Original Article

Celiac Disease: From Adherence to Gluten-Free Diet to Health-Related Quality of Life

Ehsan Vesali-Monfared[1] , Abolfazl Mohammadbeigi[2] , Sarallah Shojaei[3] , Rahim Aali[4] , Aazam Farahanie[5] , Mohammad Reza Ghadir[5*]

[1]Department of Gastroenterology and Hematology Diseases Research Center, Shahid Beheshti Hospital, Qom University of Medical Sciences, Qom, Iran

[2]Department of Biostatistics and Epidemiology, School of Health, Research Center for Environmental Pollutants, Qom University of Medical Sciences, Qom, Iran

[3]Department of Nursing and Midwifery, School of Nursing, Qom University of Medical Sciences, Qom, Iran

[4]Department of Environmental Health, School of Health, Research Center for Environmental Pollutants, Qom University of Medical Sciences, Qom, Iran

[5]Department of Internal Medicine, School of Medicine, Gastroenterology and Hepatology Diseases Research Center, Shahid Beheshti Hospital, Qom University of Medical Sciences, Qom, Iran

Abstract

Background: Celiac disease (CD) is a genetic and immune-mediated disorder in which eating gluten reduces intestinal absorption and damages the mucosa and villi of the small intestine. This study was designed to investigate adherence to a gluten-free diet (GFD) and health-related quality of life (QOL).

Methods: This cross-sectional study was conducted on 122 patients with CD in Qom in 2023. Sampling was performed in an easy and accessible way from celiac patients. The research tool was a researcher-made questionnaire. The obtained data were analyzed by descriptive and inferential statistical tests using SPSS 23.

Results: The average age of the patients was 37.57 ± 9.59 years, and 93% had a GFD. Gastrointestinal symptoms demonstrated a positive and significant correlation with GFD, age, marital status, and QOL ($P < 0.001$). The percentage of patients' QOL scores (39.57%) was lower than the average. Adherence to a GFD could predict favorable changes in patients' QOL ($\beta = 0.71$, $P < 0.001$), and CD predicted gastrointestinal symptoms ($\beta = 0.64$, $P < 0.001$). The study model showed a good fit based on two important indicators of good model fit (χ^2/pdf = 2.14 and RMSEA = 0.069).

Conclusion: The results revealed that better adherence to the GFD leads to a better clinical response and a decrease in gastrointestinal symptoms, thereby improving the QOL of celiac patients.

Keywords: Celiac disease, Adherence, Gluten-free diet, Quality of life

Introduction

Celiac disease (CD) is a common genetic and immune-mediated disability that destroys the mucosa and villi of the small intestine and reduces the absorption capacity of the intestine by eating gluten, which is present in many grains similar to wheat (1). People with CD may have gastrointestinal signs, extra-intestinal signs, or no signs at all. Generally, the CD is associated with symptoms of malabsorption, such as diarrhea, steatorrhea, and weight loss (2,3).

These gastrointestinal specifications and pathological processes emerge as an outcome of gluten-mediated intestinal damage (4). According to the results of studies, the prevalence of CD is about 0.7%–1% worldwide (5). In recent years, CD has been introduced as a public health issue. Numerous studies have estimated that the disease affects approximately 1% of the European population. Population-based data on CD prevalence have also been reported from the Middle East, India, and the like (5). The prevalence of the disease in Central Asia and Iran is similar and equals 1%–2%, which is twice as much in women as in men (6). The clinical manifestations of CD change according to the age of the patient, the duration of the malady, and its severity, and it varies from asymptomatic

patients to patients with severe malnutrition (7). Various demographic factors related to the disease and treatment can also affect the severity of the disease (8). The only effective and safe treatment for this sickness is to eliminate foods and products containing gluten (2,9). Although it is possible to control the disease and its complications with a strict gluten-free diet (GFD) and stop the autoimmune response, following this diet has serious consequences for patients' social activities and mental and physical stress caused by this challenge. It may affect the quality of life (QOL) of these patients (4,10). In addition, various studies have shown that following a GFD has a physical and psychological effect on the health-related QOL (HRQOL) in patients with CD. Due to the feature of this disease and given that the duration of adherence to a GFD is costly and requires more energy, the HRQOL of these patients can be severely pretentious by this issue (11). It is expected that the gastrointestinal symptoms associated with CD can explain the quality and extent of dietary compliance in patients with CD (9, 12). It is also predicted that adherence to GFD can have a significant impact on the HRQOL of patients with CD through changes in the severity of gastrointestinal symptoms (13-15). Therefore, the current study was implemented to investigate adherence to a GFD and related health QOL.

Materials and Methods

This cross-sectional survey was performed on celiac patients in the Gastroenterology and Liver Diseases Research Center, CD Group in Qom from June to December 2023. Sampling was conducted in an easy and accessible way and among patients who met the inclusion criteria. Suffering from this disease based on special gastrointestinal diagnostic tests (serology, endoscopy, biopsy, and tissue transglutaminase antibody test) and having a GFD diet for at least 6 months were the indications and criteria for entering the study. In case of not completing the informed consent form and the questionnaire, it was possible to exclude from the research. The sample size for the current research was based on the studies performed by Mohammadibakhsh et al (6) and Deepak et al (16), considering the prevalence of CD of 1%, the mean QOL score of 37.20 ± 11.09, the confidence interval of 95%, and d = 2 (accuracy between one-tenth and three-tenths of a standard deviation). Given a 10% attrition rate, the minimum sample size required for this study was estimated at 122 individuals.

$$n = \frac{Z_{1-\frac{\alpha}{2}}^{2}\sigma^{2}}{d^{2}}$$

A standard questionnaire was used for data collection, which was employed and evaluated in terms of validity and reliability in previous studies. The first part included demographic information, and the second section contained seven questions regarding awareness of CD.

The questions were recorded on a dichotomous (yes/no) scale. For each correct or wrong answer, a score of 1 or 0 was considered, respectively, and the total score ranged from 0 to 7. Internal consistency of the questionnaire was assessed using Cronbach's alpha value considered acceptable at 0.60 (17).

The third part of the questionnaire encompassed questions on the Gastrointestinal Symptom Rating Scale (GSRS). This questionnaire has 14 questions. Each question is scored on a 5-point Likert-type scale from no discomfort (1) to severe discomfort (5), and the total score ranges from 14 to 70. Moreover, it has 4 dimensions, namely, abdominal pain (heart pain, hunger, and nausea), diarrhea (diarrhea, loose stools, and urgent need to defecate), constipation (constipation, hard stools, and feeling of incomplete defecation), and indigestion (abdominal cramping, flatulence, belching, and increased abdominal gas). The total score is obtained from the sum of the average scores in each subscale, and the increase in the score in this scale indicates the severity of the symptoms, according to Cronbach's alpha, 0.62, 0.83, and 0.80, respectively (18). A Cronbach's alpha of 0.70 was estimated in this study. The fourth part included items related to adherence to GFD. Compatibility with the diet was assessed using the CD adherence test (CDAT) questionnaire, which evaluates adherence to a GFD using seven items on a 5-point Likert-type scale, and the total score ranges from 7 to 35. (19). Finally, the fifth part was related to questions about patients' HRQOL. HRQOL in people with CD was evaluated using the HRQOL-SF36 standard questionnaire. This is a 36-question questionnaire that assesses physical and mental health. Scores in this questionnaire range from 0 to 100. The reliability and validity of the Persian version of this questionnaire (r = 1.9-1.7) have been confirmed in Iran (20). After data collection, all analyses were performed using SPSS software, version 23. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test, and the frequency and descriptive variables were evaluated using analytical tests. In addition, the Pearson correlation test was utilized to determine the correlation between variables. Further, a regression test was employed to measure the effect of variables and predict what the QOL as a dependent variable would be with each change in the independent variables. Structural equation modeling was performed using Amos 26 software to determine the goodness-of-fit indices of the model. The value of the significance level was considered 0.05. This study has been registered at Qom University of Medical Sciences (ethical code IR.MUQ.REC.1402.107).

Results

Overall, 122 participants with CD with a mean age of 37.57 ± 9.59 years were examined in this research. Of these, 80 (66%) were women, 55 (46%) were married, and 115 patients (93%) had and followed a GFD. The mean duration of the disease was 2.1 ± 04.05 years

(Table 1). Pearson correlation coefficients between the study constructs (Table 2) revealed a positive and significant correlation between a GFD and the duration of the diet with CD. A significant correlation was also found between GFD and the duration of adherence to the diet. Statistically, a positive and significant statistical relationship was reported between QOL and adherence to the GFD ($P < 0.001$).

Among the constructs of the model, the highest mean percentage of points was related to awareness, followed by adherence to a GFD. The percentage of patients' HRQOL scores (39.57%) was reported as below average (Table 3).

The results of regression analysis for predicting HRQOL are presented in Table 4. The findings demonstrated that in stage 1, demographic characteristics could explain 1.9% of the variance in HRQOL ($P = 0.206$). By adding the disease duration variable and having a GFD, the duration of the GFD in stage 2 increased the variance of the HRQOL by 3.6% ($P = 0.13$). Eventually, dimensions of consciousness structure, GSRS, and CDAT were added to the model, which could generally explain 17% of the variance of HRQOL ($P < 0.001$).

The correlation between compliance to a GFD and gastrointestinal signs on HRQOL was analyzed through the path analysis model (Table 5). According to the results, adherence to a GFD was able to explain the changes in HRQOL in patients ($\beta = 0.71$, $P < 0.001$). The effect of gastrointestinal signs on the HRQOL was significant ($\beta = 0.27$, $P < 0.05$). Further, this model assessed the predictive power of CDAT related to changes in GSRS ($P < 0.001$, $\beta = 0.64$). The results of structural equation modeling showed that two very important indicators of the goodness of fit of the model ($\chi^2/df = 2.14$ and RMSEA $= 0.069$) were at the desirable and acceptable threshold. Furthermore, the goodness of fit index of the model (GFI $= 0.902$), adjusted fit (AGFI $= 0.878$), and relative fit (CFI $= 0.905$) were reported as acceptable. Other indications of the goodness of fit of the structural model are displayed in Figures 1 and 2 (CFI $= 0.905$, NFI $= 0.714$, TLI $= 0.862$, AGFI $= 0.878$, CMIN $= 4034.698$, df $= 1884$, $\chi^2/df = 2.14$, and RMSEA $= 0.069$).

Discussion

CD is a principal public health problem globally caused by gluten in hereditary predisposed people. This disease is of great importance due to its high prevalence, occurrence of the disease at any age, wide range of clinical pretense, and late diagnosis (3). Variables that determine the HRQOL in these patients remain largely unknown (8). Therefore, this survey investigated CD, focusing on adherence to a GFD and health-related QOL in patients suffering from this disease.

Table 1. Frequency Distribution of Demographic Characteristics (N = 122)

Variables	Category	Frequency	Percent
Age	1-20	54	44.5
	21-40	36	29.5
	40-60	32	26
Gender	Male	42	34
	Female	80	66
Marital status	Single	67	54
	Marriage	55	46
Level of education	Diploma	85	69
	BSc	28	23
	MSc/PhD	9	8
Job-status	Self-employed	19	15.5
	Employee	18	14.5
	Retired	4	3
	Scholar	41	33.5
	Unemployed	40	33
Duration disease	1-3	52	43
	4-6	26	21
	7-10	31	25
	>11	13	11
GFD regime	Yes	115	93
	No	7	7
GFD duration	0-5	80	65
	6-10	32	26.5
	>11	10	8.5
GFD adherence	Yes	112	92
	No	10	8

Note. GFD: Gluten-free diet.

Table 2. Pearson Correlation Coefficients Between the Study's Constructs (N = 122)

Variables	1	2	3	4	5	6	7
Duration disease	1						
GFD regime	-0.211*	1					
GFD duration	0.776**	-0.304**	1				
Knowledge	-0.030	-0.172	-0.081	1			
GSRS	0.082	0.167	-0.049	-0.229*	1		
CDAT	-0.048	-0.001	-0.050	-0.039	0.254**	1	
Quality of life	-0.058	0.072	-0.096	-0.141	0.463**	0.111	1

Note. GFD: Gluten-free diet; GSRS: Gastrointestinal Symptom Rating Scale; CDAT: Celiac disease adherence test. **Correlation is significant at the 0.01 level. *Correlation is significant at the 0.05 level.

Table 3. Mean, Standard Deviation, and Score Range of the Study's Constructs (N = 122)

Variables	M (SD)	Score Range	Mean Percentage of Achievable Score*
Knowledge	3.51 (.946)	0-6	58.5
CDAT	22.01 (3.59)	7-35	53.6
GSRS	28.27 (11.43)	14-70	25.3
Physical quality of life	36.24 (5.86)	28-54	31.6
Mental quality of life	40.18 (4.06)	31-51	45.9
Total quality of life	40.18 (6.36)	1-100	39.57

Note. CDAT: Celiac disease adherence test; GSRS: Gastrointestinal Symptom Rating Scale; M: Mean; SD: Standard deviation. * Calculation: (Mean − Minimum) ÷ (Maximum − Minimum) × 100

**Table 4.** Hierarchical Regression Analysis to Determine and Predict Health-Related Quality of Life

Variables	B	SE	Beta	*P* value	95.0% Confidence Interval for B	
					Lower Bound	Upper Bound
Age	-0.235	1.005	-0.031	0.815	-2.226	1.756
Gender	0.934	1.280	0.070	0.467	-1.603	3.471
Marital status	0.684	1.478	0.054	0.644	-2.244	3.613
Job	-0.566	0.453	-0.130	0.215	-1.464	0.333
Education	-1.530	1.009	-0.149	0.133	-3.530	0.471
Duration disease	-0.545	0.849	-0.090	0.522	-2.227	1.137
GFD regime	-2.996	2.973	-0.110	0.316	-8.887	2.896
GFD regime duration	0.012	1.317	0.001	0.992	-2.598	2.623
GFD adherence	2.871	2.479	0.124	0.249	-2.042	7.784
Knowledge	-0.411	0.606	-0.061	0.499	-1.611	0.789
GSRS	0.242	0.056	0.435	0.000	0.131	0.353
CDAT	-0.054	0.160	-0.030	0.737	-.371	0.263
Adjusted R²=0.17, R=0.50, *P*<0.001						

Note. GFD: Gluten-free diet; GSRS: Gastrointestinal Symptom Rating Scale; CDAT: Celiac disease adherence test; SE: Standard error.

Table 5. Regression Weights Between Structural Parameters Using Structural Equation Modeling (N=122)

Variables	Relationship	Variables	Estimate	SE*	Test Statistics	*P* value
Knowledge	→	CDAT	-0.518	0.722	-3.809	*P*<0.001
Knowledge	→	GSR	-0.114	0.447	-0.945	*P*=0.345
Knowledge	→	QOL	0.059	0.404	0.628	*P*=530
CDAT*	→	GSR	0.649	0.117	3.823	*P*<0.001
GFD adherence	→	QOL*	0.713	0.152	3.798	*P*<0.001
GSRS*	→	QOL	0.274	0.150	2.127	*P*<0.05

Note. *CDAT: Celiac disease adherence test; GSRS: Gastrointestinal Syndrome Rating Scale; QOL: Quality of life; SE: Standard error.
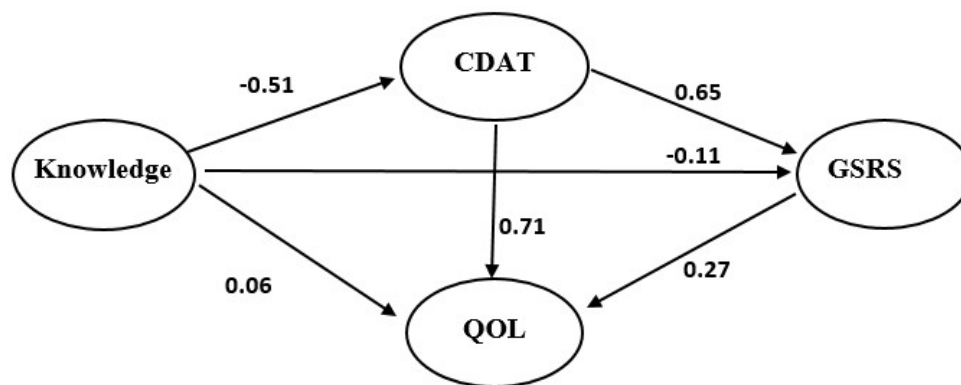
$\chi2/df = 2.14$, CFI = 0.905, GFI = 0.902, AGFI = 0.878, NFI = 0.714, TLI = 0.862, RMSEA = 0.069

Figure 1. Estimated Standardized Direct Effects for the Proposed Model. *Note.* df: Degree of freedom; CFI: Comparative fit index; GFI: Goodness-of-fit index; AGFI: Adjusted goodness-of-fit index; NFI: Normed fit index; TLI: Tucker-Lewis index; RMSEA: Root mean square error of approximation.

In the current research, a significant relationship was observed between GSRS and QOL. The average HRQOL score was below average, and the path coefficient represented that CDAT with the maximum grade predicted changes in HRQOL. In general, 92% of the studied population adhered to the GFD based on the GFD adherence questions, which is in line with the results of the study of Casellas et al, indicating an adherence rate of 71.5% (21).

Based on the findings, adherence to a GFD had a remarkable correlation with HRQOL. Moreover, a significant correlation was found between GSRS and QOL, which conforms to the results of Nikniaz et al (8). In line with the present findings, those of the study by Deepak et al (16) demonstrated a positive statistical relationship between compliance with GFD and HRQOL. Likewise, Rajpoot et al (22) and Sainsbury et al (23) concluded that adherence to GFD will reduce gastrointestinal
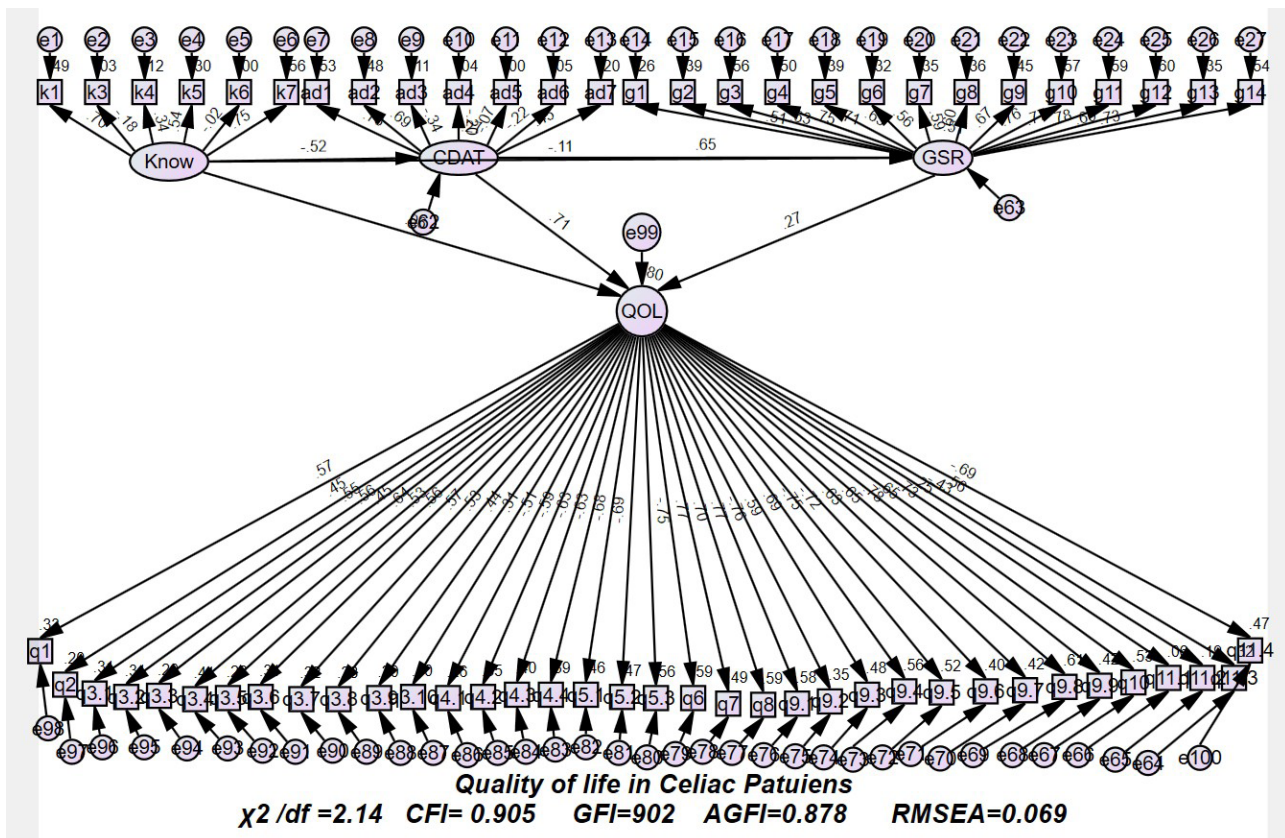
Figure 2. Estimated Standardized Direct Effects for the Proposed Model Using Structural Equation Modeling. *Note*. df: Degree of freedom; CFI: Comparative fit index; GFI: Goodness-of-fit index; AGFI: Adjusted goodness-of-fit index; RMSEA: Root mean square error of approximation.

symptoms in patients with CD and improve HRQOL. Analysis based on HRQOL revealed that better HRQOL was associated with fewer gastrointestinal symptoms and better adherence. In other words, the gradual decrease in the HRQOL and the possible increase in the symptoms of the disease will be related to the increase in the degree of difficulty in adhering to the treatment. Therefore, adaptation has been suggested as an autonomous variable intricate in the HRQOL of participants (23).

In this research, there was no statistical connection between the duration of adaptation to a GFD and HRQOL. The current findings contradict those of the study performed by Enaud et al, indicating that there was a statistical relationship between the duration of following a GFD and the HRQOL of celiac patients (14).

Our results confirmed that the gastrointestinal symptoms related to CD have a statistically significant and positive correlation with adaptation to a GFD, which corroborates the results of previous research (14). It appears to be an association between reduced gastrointestinal signs and greater compliance with the GFD. However, because of the feasible interplay between CD and irritable bowel syndrome or inflammatory bowel disease, it is difficult to interpret the level of gastrointestinal signs in people with CD and its association with compliance with a GFD (12).

The demographic findings of this survey demonstrated that there was no significant correlation between age and marital status with GFD and even CDAT. The outcome of

this survey is consistent with that of the study conducted by Barratt et al (24). The average score of the HRQOL of the participants of the present research was lower than the average, while in the study by Wolf et al (25), the average HRQOL was reported as favorable and moderate to high. This inconsistency may be partly due to differences in QOL instruments (general vs. CD specific), differences in dietary adherence instruments (self-reporting of dietary data), or geographic location. In this study, valid measures of QOL (HRQOL) were used, and the researchers relied on the participants' opinions and awareness in answering the questionnaire. Additionally, in the current research, the average score of awareness and adaptation to the gluten diet was reported as close to the average. According to Casellas et al (21) and Nachman et al (26), the HRQOL is affected by the state of awareness and compliance with a GFD in people. In other words, being aware and having extensive information about the disease cause more adherence to GFD. The results of the present survey match those of a former study that suggested the existence of a relationship between HRQOL and GFD adherence (21).

Gastrointestinal symptoms and adherence to a GFD could predict 17% of the variance in HRQOL. In line with the present results, the findings of the study by Dimidi et al confirmed that there was a statistically significant correlation among the symptoms of CD following a GFD, so that the probability of symptoms increases with decreasing compliance to a GFD. In addition, adaptation

to a GFD is consistently and significantly predicted for a better HRQOL in patients (15). The findings are in conformity with those of the study performed by Usai et al (27). The outcome of the regression analysis in the second stage showed that after improving adherence to the GFD, the HRQOL increased, and following a GFD predicted the patients' HRQOL more strongly. In line with these findings, the results of the study by Lamba et al revealed that HRQOL and health-related physical and mental quality subscales increased after following the GFD (28). The present findings corroborate the results of former surveys (14,29), demonstrating that after one year of following a GFD, the HRQOL of celiac patients improved significantly, and gastrointestinal symptoms alleviated in these patients.

In the present study, the outcome of path analysis using structural equation modeling represented that the path coefficient between CDAT and QOL was significant, and CDAT with the maximum score predicted changes in HRQOL. The GSRS could also predict 27% of changes in HRQOL. The findings of Nikniaz et al (8) confirmed the effect of CDAT and GSRS on the HRQOL of celiac patients. In line with this study, the findings of Möller et al indicated that gastrointestinal symptoms, directly and indirectly, affect the HRQOL through negative perception of the disease, inconsistent coping, catastrophizing of pain, and mental distress. An increase of 50.6% could explain the percentage of changes in HRQOL. Moreover, based on the goodness of fit indices and the results of the present study, the study model showed a good fit (13).

This study had some weaknesses. The completion of the questionnaire was self-reported, and it was performed by sending the link of the questionnaire to the personal page in the social networks of each of the patients. On the other hand, the study had some strengths. During the implementation of this study, in cooperation with the Gastrointestinal and Liver Diseases Research Center of Qom University of Medical Sciences, to improve the QOL of this group of patients, all their medical and demographic information was saved online. Patients with CD were registered, and in this way, we managed to provide financial support packages for the preparation of a GFD.

Conclusion
According to the findings of previous studies, almost all surveys confirmed a positive trace of GFD on the HRQOL of CD patients (30). The results of the current research also emphasized the effect of GFD adherence and gastrointestinal signs on the variance of HRQOL in patients with CD. Following a GFD can play a role in explaining the variance in the HRQOL of celiac patients indirectly and through digestive symptoms. Based on the findings of this study, better adherence to the GFD can lead to a better clinical response and fewer gastrointestinal symptoms, thus enhancing the HRQOL of celiac patients.

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