

ÇÖLYAK HASTALIĞI OLAN ÇOCUKLARDA DEPRESYON VE SOSYAL ANKSİYETENİN DEĞERLENDİRİLMESİ

THE EVALUATION OF DEPRESSION AND SOCIAL ANXIETY AMONG CHILDREN WITH CELIAC DISEASE

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ÖZ

AMAÇ: Çölyak hastalığı (ÇH) olan erişkin hastalarda depresyon ve anksiyete düzeyi araştırılmış ve çelişkili sonuçlar bildirilmiştir. Öte yandan çocuk hastalarda ÇH ile depresyon ve anksiyete birlikteliği ile ilgili sınırlı sayıda çalışma bulunmaktadır. Bu çalışmanın amacı ÇH olan çocuklarda depresyon ve sosyal anksiyeteye eğilimin varlığını araştırmaktır.

GEREÇ VE YÖNTEM: Bu çalışmaya en az bir yıldır glutensiz diyet alan 8 - 14 yaş grubundaki hastalar ile aynı yaş grubundaki sağlıklı kontroller dahil edilmiştir. Tüm katılımcılara Çocuklar için Depresyon Ölçeği (ÇİDÖ) = CDI ve Sosyal Anksiyete Ölçeği (ÇSAÖ-Y) = SASC-R uygulandı. Bu çalışmaya 45 çölyak hastalığı olan çocuk ve 45 sağlıklı çocuk dahil edildi.

BULGULAR: Çalışma grubunun yaş ortalaması 11.6±2,4 yıl idi ve %76'sı kızdı. Kontrol grubunun yaş ortalaması 12,0±2,1 yıl idi ve %62'si kızdı. ÇH olan çocuklarla sağlıklı kontroller arasında hem CDI hem SASC-R de skoru açısından anlamlı farklılık saptanmadı. Diyet uyumu iyi olan hastaların anksiyete düzeylerinin daha yüksek olduğu saptandı.

SONUÇ: Bu çalışma göstermiştir ki daha önce yapılan çalışmalara benzer şekilde ÇH olan çocuklarda depresyon ve sosyal anksiyete sıklığı sağlıklı çocuklardan farklı değildir.

ANAHTAR KELİMELEER: Çölyak Hastalığı, Depresyon, Sosyal Anksiyete

ABSTRACT

OBJECTIVE: Depression and anxiety levels adult patients with celiac disease (CD) have been investigated and conflicting results have been reported. However, there are limited studies on the association of CD with depression and anxiety in pediatric patients. The aim of this study was to investigate the presence of a tendency toward depression and social anxiety in children with CD.

MATERIAL AND METHODS: Patients aged between 8-14 years old and who had a gluten-free diet for at least one year and healthy controls within the same age group were included in this study. All participants were administered the Children Depression Inventory (CDI) and Social Anxiety Scale-Revised (SASC-R). 45 children with celiac disease and 45 healthy children were included in this study.

RESULTS: The mean age of the experimental group was 11.6 ± 2.4 years old and 76% were female. The mean age of the control group was 12,0±2.1 years old and 62% were female. No significant differences were found between children with CD and healthy controls in terms of CDI and SASC-R scores. Anxiety levels of the patients whose adherence to the diet was good were found to be higher.

CONCLUSIONS: This study showed that the incidences of depression and social anxiety were not different from healthy children as similar to previous studies in children with CD.

KEYWORDS: Celiac disease, Depression, Social Anxiety

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INTRODUCTION

Celiac disease is an autoimmune enteropathy that occurs following exposure to environmental factors such as gluten in diet among individuals with a genetic predisposition. Celiac disease has a clinical picture including gastrointestinal and extraintestinal symptoms. Pathogenesis of celiac disease is associated with immune dysregulation and may be accompanied by extraintestinal system symptoms associated with neurological and psychiatric disorders. Depression, disturbance in cognitive functions, attention deficit disorders, anxiety, sleeping problems, and a decrease in quality of life may be observed in individuals with celiac disease. It is known that post-treatment symptoms are regressed in celiac patients with a diagnosis of apathy, irritability, and schizophrenia especially before initiating a gluten-free diet.

It is estimated that increased proinflammatory cytokine levels may affect mental and emotional functions. On the other hand, psychological symptoms are thought to be associated with nutritional malabsorption and the difficulties caused by the presence of a lifelong gluten-free diet as the only treatment option (1 - 3). The relationship between celiac disease and psychiatric disorders such as anxiety and depression has been generally known for a long time.

The co-occurrence of depression and anxiety with celiac disease has been mostly investigated in adult patients, and conflicting results have been reported. In the literature, there are limited number of studies on depression and anxiety among children (4). The aim of this study was to investigate the presence and incidence of depression and social anxiety among children with celiac disease and its relationship with sociodemographic and clinical characteristics.

MATERIAL AND METHODS

Our study was carried out at Pediatric Health and Diseases Clinic of Afyon Kocatepe University Faculty of Medicine and Pediatric Gastroenterology Clinic of Isparta Urban Hospital between 03.06.2017 - 03.11.2017. This study was designed as a case-control study. In the study by Jafari et al. (2017), the Children Depression Inventory (CDI) was applied to both children

with celiac disease and healthy children. In the study, mean scores from Children Depression Inventory were found to be $13,4 \pm 7,95$ for children with celiac disease, and $9,6 \pm 4,6$ for healthy children (5). Based on this value, the effect size of our study was calculated to be 0.58. The sample size was found to be a total of 74 individuals including 37 in each group with an error rate of 5% and a power of 80% by using the G Power 3.1.9.2 program. 45 children with celiac disease who were aged between and 8 - 14 years old and had received a gluten-free diet at least for one year and 45 healthy children of the same age group were included in this study. The diagnosis of celiac disease was made according to the criteria of European Society for Pediatric Gastroenterology Hepatology and Nutrition.

ETHICAL COMMITTEE

Ethics approval to carry out the study was provided by Clinical Research Ethics Committee of Afyon Kocatepe University (No:02.06.2017/217-6)

DATA COLLECTION

The aim of the study was told to the parents and they were asked to complete the sociodemographic data form after giving consent. All participants were applied "Children Depression Inventory (CDI)" and "Social Anxiety Scale for Children-Revised (SASC-R).

Children Depression Inventory (CDI)

This inventory was developed by Kovacs in 1980 in order to determine the severity of depression among children and adolescents (6).

CDI is a self-rating scale and it is completed by reading it to the children or it can be read and completed directly by the children. There are 27 items in the inventory and each item has three different options. Sentence sets in the options include statements regarding the symptoms of childhood depression. Children are asked to mark the most appropriate option for their last two weeks.

While Children Depression Inventory is evaluated, each item is given 0, 1, or 2 points according to the severity of the symptom. Maximum score can be 54. The items of B, E, G, H, I, J, L, K,

O, P, S, U, and V are reverse scored. Total score increases as the severity of depression increases. Validity and reliability of Turkish version of the scale were performed by Oy (7).

Social Anxiety Scale for Children-Revised (SASC-R)

This scale was developed by La Greca et al. in 1988 (8). The scale, that had 10 questions, was reviewed in 1993; and had its latest version including 18 questions (9). While answers were chosen among three options; final version had a Likert-type scoring scale, and only one of the options including "0=never, 1=rarely, 2=sometimes, 3=often, 4=always" is chosen for each question. The scores that can be obtained from the scale is are between 18-90. Basically, SASC-R questions the cognitive aspect of social anxiety; and the scale has three components: Fear of Negative Evaluation, Social Avoidance, and Distress in General and Social Avoidance Specific to New Situations or Unfamiliar Fears. Validity and reliability study of SASC-R for Turkey was carried out by Demir et al. (10).

STATISTICAL ANALYSIS

Descriptive statistics for the whole sample were analyzed by including frequency for categorical variables, mean and standard deviation, or median with minimum and maximum for continuous variables. Chi-square test and Fisher's exact test were used to compare the percent distributions of categorical data between groups. In order to compare the mean values between the groups, the distribution of data was evaluated by the Shapiro Wilk test. In the independent groups; T-test was used for comparison when the distribution of data was normal. Mann-Whitney U test, Kruskal Wallis test, and Spearman's correlation analysis were used to compare data which were not normally distributed. Statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS) 22.0 package program. Values of $P < 0.05$ were considered as statistically significant.

RESULTS

This study was carried out to investigate the presence of tendency for social anxiety and depression among the children with CD and included 45 children with CD between 8 - 14 years old and 45 healthy children of the same age group. Celiac patients and the control group were compared for age, sex, weight, height,

body mass index, the number of family members and income of the family. No significant differences were found between groups in terms of these characteristics. 45 children with CD between 8 - 14 years old and 45 healthy children of the same age group were included in this study. Sociodemographic and clinical characteristics of patient and control groups were given in the **Table 1**.

Table 1: Sociodemographic and clinic characteristics of the study and the control groups.

	Study Group (n=45)	Control Group (n=45)	p
Age (years; mean \pm SD*)	11.6 \pm 2.4	12.0 \pm 2.1	$p=0.464$
Gender (Female/male)	34/11 (76%/24%)	28/17 (62%/38%)	$P=0.172$
Height (cm; mean \pm SD)	141.0 \pm 19.1	153.7 \pm 17.3	$p=0.003^a$
Weight (kg; mean \pm SD)	36.5 \pm 13.9	46.2 \pm 15.48	$p=0.003^a$
BMI (kg/m ² ; mean \pm SD)	17.4 \pm 3.4	18.9 \pm 3.8	$p=0.044^a$
Residence, n (%)			$p=0.088$
City center	24 (53.3%)	15 (33.3%)	
District / Village	21 (46.7%)	30 (66.7%)	
Household member (n, %)			$P=0.202$
≤ 4	29 (64.4%)	22 (58.9%)	
> 5	16 (35.6%)	23 (51.1%)	
Maternal education level (n, %)			$p=0.106$
Elementary school	16 (35.6%)	19 (42.2%)	
Middle school	16 (35.6%)	21 (46.7%)	
High school	13 (28.8%)	5 (11.1%)	
Family income (n, %)			$p=0.320$
Low	27 (60.0%)	31 (68.9%)	
Medium/High	18 (40.0%)	14 (31.1%)	

*Standard Deviation
 $^a p < 0.05$

Mean age of the experimental group was 11.6 ± 2.4 years old; and 76% were females. Mean age of the control group was 12.0 ± 2.1 years old; and 62% were females. No statistically significant differences were found between both groups in terms of age, sex, place of residency, income level, education level of the mother, and number of family members. Mean values of height (141 ± 19.1), weight (36.5 ± 13.9) and body mass index (BMI) (17.4 ± 3.4) were found to be significantly lower in the experimental group ($p=0.003$, $p=0.003$ and $p=0.036$, respectively). When celiac patients were evaluated for their follow-up times, they were less than 2 years for 20 (44.4%), 2 - 5 years for 19 (42.2%), and more than 5 years for 6 (13.4%) patients. When their adherence to the celiac diet was examined, it was seen that adherence to the diet was good in 40 (89%) and bad in 5 (11%) patients. CDI and SASC-R scores of patient and control groups were given in the **Table 2**.

Table 2: CDI and SASC-R scores for the study and control group.

	Study Group (n=45)	Control Group (n=45)	p
	Median (min-max)	Median (min-max)	
CDI	11.0 (3.0-32.0)	15.0 (2.0-31.0)	0.186
SASC-R	34.0 (18.0-64.0)	41.0 (21.0-63.0)	0.096

CDI: Children Depression Inventory; SASC-R: Social Anxiety Scale for Children

The Median value of CDI score was 11.0 (Min-Max: 3.0-32.0) in the patient group and 15.0 (Min-Max: 2.0-31.0) in the control group. There was no statistically significant difference between both groups in terms of CDI scores. The Median value of SASC-R score was 34.0 (Min-Max: 18.0-64.0) in celiac patient group and 41.0 (Min-Max: 21.0-63.0) in control group. No statistically significant difference was found between both groups in terms of SASC-R scores. When results were examined in terms of sex, median value of CDI scores of celiac patients were found to be 11.0 in females and 13.0 in males; and the median value of SASC-R score was 34.5 in females and 33.5 in males. There was no statistically significant difference between sexes in terms of these scores. In addition, no statistically significant differences were found between CDI and SASC-R scores in terms of clinical characteristics of celiac patients such as age at diagnosis and duration of disease (<2 years, 2 - 5 years, >5 years). When CDI scores and adherence to celiac diet were compared, it was found that median values of the ones showing good adherence were lower than the ones who showed bad adherence (10.0 and 16.0, respectively). This difference was not statistically significant. When adherence to celiac diet and SASC-R scores were compared, median scores of the patients who showed good adherence (35.0) were found to be significantly higher than the ones who showed bad adherence (28.0). The CDI and SASC-R scale scores associated with socio-demographic information are given in the **Table 3**.

Table 3: Relations of sociodemographic-clinical variables with CDI and SASC-R scores in study group

Gender	CDI*	SASC-R *
Female (n=34)	11.0	34.5
Male (n=11)	13.0	33.0
<i>p</i>	0.667	0.687
Adherence to gluten-free diet**		
Good adherence (n=40)	10.0	35.0
Poor adherence (n=5)	16.0	28.0
<i>p</i>	0.388	0.042*
Duration of illness		
<2 years (n=21)	10.0	46.0
2-5 year (n=19)	14.0	33.0
>5 years (n=5)	22.0	42.0
<i>p</i>	0.186	0.359
Age at first diagnosis***		
<i>r</i>	0.179	-0.004
<i>p</i>	0.244	0.979

R: Social Anxiety Scale for Children

*Median

**Good adherence to diet: patients with a serum endomysium antibody (EMA) level <20 RU/mL.

***Spearman's correlation analysis.

*p < 0.05

DISCUSSION

In our study, no significant difference was observed in depression inventory scores of children with celiac disease and healthy children in

the control group. Our results are supported by the results of Fidan et al. that reported similar depression and anxiety levels between the children and adolescents with celiac disease and control group; by Esenyel et al. that indicated no change in depression scores before the gluten-free diet, and by Simsek et al. that reported no difference between celiac patients and healthy controls in terms of depression scores (11 - 13). In the study by Ruggieri et al. which was performed with 835 celiac patients, it was indicated that neurological and psychiatric problems were common in the celiac group, but the difference was not statistically significant (14).

However, in the study by Mazzone et al. anxiety and depression scores were found to be higher among children and adolescents with celiac disease compared to the control group including healthy children (15). Pynnonen et al. reported that the major depression rate was increased among adolescents with CD (16). This situation reminded that external factors belonging to chosen sample in the studies such as social and familial characteristics might be different. Pynnonen et al. reported in their study that depressive symptoms were present in adolescents who had untreatable celiac disease (17).

This situation was associated with serotonergic dysfunction due to a lack of tryptophan. At the end of the study, it was reported that depressive symptoms might regress by gluten-free diet treatment. In the study by Simsek et al., it was concluded that adherence to diet reduced the incidence of depression (13).

Lack of a difference between groups in terms of anxiety and depression scale scores might be due to good dietary adherence (89%) of the children with celiac disease in the experimental group. Besides, no significant relationship was found between depression inventory scores and dietary adherence in our study.

Pathogenesis of the relationship between celiac disease and emotional and behavioral disorders is not certainly known yet. However, deficiencies of nutrients such as B6 and B12 vitamins, folic acid and tryptophan that develop secondary to, malabsorption concomitant autoimmune diseases such as thyroiditis and diabetes mellitus, problems in the adherence to diet and

nutritional deficiencies led by strict gluten-free diet are considered as possible etiologies of psychiatric diseases. It was reported that tryptophan and other monoamine precursors in the plasma and serotonin, dopamine and noradrenaline metabolites in the cerebrospinal fluid were at a low level in celiac patients who were have not initiated a gluten-free treatment. Meeting with a gluten-free diet, radical changes in eating habits and lifestyle and adoption of the disease may cause emotional problems among children and especially adolescents (4). Although there are many studies on the co-occurrence of celiac disease and anxiety in the literature, they present different results (18). In their study with 1641 patients with gastrointestinal system disorders, Addolorato et al. showed that the incidence of depression increased in the group with celiac disease, but the incidence of anxiety did not (19). There are many studies showing that the anxiety levels of the patients decreased after initiating a gluten-free diet (19 - 23).

In a study examining women with celiac disease, it was determined that the population having a gluten-free diet was at more risk for anxiety compared to healthy controls (22). In their large-scale cohort study, Ludvigsson et al. reported that anxiety and depression were more incidents among the patients with the mucosal improvement compared to the ones with ongoing villous atrophy (23). In the study by Jafari et al, children with a celiac disease and healthy children were evaluated for anxiety and depression (5). Celiac disease was indicated to increase depression and anxiety levels. In the study by Mazzone et al. anxiety and depression levels among children with celiac diagnosis, who had dietary adherence, were found to be higher than the healthy control group (15). In our study, no significant difference was found between experimental and control groups in terms of anxiety levels. When the relationship between dietary adherence and anxiety was examined, we found that anxiety levels of the patients, whose adherence to the diet was good, were significantly higher. This outcome supports the results of the studies showing high anxiety levels in celiac patients. This result means that children, whose adherences to diet are good, experience more anxiety.

There are some limitations in our study. This is a cross-sectional study. Therefore, our results reflect the instant depression and anxiety levels of the patients. Besides, it only represents the findings of the patients who are living in the region where the study was carried out.

CONCLUSION

With this study, we determined that depression and anxiety levels of children with celiac disease were not different from healthy children. We also found that adherence to diet did not have an effect on depression, but increased anxiety.

It is necessary to elucidate the relationship between adherence to diet and anxiety in future studies.

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