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Quality Of Life in Children with Celiac Disease: A Cross-sectional Study

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Abstract

Background

Celiac disease (CD) is a systemic autoimmune disorder due to immune response triggered by ingestion of gluten in the diet. Treatment with lifelong gluten-free diet may impact negatively on the health-related quality of life and may lead to psychological disturbances. The purpose of study was to evaluate quality of life, depression and anxiety in children with celiac disease.

Materials and Methods

In this cross-sectional study was done between 2013 and 2014 at the Gastroenterology Outpatient Clinic (Ghaem Hospital, Mashhad- Iran), patients with serology and biopsy-proven CD, on a gluten-free diet for at least one year, were included in this study and compared with non-celiac healthy children as controls. We used the questionnaire to investigate quality of life, anxiety and depression.

Results

There were statistically significant differences between the mean total anxiety (state, trait) scores and depression score in the celiac patients and control group. Correlations between state and trait anxiety and depression were statistically significant (P= 0.01, r= 0.35) and (P= 0.001, r= 0.52). Reverse correlations between quality of life of CD children and anxiety (state, trait) were statistically significant (P= 0.001, r= 0.51 and P= 0.02, r= 0.32). Mean total score of quality of life was not different in the two groups, but in the physical activity component, quality of life was better in CD patients (P=0.008).

Conclusion

In current study, anxiety and depression had a significant impact on the course of celiac disease.

Key Words: Anxiety, Celiac disease, Children, Depression, Gluten free diet.

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1- INTRODUCTION

Celiac disease (CD), an immune-mediated systemic disorder in genetically predisposed individuals (1) initiates through the ingestion of gluten and related prolamins such as cereals (wheat, rye, and barley) containing gluten, a protein complex (2). The overall global prevalence of CD is estimated to be 1%, but it varies depending on age and country of origin of the study population. Furthermore, many researchers acknowledge that the current prevalence of the disease may be underestimated due to under diagnosis (3).

In fact, the only available treatment is a lifelong gluten-free diet. However, adhering to a strict gluten-free diet every day of life may decrease the Health Related Quality of Life (HRQoL), negatively affect cost of living, and create social restrictions and stigmatization (4-8). HRQoL is defined as comprising of broad concepts of life including physical, emotional, mental, social, and behavioral components of functioning and wellbeing, as perceived by the individual and/or others (9). Several factors contribute to the negative impact that CD has on the HRQoL of affected patients. The chronic nature of CD and the fact that treatment entails a demanding, permanent, restrictive diet with periodic checkups are foremost among them (5, 10).

Celiac patients present an altered sense of well-being due to the symptoms of the disease, the associated conditions, and a sense of fatigue, among other causes (10, 11). The degree of adherence to a gluten-free diet has been shown to be an essential factor in the HRQoL of celiac patients, with better results in patients with total adherence (12). Earlier research has indicated a positive association between celiac disease and some mental disorders in both adults and children; however, the pathogenic mechanisms of mental and behavioral disorders associated with CD are not fully understood. Tryptophan deficiency and central serotoninergic hypo function have been suggested as possible causes (13). Moreover, dietary restrictions may lead to psychological and social disturbances in such patients (14) and the existence of neurologic or psychiatric dysfunctions have been shown to exist in some patients with CD (15). Interestingly, the majority of individuals with a neurological disease of unknown origin have been tested positive for anti-gliadin antibodies (16). Moreover, gluten intolerance might lead to a variety of anxiety disorders with social phobia and panic disorder being prevalent in CD cases. Depression and related mood disorders such as dysthymic disorder, and adjustment disorders are reported to be associated with celiac disease (17).

Despite various studies on HRQoL among adult cases, only a low number of studies have considered CD children, all of which have revealed inconclusive results (18-21). The HRQoL of children and adolescents with CD regarding their psychiatric symptoms has not been studied comprehensively. Hence, we have performed a cross-sectional study to compare a group of CD children (enrolled in a tertiary level pediatric gastroenterology center) with a group of healthy children, based on a validated, easy, and widely used plan for pediatric patients as well as a standard Peds Q4 questionnaire.

2- MATERIALS AND METHODS

2-1. Patients and controls

This cross-sectional study was done from November 2013 to June 2014 on the Gastroenterology Outpatient Clinic (Ghaem Hospital, Mashhad- Iran). Fifty patients (aged 7-16 years), which consisted of 24 males (48%) and 26 females (52%), with serology and biopsy-proven CD, and on a gluten free diet (GFD) for at least one year, were consecutively enrolled in this study. Patients with a history of other

medical (i.e. Insulin-Dependent Diabetes Mellitus (IDDM), autoimmune hepatitis) and psychosocial disorders were excluded. In addition, 50 non-celiac healthy children similar in age and gender, 23 males (46%) and 27 females (54%), were screened as controls during their annual pediatric visit in tertiary general pediatric clinics in the same area.

2-2. Assessment of quality of life

To investigate the quality of life, we used the PedsQL 4.0, with 23-item multidimensional generic core scales, which covers different areas including: (1) eight physical functioning parts, (2) five emotional functioning parts, (3) five social functioning parts, and (4) five school functioning parts (22). Validation and cultural adaptation of the Persian translation of the questionnaire was acquired (23).

Raw scores were evaluated based on a 5-point Likert scale (0 = never a problem; 1 = almost never a problem; 2 = sometimes a problem; 4 = almost always a problem), which was reverse-scored and linearly transformed to a 0-100 scale (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0), with higher scores indicating better HRQoL (**Table.1**).

Table-1: Health Related Quality of Life Questionnaire scores

Dimensions	Number of Items	Cluster of Items	Reversed scoring	Direction of Dimensions
Physical Functioning	8	1-8	1-8	Higher scores indicate better HRQOL.
Emotional Functioning	5	1-5	1-5	
Social Functioning	5	1-5	1-5	
School Functioning	5	1-5	1-5	

2-3. Depression and Anxiety

The Child Depression Inventory (CDI), as a widely used scale of children's depression symptoms, is a 27-item self-rating assessment commonly applied to study depression in children and adolescents between 6 and 17 years old. Each part of this measure evaluates the severity of depression symptoms using three scales (0, 1, 2 points), the maximum score is 54 and those with a score of 19 or higher should be assessed for depression disorders (24).

Validation and cultural adaptation of the Persian translation of the questionnaire was acquired by Dehshri et al. and reliability and internal consistency is considered to be 0.82 and 0.83 respectively (25). The State-Trait Anxiety Inventory for Children (STAIC) covers 20 parts in each of the two subscales to assess state-trait anxiety. Each item is scored from 1 to 3 based on the intensity of the symptom. Hence, 60 is the highest possible score and 20 is the lowest possible score (26). Reliability and validity of the inventory in Persian was studied and reliability and internal consistency for state anxiety is 0.92 and for trait anxiety is 0.90 (27).

2-4. Statistical analysis

Statistical analysis was done using SPSS software, version 11.5. The Mann Whitney test, Independent samples t- test, were used for comparing variables between groups and Spearman correlation coefficient were used for correlation test. P-value less than 0.05 were considered significant.

2-5. Ethics

The Research and Legal Committee of the Medical Center of the Mashhad University of Medical Sciences, Iran approved the study protocol.

3- RESULTS

One hundred children (aged 7-16 years) were initially invited to participate in our study. They were divided into two groups of 50 patients with celiac disease (24 males and 26 females), and 50 controls (23 males and 27 females). According to their age, they were classified further into three age groups (7-10, 11-13, 16-14 years), most of the studied children were between 7 to 10 years, in which 23 out of 50 (46%) were in the case groups and 33 out of 50 (66%) were in the control group. Children aged 14-16 years were frequent in the CD group. **Table.2** shows the demographic characteristics of the enrolled subjects.

3-1. Quality of life

In this study, the mean score of quality of life in the case group was 76.8±13.6 and in the control group it was 80.5±11.3 (total score: 100), which was not statistically significant. In the physical activity component, the mean scores in the case group was 84.37 and in the control group it was 75.87(total score: 100), which was statistically significant (P= 0.008). Quality of life in the subgroup of physical activity was better in CD patients. However, there was no statistical significance between the emotional function and social function in the two groups.

Figure.1 shows the results of the psychosocial evaluation of CD patients and controls (PedsQL 4.0 scores).

3-2. Depression and Anxiety

The mean state anxiety score in the CD group was 35.88± 5.67, and in the control group it was 31.18±5.62 (total score: 60), which was statistically significant (P<0.001). Mean trait anxiety score in the CD group was 34.4±7.95, and in the control group it was 30.68±6.92 (total score: 60), which was statistically significant (P= 0.014). Mean depression score was 13.44±7.95 in the celiac disease group. In the control group it was 9.6±4.69 (total score: 54), which was statistically significant (P= 0.018).

Table.3 shows the mean STAIC, CDI and PedsQL 4.0 score of children with or without celiac disease. There was a statistically significant correlation between state and trait anxiety (P= 0.001, r = 0.53). Also, there were statistically significant correlations between state and trait anxiety and depression (P= 0.014, r= 0.35 and P=0.001, r: 0.52). In addition, there were statistically significant reverse correlations between the quality of life of CD children and anxiety (state, trait) (P= 0.001, r= 0.51 and P= 0.02, r= 0.32). However, there was no correlation between quality of life and depression. **Table**.**4** shows the correlation coefficient of anxiety, depression, and quality of life in children with or without celiac disease.

Table-2: Demographic features of the celiac patients and control group

Variables	With celiac disease		Healthy control group	
	Number	Percent	Number	Percent
Gender				
Female	26	52%	27	54%
Male	24	48%	23	46%
Age (year)				
7-10	23	46%	33	66%
11-13	14	28%	14	28%
14-16	13	26%	3	6%

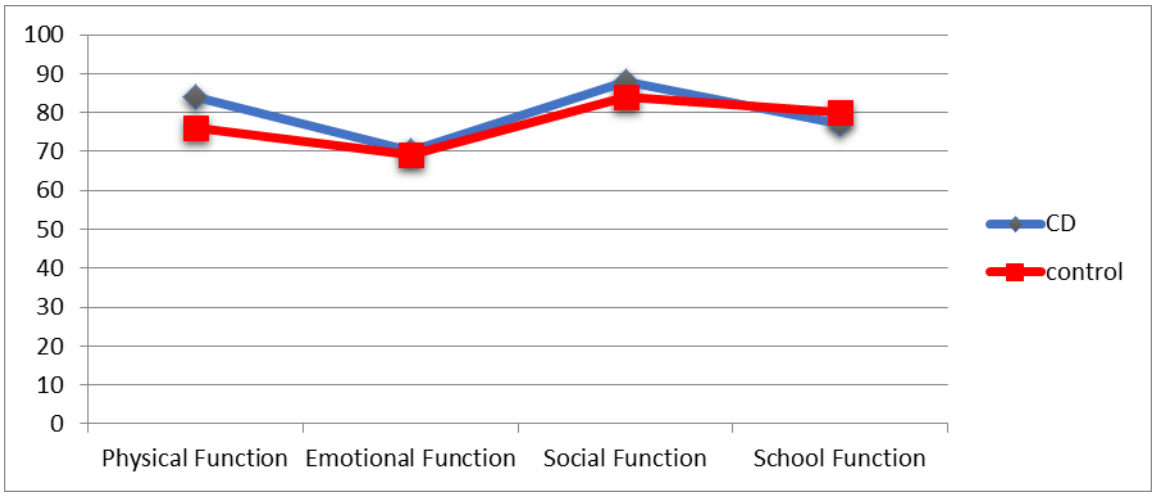

Fig.1: PedsQL mean scores in case and control groups.

Table-3: Mean STAIC, CDI and PedsQLTM score of patients with or without celiac disease

Variables	With Celiac disease	Healthy control group	
	Mean ± SD	Mean ± SD	P- value
STAIC state	34.4±7.95	30.68±6.92	0.014
STAIC trait	35.88±5.62	31.18±5.67	0.001
CDI	13.4±7.95	9.6±4.6	0.018
PedsQLTM	80.5±11.3	76.8±13.6	0.148

Child Depression Inventory (CDI), Pediatric Quality of Life Inventory (PedsQLTM), State-Trait Anxiety Inventory for Children (STAIC).

Table-3: Correlation coefficient of anxiety, depression, and quality of life in patients with or without celiac disease

Variables	Celiac patient		Healthy control	
	Correlation coefficient	P-value	Correlation coefficient	P-value
Anxiety (state) and (trait)	0.56	<0.001	0.51	<0.001
Anxiety (state) and depression	0.51	<0.001	0	0.63
Anxiety (trait) and depression	0.5	<0.001	0.6	<0.001
Quality of life and anxiety (state)	-0.23	0.02	-0.32	0.02
Quality of life and anxiety (trait)	0.2	0.02	-0.2	0.04
Quality of life and depression	0.12	0.2	0.17	0.08

R=Correlation coefficient (Spearman Correlation Test).

4- DISCUSSION

The gluten-free diet has a positive effect in celiac children. However, a new strategy is needed to improve the quality of life of CD patients alongside disease treatment. HRQoL as a crucial aim of therapeutic interventions assesses clinical settings to ameliorate the quality of care in different chronic illnesses including CD and inflammatory bowel diseases (28). In this

study, PedsQL 4.0 as a well-known, easy and valid tool for children was applied to compare the condition of CD cases with healthy individuals. In our study, depression and anxiety (state, trait) levels were statistically different in children with celiac disease than healthy children. We did not find any significant difference in the PedsQL score distributions between celiac patients and controls. However, in subgroup analysis, physical activity component, mean number in the case group, and control group was statistically significant. Quality of life in this subgroup was better in CD patients.

Recent studies have evaluated the impact of GFD on quality of life in children with celiac disease. In the study of Biagetti et al., not only no significant differences were shown regarding the quality of life between groups, but also celiac patients had generally good quality of life in comparison with the controls. In that study, cases with diet difficulties revealed lower scores of QoL regarding their characteristics in the physical activity and total scores. They suggested that probably the difficulty in adhering to the diet could have an impact on all the aspects of the QoL (29). Similar results obtained in other studies about the total scores of quality of life were not significantly different between the CD cases and healthy controls (20). Applying the generic questionnaire of QoL in other previous studies revealed compatible results with those obtained in our study (30, 31).

Fabiani et al. evaluated the compliance with GFD in adolescents with CD and found that adhering to a strict diet is not easy in this age group, which is a critical period for adherence to the diet (32). In our study, the subgroup with 14-16 years age was frequent in CD patient than in controls. Negative experiences eventually adversely affect the life of CD adult patients regarding their social relationships and management of daily life in order to adhere to the GFD (33); similar difficulties for CD children have been also proposed in other studies (18, 19, 34-37). It has been shown that relief of gastrointestinal symptoms could lead to improvements of QoL in adults, within one year of diagnosis of the CD symptomatic cases (38). Conversely, no improvement or deterioration has been reported in asymptomatic or in screening-detected celiac patients at one year follow-up (38, 39). In our country, we did not have a screening test for celiac disease so all the patient referred to a physician are symptomatic and when treated with GFD, their symptoms are relieved and their quality of life improves.

The progressive effects of the GFD on physical health might be due to a significantly higher energy intake in patients on GFD than controls, with no impact on body mass index (40). Another study by Samasca et al. has shown positive effects of GFD in CD cases, including body mass index elevation, higher energy intakes, decreased adiposity gain, and controlled risk of the associated complications (41). Sex related differences have been also reported in the study of Sverker et al. Negative effects have been observed in some studies performed on the Qol of female patients after being diagnosed (42, 43); however, no relation was observed between the sexes and QoL in our study.

Furthermore, the relation between psychiatric disorders and chronic diseases has been studied. We obtained a significant positive relation between CD in children and the level of depression and anxiety; which was consistent with other studies that proposed a higher prevalence of depression and disruptive behavior syndromes in adolescents with CD (44). Conversely, another study did not obtain this significant relation regarding the depression parameters in CD children and adolescents compared to healthy controls

(13). Compromised absorption of vitamins and amino acids might be responsible for reduced neurotransmitter levels in the central nervous system, which leads to immunological dysregulation and eventually psychiatric symptoms in CD cases (45). In this regard, although, the plasma level of tryptophan has shown to be decreased in CD cases with untreated behavioral complications, emotional and mental parameters have been ameliorated following the administration of the gluten free diet (46). On the other hand, the regulation of serum tryptophan levels has been reported to improve depression symptoms (47).

Poor dietary compliance in CD children and adolescents might lead to different levels of anxiety and depression between these two age groups. Depression and disruptive behavior disorders are more common in adolescents with celiac disease (48); CD patients were mostly adolescents in our study. Studies have not shown any relation between the depression complaints observed in CD patients and age, gender, and socio-economic variables (49). Also, there is no relation between physical symptoms, such as abdominal pain and diarrhea, and depression symptoms (50). In this study, we did not check these relations. Depression could be also proposed as a major reason for noncompliance with the treatment of chronic diseases (51).

Based on the study of Rapaport et al., CD patients might have different degrees of anxiety disorders, but all have shown significant QoL impairment (52). We also observed significant impairment in QoL of CD children with anxiety. Hence, psychological supports are crucial for CD cases with depression and anxiety disorders to improve psychological parameters that might lead to better acceptance of GFD, higher treatment compliance, and lower disease-associated complications (53).

4-1. Limitations of the study

Limitation of our study included not checking the patients' age and sex, along with time of diagnosis, and length of time on a gluten-free diet, which were all independent determinant factors of certain dimensions of HRQoL. Additionally, our sample size was small and we did not focus on patients' adherence to the diet, an important factor in the assessment of quality of life.

5- CONCLUSION

Adhering to a strict GFD for managing celiac disease may impact negatively on patients' health related quality of life (HRQoL) and may lead to depression and anxiety. Our study compares a group of CD children with healthy counterparts, based on a validated questionnaire. In our finding, the physical activity component of quality of life was better in CD patients. However, the mean total anxiety or depression scores were higher in this group. There were significant correlations between anxiety and depression and reverse correlations between quality of life of CD children and anxiety. It seems that anxiety and depression are important aspects in celiac disease and may have a significant impact on the course of the disease.

6- AUTHOR CONTRIBUTIONS

Jafari SA, Mostafavi N, Moharreri F, and Kianifar HR contributed to study conception and design, Talebi S, Jafari SA, Mostafavi N, Moharreri F, and Kianifar HR, contributed to data acquisition, data analysis and interpretation, and writing of the article; Talebi S, Jafari SA, and Kianifar HR contributed to editing, reviewing and final approval of the article.

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8- CONFLICT OF INTEREST

All of the authors have declared no conflict of interest.

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