolated at home. The difficulty of maintaining a GFD and how pandemic stress affects patients with CD remain unknown. There is no comparative study on this subject before and during the COVID-19 pandemic. There have been no studies or predictions published regarding the risk and prognosis of COVID-19 infection in CD patients.

In this study, the frequency and clinical course of COVID-19 infection in our CD patients were investigated. CD patients' adherence to purchasing GFPs, the strict diet, and how patients' anxiety affects CD symptoms during the COVID-19 outbreak were also examined.

Materials and methods

In this study, informed consent was obtained from all participants whose data could be analyzed and published for scientific purposes. A detailed questionnaire was then administered by telephone or e-mail. Patients who were followed by our gastroenterology clinic and were >18 years old, positive for celiac autoantibodies, diagnosed with endoscopic, and pathological CD, and who followed a GFD for at least 1 year were included in the study. Patients who had an incomplete CD diagnosis, were <18 years old, had incomplete data, could not be reached by phone and e-mail, and did not agree to participate in the study were excluded from the study. A questionnaire was administered to determine the status of these patients in

Table 1. — Descriptive Statistics

Gender(n: 101)	n (%)
Females	77 (76.2%)
Males	24 (23.8%)
Age (n: 101) (Mean± SD, Median)	n (%)
≤ 24	14 (13.9%)
25-34	28 (27.7%)
35-44	29 (28.7%)
≥ 45	30 (29.7%)
Educational Status (n: 101)	n (%)
Primary School	46 (45.5%)
High School	29 (28.7%)
University	26 (25.7%)
Working Status (n:101)	n (%)
Housewife	42 (41.6%)
Other workers	41 (40.6%)
Student	11 (10.9%)
Healthcare professional	7 (6.9%)
Marital Status (n:101)	n (%)
Marriage	70 (69.3%)
Single	31 (30.7%)
Period of CD diagnosis/year (n:101)	n (%)
(Mean± SD, Median)	5.5 ± 6.1 (3.0)
≤2 years	22 (21.8%)
3-5 years	42 (41.6%)
≥ 6 years	37 (36.6%)
Age of CD diagnosis (n:101) (Mean± SD, Median)	n (%)
≤17	11 (10.9%)
18-24	17 (16.8%)
25-34	28 (27.7%)
≥35	45 (44.6%)
Additional chronic disease (n:101)	n (%)
+	43 (42.6%)
-	58 (57.4%)
Familial CD history (n:101)	n (%)
+	20 (19.8%)
-	81 (80.2%)
Considering themselves at high risk of becoming infected with COVID-19 (n:101)	n (%)
Yes	48 (47.5%)
No	53 (52.5%)

CD : Celiac Disease

obtaining GFPs (easy, difficult, inaccessible) and dietary compliance (complete, mostly, rarely, incompatible) between 1 March 2020 and 1 June 2020, when COVID-19 cases were seen in our country.

Patients were interviewed about the changes in their current symptoms related to CD compared to before the pandemic using this questionnaire (Table 1). Detailed information for the CD patients was recorded. The effects of the pandemic on economic conditions, GFP supply, and diet compliance were investigated. Additionally, state and trait anxiety levels of patients were evaluated using the State-trait Anxiety Inventory (STAI) scale (22).

Also, whether patients with CD were diagnosed with COVID-19, and if diagnosed, their symptoms and

clinical course of the disease were investigated. Patients were also interviewed about whether they considered themselves to be at risk for COVID-19 infection. The relationship between changes in each patient's weight, cigarette and alcohol intake, their economic status, GFP supply, GFD compliance, and anxiety level during the pandemic were investigated. However, two patients did not agree to provide information about their monthly income, while one patient refused to provide information about alcohol intake and smoking.

Statistical Analysis

The data were analyzed using the Statistical Package for Social Sciences version 20.0 statistical program (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as the mean \pm standard deviation, and median, and categorical variables were presented as the number and percentage. The Shapiro–Wilk test was used to evaluate the normality of the data distribution.

In the analysis Chi-square, Pearson's Chi-square, and Fisher's exact Chi-square test, independent *t*-tests, Wilcoxon test, and McNemar and McNemar–Bowker tests were used to detect changes within the groups

(variables). A one-way analysis of variance (ANOVA) was also used in the comparisons between more than two independent groups. Additionally, $p < 0.05$ was considered to be statistically significant.

Results

One hundred one (70.6%) of 143 patients followed in our center were included in the study. Of the 101 patients 77 (76.2%) were female, 24 (23.8%) were male). The mean age was 37.9 ± 11.8 years (37.4 ± 10.8 years in women and 39.7 ± 14.7 years in men). The history of CD was less than 2 years in 22 (21.8%) patients, 2-5 years in 42 (41.6%) patients, and more than 5 years in 37 (36.6%) patients. Forty-three (42.6%) patients also had additional chronic disease, and 20 (19.8%) patients had a family history of CD (Table 1).

In the pandemic, patients' weight gain was significantly higher ($p=0.003$), but no difference was observed in terms of alcohol and smoking intake. There were 36 (35.6%) and 20 (19.8%) patients, respectively, who easily obtained GFPs before and during the pandemic, and this difference was significant (Table 2). The total number of the patients who can obtain GFPs before the pandemic

Table 2. — Distribution of variables before and in the pandemic

	Before the Pandemic	In the Pandemic	P value
Weight	(n: 101)	(n: 101)	
Mean \pm SD	61.7 \pm 13.4	62.4 \pm 14.2	0.003*
(Median)	(61.0)	(62.0)	
BMI	(n:101)	(n:101)	
Mean \pm SD	23.4 \pm 3.9	23.7 \pm 4.1	0.001*
(Median)	(23.7)	(24.0)	
Monthly income n (%)	(n:99)	(n:99)	
\leq 1999 TL	10 (10.1%)	38 (38.4%)	<0.001**
2000 - 2999 TL	50 (50.5%)	36 (36.4%)	
3000 - 4999 TL	29 (2.3%)	20 (20.2%)	
\geq 5000	10 (10.1%)	5 (5.1%)	
Alcohol intaken (%)	(n:100)	(n:100)	
+	2 (2%)	2 (2%)	1.000***
-	98 (98%)	98 (98%)	
Smoking n (%)	(n:100)	(n:100)	
+	19 (19%)	18 (18%)	1.000***
-	81 (81%)	82 (82%)	
GFD Compliance n (%)	(n:101)	(n:101)	
Complete	66 (65.3%)	59 (58.4%)	0.091**
Mostly	25 (24.8%)	33 (32.7%)	
Rarely	7 (6.9%)	6 (5.9%)	
Incompatible	3 (3.0%)	3 (3.0%)	
Gluten Containing Meal Consumption n (%)	(n:101)	(n:101)	
+	37 (36.6%)	41 (40.6%)	0.424***
-	64 (63.4%)	60 (59.4%)	
Skip a Meal n (%)	(n:101)	(n:101)	
+	49 (48.5%)	56 (55.4%)	0.016***
-	52(51.5%)	45 (44.6%)	
Difficulty in GFP Supply n (%)	(n:101)	(n:101)	
Never	36 (35.6%)	20 (19.8%)	<0.001**
Sometimes	46 (45.5%)	39 (38.6%)	
Always	19 (18.8%)	42(41.6%)	

* Wilcoxon test, ** McNemar-Bowker Test, *** McNemar Test. **GFD** : Gluten Free Diet

Table 3. — Situations of considering themselves to be at high risk of becoming infected with COVID-19 based on the sociodemographic characteristics of the patients

	Yes	No	P value
Gender (n:101)			
Males	16 (66.7%)	8 (33.3%)	0.032
Females	32 (41.6%)	45 (58.4%)	
Marital Status (n:101)			
Marriage	37 (52.9%)	33 (47.1%)	0.107
Single	11 (35.5%)	20 (64.5%)	
Age (n:101)			
≤ 24	7 (50.0%)	7 (50.0%)	0.272
25-34	9 (32.1%)	19 (67.9%)	
35-44	15 (51.7%)	14 (48.3%)	
≥ 45	17 (56.7%)	13 (43.3%)	
Period of CD/year (n:101)			
≤ 2	11 (50.0%)	11 (50.0%)	0.312
3-5	23 (54.8%)	19 (45.2%)	
≥ 6	14 (37.8%)	23 (62.2%)	
Age of CD diagnosis (n:101)			
≤ 17	4 (36.4%)	7 (63.6%)	0.162
18-24	6 (35.3%)	11 (64.7%)	
25-34	11 (39.3%)	17 (60.7%)	
≥ 35	27 (60.0%)	18 (40.0%)	
Educational Status (n: 101)			
Primary School	25 (54.3%)	21 (45.7%)	0.272
High School	14 (48.3%)	15 (51.7%)	
University	9 (34.6%)	17 (65.4%)	
Additional chronic disease (n:101)			
+	24 (55.8%)	19 (44.2%)	0.151
-	24 (41.4%)	34 (58.6%)	
Familial CD history (n:101)			
+	13 (65.0%)	7 (35.0%)	0.081
-	35 (43.2%)	46 (56.8%)	
Gluten-containing food snack habit before the Pandemic (n:101)			
+	14 (37.8%)	23 (62.2%)	0.138
-	34 (53.1%)	30 (46.9%)	
Gluten-containing food snack habit in the Pandemic (n:101)			
+	16 (39.0%)	25 (61.0%)	0.157
-	32 (53.3%)	28 (46.7%)	
Monthly income before the Pandemic (n:99)			
≤ 1999 TL	5 (50.0%)	5 (50.0%)	0.086
2000 - 2999 TL	29 (58.0%)	21 (42.0%)	
3000 - 4999 TL	9 (31.0%)	20 (69.0%)	
≥ 5000	3 (30.0%)	7 (70.0%)	
Monthly income in the Pandemic (n:99)			
≤ 1999 TL	23 (60.5%)	15 (39.5%)	0.010
2000 - 2999 TL	18 (50.0%)	18 (50.0%)	
3000 - 4999 TL	5 (25.0%)	15 (75.0%)	
≥ 5000	0 (0%)	5 (100.0%)	
Difficulty in GFP Supply before the Pandemic (n:101)			
Never	11 (30.6%)	25 (69.4%)	0.039
Sometimes	26 (56.5%)	20 (43.5%)	
Always	11 (57.9%)	8 (42.1%)	
Difficulty in GFP Supply in the Pandemic (n:101)			
Never	5 (25.0%)	15 (75.0%)	0.075
Sometimes	20 (51.3%)	19 (48.7%)	
Always	23 (54.8%)	19 (45.2%)	

* Pearson Chi-Square Test. CD : Celiac Disease. GFP : Gluten Free Product

Table 4. — Sociodemographic data and Anxiety Scores of the patients

	State Anxiety Score (Mean ± SD)	P value	Trait Anxiety Score (Mean ± SD)	P value
	40.7 ± 7.9		44.5 ± 8.5	
Gender (n:101)				
Male	41.9 ± 6.9	0.382 *	44.9 ± 8.7	0.783 *
Female	40.3 ± 8.2		44.3 ± 8.5	
Age (n:101)				
≤ 24	39.6 ± 7.6	0.622 **	43.5 ± 9.1	0.758 **
25-34	39.4 ± 7.9		44.0 ± 7.6	
35-44	41.3 ± 7.8		45.9 ± 8.8	
≥ 45	41.8 ± 8.3		43.9 ± 8.9	
Period of CD/year (n:101)				
≤ 2	39.3 ± 7.2	0.654 **	45.5 ± 8.6	0.379 **
3-5	41.1 ± 8.2		44.5 ± 8.9	
≥ 6	41.1 ± 8.2		44.5 ± 8.5	
Age of CD diagnosis (n:101)				
≤ 17	40.3 ± 8.2	0.541 **	46.8 ± 8.3	0.204 **
18-24	38.3 ± 6.4		41.1 ± 8.3	
25-34	40.9 ± 8.0		46.1 ± 8.4	
≥ 35	41.6 ± 8.4		44.2 ± 8.5	
Educational Status (n:101)				
Primary School	42.8 ± 8.1	0.056 **	47.0 ± 7.5	0.022 **
High School	38.9 ± 6.8		42.6 ± 9.5	
University	39.0 ± 8.2		42.1 ± 7.9	
Additional Chronic Disease (n:101)				
+	41.6 ± 9.2	0.322 *	44.8 ± 8.9	0.766 *
-	40.0 ± 6.9		44.3 ± 8.2	
Familial CD history (n:101)				
+	43.5 ± 7.9	0.080 *	47.8 ± 7.5	0.052 *
-	40.0 ± 7.8		43.7 ± 8.6	
Skip a meal before the Pandemic (n:101)				
+	40.6 ± 8.3	0.942 *	44.3 ± 8.1	0.812 *
-	40.8 ± 7.6		44.7 ± 8.9	
Skip a meal in the Pandemic (n:101)				
+	40.8 ± 8.3	0.899 *	44.3 ± 8.1	0.839 *
-	40.6 ± 7.6		44.7 ± 9.0	
Monthly income before the Pandemic (n:99)				
≤ 1999 TL	9.3 ± 2.9	0.027 **	45.6 ± 9.7	0.124 **
2000 - 2999 TL	7.4 ± 1.0		46.4 ± 7.9	
3000 - 4999 TL	7.9 ± 1.4		42.2 ± 8.5	
≥ 5000 TL	7.2 ± 2.3		41.8 ± 9.0	
Monthly income in the Pandemic (n:99)				
≤ 1999 TL	41.6 ± 7.4	0.011 **	46.2 ± 7.5	0.126 **
2000 - 2999 TL	42.8 ± 8.3		45.3 ± 8.8	
3000 - 4999 TL	35.8 ± 7.2		41.7 ± 9.0	
≥ 5000	39.0 ± 6.3		39.6 ± 8.3	
GFD Compliance before the Pandemic (n:101)				
Complete	40.8 ± 7.6	0.805 **	44.0 ± 8.6	0.346 **
Mostly	40.7 ± 9.3		46.2 ± 8.5	
Rarely	38.1 ± 7.7		40.8 ± 7.9	
Incompatible	43.0 ± 2.6		49.3 ± 5.8	
GFD Compliance in the Pandemic (n:101)				
Complete	41.1 ± 7.6	0.745 **	44.2 ± 8.3	0.628 **
Mostly	40.2 ± 8.9		45.0 ± 9.2	
Rarely	38.0 ± 7.0		41.8 ± 7.8	
Incompatible	43.0 ± 2.6		49.3 ± 5.8	

* Independent Samples t test, ** Oneway ANOVA. CD : Celiac Disease. GFD : Gluten Free Diet.

	State Anxiety Score (Mean ± SD)	P value	Trait Anxiety Score (Mean ± SD)	P value
	40.7 ± 7.9		44.5 ± 8.5	
Difficulty in Dietary Compliance in the Pandemic (n:101)				
Always	44.7 ± 7.8	0.344 **	46.7 ± 9.4	0.190 **
Sometimes	42.4 ± 8.0		47.2 ± 6.4	
Rare	39.8 ± 7.8		46.0 ± 8.7	
Never	39.8 ± 7.9		43.0 ± 8.9	
Suspicious Symptom of COVID-19 (n:101)				
+	41.2 ± 7.7	0.599 *	46.7 ± 7.8	0.027 *
-	40.4 ± 8.2		42.9 ± 8.6	
Considering themselves at high risk of becoming infected with COVID-19				
+	41.9 ± 8.3	0.156 *	45.9 ± 8.3	0.111 *
-	39.6 ± 7.5		43.2 ± 8.5	

* Independent Samples t test, ** Oneway ANOVA. CD : Celiac Disease. GFD : Gluten Free Diet.

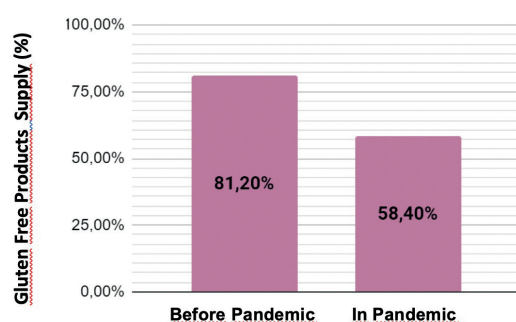


Fig. 1. — Gluten-free product supply before and in the pandemic.

decreased from 82 (81.2%) patients to 59 (58.6%) patients in the pandemic, this difference was significant (Figure 1). The most common reason for difficulty in obtaining GFPs both before and during the pandemic was the high price and not being able to find GFPs at the store. Among the reasons for the difficulty obtaining GFPs during the pandemic were the curfew in 19 (19.2%) patients and anxiety about becoming infected with COVID-19 in 5 (5.1%) patients. During the pandemic, significantly more patients skipped a meal than before the pandemic ($p=0.016$). The most common reason for skipping a meal was sleep disturbance and late awakening. No significant difference was observed between patients in terms of dietary compliance before and after the pandemic ($p=0.091$) (Table 2). Patients' education levels were investigated, and primary school graduates had more difficulties obtaining GFPs than high school and higher education graduates ($p=0.006$). However, no difference was observed between the groups during the pandemic ($p=0.064$). During the pandemic, there was a significant decrease in patients' monthly income compared to before the pandemic ($p<0.001$) (Table 2).

In patients with CD, while dyspeptic complaints ($p=0.030$) such as gas, bloating, and constipation ($p=0.021$) symptoms were significantly increased during the pandemic, there was no significant difference in other symptoms such as weakness, fatigue, diarrhea,

nausea, vomiting, and headache. When the patients were evaluated according to the age of CD diagnosis, additional chronic disease, and familial CD history, there was no significant difference in access to GFPs, GFD compliance, and skipping a meal before or during the pandemic. When patients were evaluated according to their period of CD, there was no significant difference in terms of access to GFPs and skipping a meal before and during the pandemic. However, the patients had difficulty with GFD compliance during the pandemic. Patients who were diagnosed with CD less than 2 years before had more difficulty with GFD compliance than patients who were diagnosed with CD for more than 2 years ($p=0.019$). In patients with additional chronic diseases, gluten-containing food snack habits were significantly higher than those without an additional chronic disease before the pandemic ($p=0.028$), but this difference was not observed during the pandemic.

When patients were interviewed about whether they considered themselves to be at high risk of becoming infected with COVID-19 because of their CD, there was no significant difference in their period of CD, age at CD diagnosis, marital status, education level, additional chronic disease, and familial CD history. However, significantly more male patients (66.7%) considered themselves to be at high risk of becoming infected with COVID-19 than female patients (41.6%) ($p=0.0302$).

Before the pandemic, patients who were unable to access GFPs or who had difficulty obtaining GFPs were significantly more concerned about becoming infected with COVID-19 than patients who had easy access to GFPs ($p=0.039$). However, this significant difference was not observed during the pandemic ($p=0.075$) (Table 3). During the pandemic, 17 (16.6%) patients had symptoms potentially related to CD, but 11 (64.7%) of these patients did not go to the hospital because of their concern of becoming infected with COVID-19.

The patients' state anxiety index was 40.7 ± 7.9 , and the trait anxiety index was 44.5 ± 8.5 based on the STAI scale, and all patients were evaluated as mildly anxious.

There was no significant difference in patients' age, gender, period of CD, age at CD diagnosis, additional chronic disease, and familial CD history for the state and trait anxiety levels (Table 4).

While there was no significant difference between the patients' education levels and their state anxiety score ($p=0.056$), there was a significant difference between education level and the trait anxiety score ($p=0.022$). The trait anxiety score was significantly higher in primary school graduates than in higher education (university) graduates ($p=0.046$). In monthly income category, there was a significant difference in state anxiety levels (before the pandemic, $p=0.027$; during the pandemic, $p=0.011$), but the difference in trait anxiety levels was not significant. (Table 4). The state anxiety score was lower in patients with a high income. There was no significant difference between patients' GFD compliance and anxiety levels before and during the pandemic (Table 4). There was no significant difference in the anxiety level in patients with at least one COVID-19 symptom and in patients without any COVID-19 symptoms ($p=0.599$), but there was a significant difference in trait anxiety levels ($p=0.027$) between these groups.

During the pandemic, two (1.9%) female patients were diagnosed with COVID-19. A 27-year-old patient with a diagnosis of CD for 9 years was an active healthcare worker in the pandemic hospital. She had symptoms of taste-smell disorder, myalgia, high fever, respiratory distress, and a positive COVID-19 PCR test. The patient was followed up at her home 1 day after hospitalization, and she received hydroxychloroquine sulfate, azithromycin, and oseltamivir treatments. After 14 days of follow-up, her control PCR test was negative. The patient's state anxiety score was 32, and the trait anxiety score was 36. The other patient who was COVID-19-positive was a 42-year-old housewife. This patient had CD for 14 years and had a mild cough, and her COVID-19 PCR test was positive. This patient was followed-up at home and only symptomatic treatment was given during COVID-19 infection. This patient's state anxiety score was 51, and the trait anxiety score was 55. These two patients had always followed a strict GFD before and during the pandemic. However, both patients had difficulty obtaining GFPs during the pandemic.

Discussion

Recently, there has been a significant increase in the number of new CD cases because of extensive screening of individuals who are considered to be at high risk and the development of diagnostic methods (23). CD occurs in all age groups including the elderly and affects 0.6-1% of the world's population (24). CD prevalence was 0.47% in Turkey, based on antibody test and intestinal biopsy results (25). The main treatment for patients with CD is lifelong adherence to a strict GFD. These patients should be advised to eat a high-fiber diet enriched with whole grain rice, corn, potatoes, and lots of vegetables. Strict adherence to a GFD is essential to control

symptoms, improve quality of life, and reduce the risk of complications (23).

As in many countries, high-quality GFPs can be obtained from supermarkets, private health food stores, and online orders in Turkey. However, GFPs are more expensive than equivalent wheat-based foods. These products are easily accessible, and the prices of gluten-containing products are reasonable, which facilitates compliance with a GFD. Strict adherence to a GFD is challenging and requires considerable special effort in everyday life. Additionally, quarantine measures and curfew implementation during the pandemic may make adherence to GFD difficult. The COVID-19 pandemic is an emergency health problem that affects the entire world. Although COVID-19 is spread via droplets, it can also be found in the lower GIT (26). However, there are no up-to-date data on the risk of COVID-19, treatment management in case of infection, and a GFD during the pandemic for patients with CD. There is also no information on how state and trait anxiety levels were affected in patients with CD because of the significant changes in the daily routine during the pandemic. Studies that were conducted before the pandemic reported that the prevalence and severity of anxiety was not different in patients with CD compared to healthy adults, but the anxiety level has generally increased in these patients (27).

In our study, when patients were evaluated using the state and trait anxiety scales during the pandemic, anxiety levels were found to be slightly high. However, current anxiety levels of the patients did not cause a significant change in dietary compliance during the pandemic. State anxiety expresses the psychological and physiological transient reactions that are directly related to adverse conditions at a certain moment. Conversely, the term trait anxiety refers to a personality trait and describes individual differences related to a propensity toward current state anxiety. Therefore, trait anxiety is comparatively stable over time, and it is considered to be a significant characteristic of patients with anxiety disorders because they have higher persistent anxiety than healthy individuals (28). In our study, it was found that patients with low monthly income before and during the pandemic had higher state anxiety. This may be because of the high cost of GFPs in both periods compared to wheat-based foods, and the additional difficulties that are caused by low purchasing power.

In Turkey, after the announcement of the first COVID-19 case on 11 March 2020, pandemic measures were increased in accordance with the recommendations of the Ministry of Health and Science Board. Serious protective measures such as mandatory masks and gloves and strict social distancing rules in public spaces, partial curfew, and stores open only at certain time intervals have been taken. People who are <20 years, >65 years, and/or have chronic illnesses are also restricted from leaving their homes. The uncertainty of how long the pandemic will continue has led some people to stockpile more

food than they need. Therefore, it has been difficult for patients to access GFPs during the pandemic. However, despite serious changes in the daily routine and social life during the pandemic, our study suggests that the effect of COVID-19 on GFD compliance of CD patients was limited in our country.

Four percent of patients with CD consider themselves to be at very much higher risk, and 6.5% of them consider themselves at much higher risk in terms of becoming infected with COVID-19 in Italy (29). In that previous study, CD patients who were women, >50 years old, and had additional chronic disease considered themselves to be at higher risk of becoming infected with COVID-19. Additionally, 59.1% of these patients were afraid to go to the hospital because of the risk of COVID-19 infection. However, in our study, 47.5% of the patients considered that CD posed a risk for COVID-19 infection during the pandemic. Male patients were especially more concerned about COVID-19. During this period, 16.8% of the patients needed to go to the hospital because of CD-related complaints, but 64.7% of them did not attend any health center for fear of becoming infected with COVID-19. Although there was no significant difference, young patients considered themselves to be at a higher risk of becoming infected with COVID-19 compared to older patients. The differences between Italian study and ours may have resulted from different traditional, cultural, and social life characteristics and from the lower average age of our patients and lower mortality rates due to COVID-19 in Turkey. CD patients were economically affected during the pandemic, but patients were able to obtain GFPs, albeit with difficulty, and followed their GFD. During the pandemic, limited working hours and home office work practices caused patients to skip more meals than before the pandemic. However, an increase in their weight was observed as patients' daily mobility was restricted. During the pandemic, our patients with a history of CD for <2 years had difficulty following GFD. Patients who had CD for more than 2 years had no difficulty following the diet during the pandemic because GFD had become a routine for them. During the pandemic, two CD patients with COVID-19 infection had CD for over 5 years and were strictly compliant with their diets. In these patients, the infection was mild, and one patient received only symptomatic treatment, while the other patient received medical treatment for COVID-19, and both patients recovered. Our clinical experience has shown that CD does not pose an additional risk for COVID-19 infection in patients on a GFD, and these patients will have a similar clinical course as individuals without CD, even if they become infected with COVID-19. Based on our experience, we cannot comment on how the COVID-19 infection clinical symptoms will progress in patients with CD who cannot be compliant with a GFD. Moreover, there is no up-to-date data published on this subject.

Our study had some strengths. It was the first study to investigate the effect of COVID-19 pandemic in

patients with CD in detail and to compare it with the period before the pandemic. Additionally, it was the first study to present data from adult CD patients who were COVID-19-positive.

Also there was some limitations in this study. One of the limitations was the lack of having a healthy control group to compare CD patients' anxiety levels. Additionally, there were no data about our patients' general anxiety levels and their ability to manage anxiety before the pandemic. However, the COVID-19 pandemic began suddenly, making it impossible to perform a pre-test. Another limitation was that the questionnaires were distributed between March and June. In this study, it cannot exclude that patients who responded to the questionnaire in March were not later infected.

In conclusion, the COVID-19 pandemic caused difficulty in obtaining GFPs and GFD compliance in patients with CD, but although there was a significant difference in obtaining GFPs, the difference in GFD compliance was not significant compared to before the pandemic. Approximately half of the patients with CD considered themselves to be at risk of becoming infected with COVID-19. However, the patients with CD did not have any additional risk compared to other individuals in terms of becoming infected with COVID-19 for patients under GFD, and these patients will have a similar clinical course as individuals without CD, even if they catch the COVID-19 infection.

Statement of Ethics

The study approved by the institutional and national research ethics committee and was carried out according to the principles of the Helsinki Declaration [No : 48670771-514.10 (05.27.2020)].

Disclosure Statement

All authors declare that they have no conflicts of interest and no financial support was obtained.

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