Düşünen Adam The Journal of Psychiatry and Neurological Sciences 2013;26:232-238
DOI: 10.5350/DAJPN2013260301

Research / Araştırma

Depression-anxiety Levels and the Quality of Life Among Children and Adolescents with Coeliac Disease

Tulin Fidan[1], Vildan Ertekin[2], Kezban Karabag[3]

[1]Assist. Prof. Dr., Eskisehir Osmangazi University, Faculty of Medicine, Department of Pediatrics, Eskisehir - Turkey
[2]Assoc. Prof. Dr., Istanbul University Istanbul Faculty of Medicine, Department of Pediatric Gastroenterology, Istanbul - Turkey
[3]Pediatrician, Erzurum Training and Research Hospital, Department of Pediatrics, Erzurum - Turkey

ABSTRACT

Depression-anxiety levels and the quality of life among children and adolescents with coeliac disease

Objective: Coeliac disease is a chronic and inflammatory disease of the upper small intestine resulting from faulty gluten ingestion in genetically susceptible individuals. There is no sufficient data about the psychiatric symptoms and quality of life in children and adolescents with coeliac disease. The aim of this study was to investigate the quality of life in children and adolescents with coeliac disease.

Methods: Thirty children and adolescents with coeliac disease and 30 healthy controls were included in the study. Children Depression Inventory (CDI), State and Trait Inventory for Children (STAI-C) and Quality of Life Inventory for Child and Adolescents (PedsQL) were performed. Chi-square and t-test were used for statistical evaluations.

Results: Of the children and adolescents with coeliac disease, 56.7% were male and the mean age was 11.6±3.1. There were no statistically significant difference in the mean scores of CDI and STAI-C between the study group and healthy controls. But psychosocial and total mean scores of quality of life were found statistically significantly different.

Conclusions: In this study, no difference was found in depression and anxiety levels among children and adolescents with coeliac disease and healthy controls. However, coeliac disease has a negative effect on the quality of life and this might be related to dietary treatment.

Key words: Child and adolescents, coeliac disease, psychiatric symptoms, quality of life

ÖZET

Çölyak hastalığı olan çocuk ve ergenlerde depresyon - kaygı düzeyleri ve yaşam kalitesi

Amaç: Çölyak hastalığı, yatkın bireylerde gluten içeren besinlerin alınmasına bağlı olarak ince bağırsaklarda oluşan mukozal inflamasyonla karakterize süreğen bir hastalıktır. Çölyak hastalığı olan çocuk ve ergenlerde psikiyatrik belirtiler ve yaşam kalitesi ile ilgili bilgilerimiz yetersizdir. Bu çalışmanın amacı çölyak hastalığı olan çocuk ve ergenlerin yaşam kalitesi açısından değerlendirilmesidir.

Yöntem: Çalışmaya 30 çölyak tanılı, 30 sağlıklı çocuk-ergen dahil edilmiş olup, Çocuklar İçin Depresyon Ölçeği (ÇDÖ), Çocuklar İçin Durumluk-Sürekli Kaygı Envanteri (ÇDSKE) ve Çocuklar İçin Yaşam Kalitesi Ölçeği (ÇYKÖ) katılımcılara uygulanmıştır. İstatistiksel değerlendirmede ki-kare testi ve t-testi kullanılmıştır.

Bulgular: Çölyak hastalığı tanısı almış çocuk ve ergenlerin %56.7'si erkek olup, yaş ortalamaları 11.6±3.1'dir. Çölyak hastalığı tanısı bulunan çocuk ve ergenlerin ÇDÖ, ÇDSKE puan ortalamaları sağlıklı kontrol grubundan farklı bulunmamıştır. Ancak ÇYKÖ'den alınan sonuçlarda, psikososyal sağlık toplam puanı ve ölçek toplam puanları arasındaki fark istatistiksel olarak anlamlı bulunmuştur.

Tartışma: Bu çalışmada, çölyak hastalığı tanılı çocuk ve ergenler depresyon ve anksiyete düzeyleri bakımından değerlendirildiklerinde, sağlıklı kontrol grubundaki çocuklardan farklı bir durum bulunamamıştır. Ancak çölyak hastalığı, çocuk ve ergenlerin yaşam kalitesine olumsuz biçimde etki etmektedir ve bu durum kısıtlı diyet tedavisine bağlı olabilir.

Anahtar kelimeler: Çocuk ve ergen, çölyak hastalığı, psikiyatrik belirtiler, yaşam kalitesi

Address reprint requests to / Yazışma adresi:
Assist. Prof. Dr. Tulin Fidan,
Eskisehir Osmangazi University, Faculty of Medicine, Department of Pediatrics
Meselik Kampusu 26480 Eskisehir - Turkey

Phone / Telefon: +90-222-239-2979/3051

Fax / Faks: +90-222-229-1416

E-mail address / Elektronik posta adresi:
tulincps@hotmail.com

Date of receipt / Geliş tarihi:
June 1, 2012 / 1 Haziran 2012

Date of acceptance / Kabul tarihi:
October 13, 2012 / 13 Ekim 2012

INTRODUCTION

Coeliac disease is chronic disorder characterized with mucosal lesions of the small intestine due to genetic, immunological and environmental factors. Inflammation of the small intestine depends on intake of gluten with diet in genetically predisposed individuals and improves with having gluten-free diet (1). Coeliac disease affects small intestine essentially, however, it is a systemic disorder which can also affect liver, skin, joints, reproductive organs, nervous system and heart (2). It is known to be more common in individuals with Down syndrome (4–15%), type 1 diabetes mellitus (3–8%), Turner syndrome, Williams syndrome and selective Immunoglobulin A deficiency (10%) (3,4). Other autoimmune disorders frequently seen with Coeliac disease are Addison disease, autoimmune thyroiditis, alopecia areata, primary biliary cirrhosis, and autoimmune hepatitis (5,6). Signs of classical Coeliac disease include diarrhoea with or without steatorrhea, constipation, lack of appetite, vomiting, abdominal pain, abdominal distention, weight loss and failure to thrive (7-11). Most common signs in children diagnosed during early childhood are related with the intestinal system. Atypical signs increase with age (12). Neurological signs of Coeliac disease include ataxia, epilepsy, neuropathy, headache and cognitive impairment. This signs may be due to B12, D, and E vitamin deficiency because of malabsorption (13). Coeliac crisis, a medical emergency, can present itself with severe diarrhea, electrolyte imbalance and liquid loss in untreated or undiagnosed cases (2).

Principal approach for diagnosis is intestinal biopsy done by a gastroenterologist during both gluten-free diet and non-restricted diet periods. A significant histological improvement will happen in a short time after gluten-free diet (2).

It has been known that, psychiatric symptoms are common and quality of life is lower in subjects with Coeliac disease, particularly during adulthood, however, there are conflicting results on children in the literature (14).

Quality of life can be impaired in children due to chronic diseases. Children's social and emotional world change with physical restrictions. For this reason, it is important to evaluate the effect of disease on the child's life when assessing quality of life in children (15). Health dependent quality of life is a multidimensional concept, including physical, emotional and social components, which draws attention increasingly (16).

Data is limited on psychiatric signs of children and adolescents with Coeliac disease and the impact of these on quality of life (14). In this study, our aim was to investigate the depression and anxiety levels of children and adolescents with Coeliac disease and the impact of these on quality of life.

METHOD

Sample

This study was conducted during January 2009-May 2009 at Ataturk University Pediatric Gastroenterology Outpatient Clinic and included 30 children-adolescents who were followed-up for Coeliac disease for at least one year and 30 healthy control participants with similar age, gender and socioeconomic status. Subjects without grade 2 level literacy and who had mental retardation due to clinical examination or test (Weschler Intelligence Scale for Children or Stanford-Binet test) results were excluded from the study. Child Depression Inventory (CDI), State-Trait Anxiety Inventory for Children (STAIC) and Pediatric Quality of Life Inventory (PedsQL) were applied to all children and adolescents.

Detailed information on the study was given to every participant in accordance with Helsinki Declaration and written informed consent was obtained from the participants and their families. Institutional review board approval was obtained.

Measures

Child Depression Inventory (CDI): CDI is a 27-items self-rating scale frequently used to investigate depression in children and adolescents between 6 and 17 years of age. Kovacs (17) developed the inventory

based on Beck Depression Inventory and it was adapted to Turkish by Oy (18). Test validity (r=0.70) and internal consistency (a=0.80) of the inventory is high. Each item of the inventory investigates the severity of depression symptoms with three options (0, 1, 2 points). Maximum score is 54. Those with a score of 19 or higher is evaluated for depressive disorder (18).

State-Trait Anxiety Inventory for Children (STAIC): This inventory is developed by Spielberger (19) and consists of two subscales of multi-choice 20 items in each for evaluating state and trait anxiety. Each item is scored from 1 to 3 according to the severity of the symptom, maximum possible score is 60 and minimum possible score is 20. State anxiety refers to anxiety experienced by the individual on certain times under certain conditions and can change with external factors. On the other hand, trait anxiety corresponds to individual's general disposition to anxiety. Reliability and validity of the inventory in Turkish was studied by Ozusta (20).

Pediatric Quality of Life Inventory (PedsQL): It is a general quality of life inventory used in children and adolescents from age 2 to 18 (21). There are four different forms of the inventory with appropriate wording for 2–4, 5–7, 8–12 and 13–18 age groups. PedsQL consists of four subsections which investigate physical, emotional, social and school functioning. Inventory yields emotional functioning score (EFS), social functioning score (SFS), school functioning score, (ScFS), physical health summary score (PHSS), psychosocial health summary score (PsHSS) and total scale score (TSS).

5 choice Likert type visual scale is used in the inventory (0=never, 1=almost never, 2=sometimes, 3=often, 4=her almost always). Points obtained from the items are converted linearly to a value ranging between 0 and 100 (0=100, 1=75, 2=50, 3=25, 4=0). Higher scores reflect higher quality of life (22). Reliability and validity of the Turkish PedsQL 8–12 and 13–18 age group forms have been studied by Memik and colleagues (23,24) reported to have high reliability and validity.

Composite index was used to detect socioeconomic status of the families. Presence of water and sewer systems inside the house, parental education, maternal employment status and number of household residents per room were asked for this purpose. A score lower than 4 reflected low, 4-8.4 reflected middle and higher than 8.5 reflected high socioeconomic status, respectively (25). Composite index has been used in previous studies in our country (26).

Data Analysis

Study data was analyzed with Statistical Package for Social Sciences (SPSS) for Windows 15.0 software. Continuous variables were defined with mean, standard deviation; categorical variables were defined with number and percents. Kolmogorow-Smirnov test was used to assess the normality of distribution in continuous variables; in order to compare the groups, Student's t test was used in variables with normal distribution and Mann Whitney-U test in other variables. Two sided hypothesis was set for the study, 95% confidence intervals were provided and $p<0.05$ was reported as statistically significant. Besides, Cohen's "d" index (27) was used to interpret the effect sizes. Cohen set up certain cut-offs for interpretation of d: an effect size of d=0.02-0.5 is "small", d=0.05-0.8 is "medium" and d>0.8 is "large".

RESULTS

In this study, the data obtained from 30 children aged 7 to 18 years with Coeliac disease and 30 healthy children as the control group. Mean age of children and adolescents in the Coeliac disease group was 12.4±3.1 years and 56.7% were girls. There were no statistical differences between the groups in terms of age, gender, and socioeconomic level (Table 1).

Children and adolescents with Coeliac disease had this diagnosis for a mean of 4.1±2.3 years and they were on diet for a mean of 3.6±2.1 years. While twenty six patients were compliant with diet (86.7%) four were not (13.3%) (Table 2).

Table 1: Demographic features

Variables	With Coeliac disease (n=30)		Healthy control group (n=30)			
	n	%	n	%	χ^2	p
Gender						
Female	17	56.7	17	56.7	1.00	1
Male	13	43.3	13	43.3		
Age						
7-11 years	13	43.3	20	66.7	3.30	0.69
12-18 years	17	56.7	10	33.3		
Socioeconomic level						
Poor	5	16.7	5	16.7		
Middle	21	70.0	16	53.3	2.60	0.27
Good	4	13.3	9	30.0		

χ^2: Chi-square test

Table 2: Variables related with the disorder in children and adolescents with Coeliac disease

	Min-max	Mean±SD
Duration of the signs of Coeliac disease (years)	1-15	5.2±2.9
Duration of the Coeliac disease diagnosis (years)	1-10	4.1±2.3
Duration of being on diet	1-10	3.6 ±2.1
Diet compliance	**n**	**%**
Good	26	86.7
Poor	4	13.3

SD: Standard Deviation

Only three children (10%) with Coeliac disease or in the control group had a CDI score of 19 or higher. Mean state anxiety score was 34.6±6.1, trait anxiety score was 33.7±6.5, and depression score was 10.8±7.4 in the Coeliac disease group. In the control group these figures were 32.8±7.2, 33±6.3, 8.8±6.8, respectively. There were no statistically significant differences between children with Coeliac disease and healthy children in terms of mean CDI and STAIC state and trait anxiety scores (p=0.28, Cohen d=0.21, p=0.30, Cohen d=0.25, p=0.64, Cohen d=0.07) (Table 3). The difference of CDI and STAIC mean scores had a small effect size.

Pediatric Quality of Life Inventory PHSS, PsHSS and TSS mean scores of children and adolescents with Coeliac disease were 67.5±16.4, 66.0±23.0, 69.1±17.1, respectively. When compared with healthy children and adolescents, children and adolescents with Coeliac disease had lower mean subscale scores; while the difference of PsHSS and TSS mean scores were statistically significant with a medium effect size (p=0.002, Cohen d=0.67, p=0.004, Cohen d=0.74), the difference of mean PHSS score was not statistically significant and the effect size was small (p=0.11, Cohen d=0.37) (Table 4).

There were no significant differences between children with Coeliac disease who were compliant or non-compliant with diet in terms of PHSS, PsHSS and TSS scores (p<0.05).

When the children and adolescents with Coeliac disease were divided into two age groups regarding age (7-11 age: 1st Group, 12-18 age: 2nd Group), there were no significant differences in terms of mean PHSS, PsHSS and TSS scores (p<0.05).

Table 3: Mean STAIC and CDI scores

	With Coeliac disease		Healthy Control Group			
	Min-max	Mean±SD	Min-max	Mean±SD	t	p
STAIC-State Anxiety	22-49	34.6±6.1	20-44	32.8±7.2	1.035	0.30
STAIC-Trait Anxiety	20-45	33.7±6.5	21-46	33±6.3	0.461	0.64
CDI	1-33	10.8±7.4	0-25	8.8±6.8	1.078	0.28

STAIC: State-Trait Anxiety Inventory for Children, CDI: Child Depression Inventory, SD: Standard Deviation

Table 4: Mean Pediatric Quality of Life subscale scores

	With Coeliac disease		Healthy control group			
	Min-max	Mean±SD	Min-max	Mean±SD	t	p
PHSS	25.0-93.7	67.5±16.4	37.5-100.0	77.5±19.0	-1.617	0.11
PsHSS	7.3-93.3	66.0±23.0	55.0-95.0	77.4±11.7	-2.400	0.02*
TSS	26.0-89.9	69.1±17.1	48.9-95.6	77.3±12.9	-2.104	0.04*

PHSS: Physical Health Summary Score, PsHSS: Psychosocial Health Summary Score, TSS: Total Scale Score, SD: Standard Deviation, *p< 0.05 statistically significant

DISCUSSION

Coeliac disease is a chronic disorder characterized with impaired absorption in small intestine. It is known that psychiatric disorders are common in chronic disorders. However, in this study, depression and anxiety levels were not different in children and adolescents with Coeliac disease than healthy children and adolescents. In a study supporting these results, while psychiatric/neurological symptoms were more common in 835 children and adolescents diagnosed with Coeliac disease who were followed-up from 1991 to 2004, the difference was not statistically significant (28). In a similar study in which adolescents with Coeliac disease were evaluated with a semi-structured clinical interview for present and life-time psychiatric disorders (Kiddie Kiddie-SADS), Child Behavior Checklist, Youth Self Report, Hamilton Depression Ratings Scale, Hamilton Anxiety Rating Scale, Beck Anxiety and Depression Inventory, it was reported that while there were no differences between the present psychiatric evaluations, lifetime risk of major depressive disorder and disruptive behavior problems were increased in the patient group. It was argued that this increased risk was associated with the period before dietary restrictions (29).

On contrary to the results of the present study, there have been several case examples implying association of Coeliac disease with depression, schizophrenia and anxiety disorders. It has been suggested that impaired absorption of vitamins and amino acids in patients with Coeliac disease might lead to decreased levels of neurotransmitters in the central nervous system and that psychiatric symptoms might be due to immunological dysregularities (30). Depressive symptoms are part of the clinical picture in adults with Coeliac disease and these symptoms are seen in similar frequency in children and adolescents (31). Pynnönen and associates (29), found that lifetime prevalence rates of major depression and disruptive behavior disorders are increased in adolescents with Coeliac disease. Ljungman and Myrdal (32) reported that adolescents diagnosed with Coeliac disease before 2 years of age were as healthy as the comparison group of healthy adolescents.

Pathogenesis and related mechanisms of emotional and behavioral disorders in Coeliac disease are not clear yet. Previous studies suggested impaired tryptophan metabolism and serotonergic functions as possible mechanisms. Plasma tryptophan level is low in Coeliac disease patients with untreated behavioral problems and in some of these patients emotional or mental activity can recover after gluten free diet implementation (33).

In this study, mean scores of depression inventory and state trait anxiety inventory for children and adolescents with Coeliac disease were not different when compared with scores of healthy children and adolescents. This might be due to early diagnosis and early, pre-adolescence onset of gluten free diet implementation. It can be argued that early implementation of gluten free diet might have a protective effect on future depression and anxiety disorders. At the same time, good compliance of almost all of the children and adolescents with Coeliac disease to diet might be a reason for the lack of difference of anxiety and depression levels between children and adolescents with Coeliac disease and control group.

On the other hand, former studies reported that depression and disruptive behavior disorders were more common in adolescents with Coeliac disease particularly before gluten free diet and that in some

patients psychiatric symptoms recovered after treatment (34). Increased rate of depression and disruptive behavior disorders in adolescents with Coeliac disease might be consistent with the hypothesis that central serotonergic functioning is impaired in Coeliac disease. However, this mechanism is not clear, yet (28).

In this study, results indicated that children and adolescents with Coeliac disease did not have a problem in terms of physical health related quality of life, but that they have impaired psychosocial health and overall quality of life when compared with healthy children and adolescents. Gluten-free products are not very easily accessible and common particularly in Turkey and very restricted presence of products suitable for children and adolescents with Coeliac disease might lead to decreased psychosocial quality of life. In a study with 133 children between 8-16 years of age and adolescents with Coeliac disease, there was only borderline difference in quality of life in treated children and adolescents with Coeliac disease and it was argued that this lack of significant difference might be due to treatment (35).

Like all studies, there were some limitations of the present study. First, lack of clinical assessment regarding psychiatric disorders and small sample size, and second, the selection of the sample among patients who applied to hospital made it difficult to generalize the findings.

CONCLUSIONS

Results indicated that children and adolescents with Coeliac disease were negatively affected in terms of psychological and social quality of life during their struggle with a chronic disease. Decreased quality of life can be associated with dietary restrictions and it is important to make products suitable for the diets of children and adolescents with Coeliac disease are more readily and commonly available. Child psychiatrists must be in the treatment team of children and adolescents with Coeliac disease to help these patients solve their psychological and social problems. In order to define the psychiatric disorders accompanying Coeliac disease and the mechanism of these disorders, prospective follow-up studies with bigger sample sizes using structured clinical interviews are necessary.

REFERENCES

1. Mearin ML. Celiac disease among children and adolescents. Curr Probl Pediatr Adolesc Health Care 2007; 37:86-105.
2. Zawahir S, Safta A, Fasano A. Pediatric celiac disease. Curr Opin Pediatr 2009; 21:655-660.
3. Wouters J, Weijerman ME, van Furth AM, Schreurs MW, Crusius JB, von Blomberg BM, de Baaij LR, Broers CJ, Gemke RJ. Prospective human leukocyte antigen, endomysium immunoglobulin A antibodies, and transglutaminase antibody testing for celiac disease in children with Down syndrome. J Pediatr 2009; 154:239-242.
4. Korponay-Szabó IR, Dahlbom I, Laurila K, Koskinen S, Woolley N, Partanen J, Kovács JB, Mäki M, Hansson T. Elevation of IgG antibodies against tissue transglutaminase as a diagnostic tool for coeliac disease in selective IgA deficiency. Gut 2003; 52:1567-1571.
5. Gianfrani C, Troncone R, La Cava A. Autoimmunity and celiac disease. Mini Rev Med Chem 2008; 8:129-134.
6. Leeds J, Hopper A, Sanders D. Coeliac disease. Br Med Bull 2008; 88:157-170.
7. Cassinotti A, Birindelli S, Clerici M, Trabattoni D, Lazzaroni M, Ardizzone S, Colombo R, Rossi E, Porro GB. HLA and autoimmune digestive disease: a clinical oriented review for gastroenterologists. Am J Gastroenterol 2009; 104:195-217.
8. Catassi C, Fasano A. Celiac disease. Curr Opin Gastroenterol 2008; 24: 687-691.
9. Garrote JA, Gómez-González E, Bernardo D, Arranz E, Chirdo F. Celiac disease pathogenesis: the proinflammatory cytokine network. J Pediatr Gastroenterol Nutr 2008; 47:27-32.
10. Branski D, Fasano A, Troncone R. Latest developments in the pathogenesis and treatment of celiac disease. J Pediatrics 2006; 149:295-300.
11. Lebenthal E, Shteyer E, Branski D. The Changing Clinical Presentation of Celiac Disease: In Fasano A, Troncone R, Branski D (editors). Frontiers in Celiac Disease. Basel: Karger, 2008, 18-22.
12. Kurppa K, Koskinen O, Collin P, Mäki M, Reunala T, Kaukinen K. Changing phenotype of celiac disease after long-standing gluten exposure. J Pediatr Gastroenterol Nutr 2008; 47:500-503.

13. Grossman G. Neurological complications of celiac disease: what is the evidence? Pract Neurol 2008; 8:77-89.

14. Fidan T, Ertekin V, Selimoglu A. Depression and anxiety levels among children with coeliac disease: a preliminary report. Acta Pædiatr 2008; 459 (Suppl.):133.

15. Eiser C, Morse R. Can parents rate their child's health related quality of life? Results of a systematic review. Qual Life Res 2001; 10:347-357.

16. Petersen C, Schmidt S, Power M, Bullinger M. The DISABKIDS Group. Development and pilot-testing of a health related quality of life chronic generic module for children and adolescents with chronic health conditions: a European perspective. Qual Life Res 2005; 14:1065-1077.

17. Kovacs M. Rating scales to assess depression in school-age children. Acta Paedopsychatr 1980; 46:305-315.

18. Oy B. Çocuklar için depresyon ölçeği geçerlilik ve güvenilirlik çalışması. Turk Psikiyatri Derg 1991; 2:132-137 (Article in Turkish).

19. Spielberger CD. Manual for the State-Trait Anxiety Inventory for Children. Palo Alto, CA: Consulting Psychologists Press, 1973.

20. Ozusta Ş. State-Trait Anxiety Inventory for Children: a study of realibility and validity. Türk Psikoloji Dergisi 1995; 10:32-44.

21. Varni JW, Seid M, Rode CA. The PedsQL: measurement model for the Pediatric Quality of Life Inventory. Med Care 1999; 37:126-139.

22. Varni JW, Seid M, Kurtin PS. The PedsQLTM 4.0: reliability and validity of the Pediatric Quality of Life Inventory TM version 4.0 generic core scales in healthy and patient populations. Med Care 2001; 39:800-812.

23. Memik NC, Agaoglu B, Coskun A, Uneri OS, Karakaya I. The validity and reliability of the Turkish Pediatric Quality of Life Inventory for children 13-18 years old. Turk Psikiyatri Derg 2007; 18:353-363.

24. Memik NC , Agaoglu B, Coskun A, Uneri OS, Karakaya I. The validity and reliability of the Turkish pediatric quality of life inventory for children 8-12 years old. Turkish Journal of Child and Adolescent Mental Health 2008; 15:87-99.

25. Cohen L, Holliday M. Statistics for Social Scientist. London: Harper & Row, 1983; 69-75.

26. Altinkaynak S, Ertekin V, Arik A, Guraksin A. Diphtheria seroprevalence in children living in the eastern Turkey. East African Medical 2003; 80: 617-621.

27. Cohen J. Statistical Power Analysis for The Behavioral Sciences. Second ed., Hillsdale, NJ: Lawrence Erlbaum, 1988.

28. Ruggieri M, Incorpora G, Polizzi A, Parano E, Spina M, Pavone P. Low prevalence of neurologic and psychiatric manifestations in children with gluten sensitivity. J Pediatr 2008; 152:244-249.

29. Pynnönen PA, Isometsä ET, Aronen ET, Verkasalo MA, Savilahti E, Aalberg VA. Mental disorders in adolescents with celiac disease. Psychosomatics 2004; 45:325-335.

30. Potocki P, Hozvasz K. Psychiatric symptoms and coeliac disease. Psychiatr Pol 2002; 36:567-578.

31. Ciacci C, Iavarone A, Mazzacca G, De Rosa A. Depressive symptoms in adult coeliac disease. Scand J Gastroenterol 1998; 33:247-250.

32. Ljungman G, Myrdal U. Compliance in teenagers with coeliac disease - a Swedish follow-up study. Acta Paediatr 1993; 82:235-238.

33. Hernanz A, Polanco I. Plasma precursor amino acids of central nervous system monoamines in children with coeliac disease. Gut 1991; 32:1478-1481.

34. Pynnönen P, Isometsä E, Aalberg V, Verkasalo M, Savilahti E. Is coeliac disease prevalent among adolescent psychiatric patients? Acta Paediatr 2002; 91:657-659.

35. Kolsteren M, Koopman HM, Schalekamp G, Mearin ML. Health-related quality of life in children with celiac disease. J Pediatr 2001; 138:593-595.