ORIGINAL PAPERS

Adv Clin Exp Med 2009, **18**, 2, 153–158
ISSN 1230-025X

Barbara Iwańczak[1], Krystyna Mowszet[1], Ewa Waszczuk[2], Agata Szlachcic[1], Leszek Paradowski[2]

Clinical Differences of Celiac Disease in Schoolchildren and Adults

Odrębności kliniczne choroby trzewnej ujawniającej się u dzieci w wieku szkolnym i u pacjentów dorosłych

[1] Second Department of Pediatrics, Gastroenterology, and Nutrition, Wroclaw Medical University, Poland
[2] Department of Gastroenterology and Hepatology, Wroclaw Medical University, Poland

Abstract

Background. In recent decades an increase in newly diagnosed celiac disease in both schoolchildren and adults has been observed. Celiac disease is the most common genetically determined disease of the gastrointestinal system and is most frequently diagnosed in the first three years of life and between the ages of 44 and 64. Asymptomatic, silent, and late-onset celiac disease are the predominant forms.
Objectives. Analysis of the frequency of clinical symptoms and coexisting diseases in schoolchildren and adults with diagnosed celiac disease.
Material and Methods. The study comprised 59 children aged 7 to 18 years (mean: 12.5 years) and 52 adults aged 19 to 75 years (mean: 32 years) in whom celiac disease was diagnosed based on histological study of intestinal specimens and positive serologic tests (EmA, tTG). Clinical symptoms, nutritional status, and coexisting diseases were analyzed in all the patients.
Results. Low body mass (69.5%), abdominalgia (59.3%), recurrent diarrhea (39%), and anemia (28.8%) were most frequently observed in the children. The most frequent symptoms in the adults were anemia (80.7%), flatulence (76.9%), increased aminotransferase activity (AST and ALT, 73.1%), chronic diarrhea (59.6%), and low body mass (59.6%).
Conclusions. Deficiency in body mass and height as well as abdominal pains and recurrent diarrhea were the most frequent symptoms in the schoolchildren with celiac disease. In adults the most frequently observed were anemia, chronic diarrhea, flatulence, and increased AST and ALT activity as well as more frequent occurrence of diabetes mellitus, diseases of the thyroid gland, and osteoporosis (**Adv Clin Exp Med 2009, 18, 2, 153–158**).

Key words: celiac disease, children, adults, clinical differences.

Streszczenie

Wprowadzenie. W ostatnich dekadach zaobserwowano wzrost liczby rozpoznań choroby trzewnej u dzieci i dorosłych. Chorobę trzewną najczęściej rozpoznaje się w pierwszych trzech latach życia oraz w wieku 44–64 lat. W obrazie klinicznym choroby przeważają postacie skąpoobjawowe lub ukryte (*silent celiac disease*) oraz późno ujawniające się (*late-onset celiac disease*).
Cel pracy. Ocena porównawcza częstości występowania objawów chorobowych oraz chorób współistniejących u dzieci w wieku szkolnym i u dorosłych z rozpoznaną chorobą trzewną.
Materiał i metody. Analizą objęto 59 dzieci w wieku od 7 do 18 lat (średni wiek 12,5 lat) oraz 52 pacjentów dorosłych w wieku od 19 do 75 lat (średni wiek 32 lata), u których na podstawie wyniku badania histopatologicznego wycinków błony śluzowej jelita cienkiego oraz dodatnich testów serologicznych (tTG, EmA) rozpoznano chorobę trzewną. U pacjentów analizowano objawy chorobowe i stan odżywienia oraz choroby współistniejące.
Wyniki. U dzieci najczęściej obserwowano niedobór masy ciała i/lub wzrostu (69,5%), bóle brzucha (59,3%), nawracające biegunki (39%), niedokrwistość (28,8%). U pacjentów dorosłych najczęściej obserwowano niedokrwistość (80,7%), wzdęcia brzucha (76,9%), wzrost aktywności aminotransferaz AspAT, ALAT (73,1%), przewlekłe biegunki (59,6%) oraz niedobór masy ciała (59,6%).

Wnioski. Najczęstszymi objawami choroby trzewnej u dzieci w wieku szkolnym był niedobór masy ciała i wzrostu, bóle brzucha i nawracające biegunki. U pacjentów dorosłych najczęściej obserwowano: niedokrwistość, przewlekłą biegunkę, wzdęcia brzucha i wzrost aktywności AspA, ALAT oraz częstsze występowanie cukrzycy, chorób tarczycy i osteoporozy (**Adv Clin Exp Med 2009, 18, 2, 153–158**).

Słowa kluczowe: dzieci, dorośli, odrębności kliniczne, choroba trzewna.

Celiac disease is a gluten-dependent enteropathy caused by excessive immunological response of the organism to gluten in genetically predisposed subjects. Damage to and atrophy of the intestinal villi, hypertrophy of crypts, and increased numbers of intraepithelial lymphocytes occur in the course of the disease. Consequential disturbance of intestinal absorption and gastrointestinal symptoms in the classical form of the disease, atypical symptoms in the asymptomatic or silent forms, as well as latent and late-onset celiac disease are observed. In recent decades an increase in newly diagnosed cases of celiac disease in both schoolchildren and adults has been observed. This pertains mainly to the asymptomatic and silent forms of the disease, while the number of classical celiac cases has diminished. However, the great number of cases of celiac disease diagnosed too late is emphasized [1–3].

Based on numerous studies it is assumed that the frequency of celiac disease is 1:100 in the general European population and this increases in the high-risk group, which includes family members of celiac patients and persons with diabetes mellitus type 1, short stature, iron deficiency anemia, IgA deficiency, Down's syndrome, and others [4, 5]. Celiac disease is the most frequent genetically determined disease of the gastrointestinal system and is most frequently diagnosed in the first three years of life and between the ages of 44 and 64 [2, 4]. The aim of this study was an analysis of the frequency of clinical symptoms and coexisting diseases in schoolchildren and adults with diagnosed celiac disease.

Material and Methods

The study comprised 111 patients aged 7 to 75 years hospitalized in gastroenterology clinics for children and adults due to body mass and height deficiency, anemia, chronic abdominalgia, chronic diarrhea, or increased activity of aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The patients were divided into two groups. The first consisted of 59 children (38 girls and 31 boys) aged 7 to 18 years (mean: 12.5 years) and the second of 52 adult patients (41 women and 11 men) aged 19 to 75 years (mean: 32 years) treated in the clinics in the period of 2001–2007. In all patients, celiac disease was diagnosed based on histological study of intestinal specimens obtained during endoscopic examination and assessed according to the Marsh scale (grades III a, b, c) and elevated titers of antibodies against the endomysium of smooth muscles (EmA) and/or tissue transglutaminase (tTG) [1, 6–9].

For all patients a questionnaire was prepared which included symptoms of the disease, clinical laboratory deviations, and coexisting diseases. For the assessment of growth disturbances in the children, percentile scales according to Palczewaska and Niedźwiedzka [10] were used in which body mass and height below the 3rd percentile were regarded as deficient. In the adults the nutritional status was assessed based on the body mass index (BMI), where an index value below 16.9 was treated as moderate or severe malnutrition. The data were statistically analyzed by the chi-squared Pearson's test using Microsoft Excel and Statistica 6.0 packages. For four-field tables the Yates' correction or Fisher's exact test were used. Values of $p < 0.05$ were regarded as statistically significant.

Results

The numbers of patients according to age and sex are presented in Table 1, where it can be seen that celiac disease was diagnosed in females significantly more frequently than in males in both groups of patients. Table 2 presents the gastrointestinal symptoms. Chronic abdominalgia was the most frequent symptom in both groups and the difference in its frequency between the groups was not significant. Abdominal flatulence and chronic diarrhea in adults and recurrent diarrhea in children were among the other symptoms which occurred significantly more frequently. In some of the patients, lack of appetite (16.0% vs. 9.6% in groups 1 and 2) and sporadic vomiting (1.7% vs. 5.8%) were observed.

Body mass deficiency draws attention among the general symptoms in both the children and adults (Table 3). Disturbances of the menstrual cycle in women should be regarded as significantly frequent. Bone fractures were observed in 13.5% and tetany in 5.8% of the adult patients. In 13% of the children, emotional disturbances and worse school achievement were present.

Table 1. Number, age, and sex of the patients

Tabela 1. Liczba, wiek i płeć pacjentów

Group (Grupa)	Total (Ogółem)	Age – years (Wiek – lata)		Sex (Płeć)		*p*
		mean	range	females n (%)	males n (%)	
Group 1 – children (Grupa 1 – dzieci)	59	12.5	7–18	38 (64.4%)	21 (35.6%)	0.01
Group 2 – adults (Grupa 2 – dorośli)	52	32.0	19–75	41 (78.8%)	11 (21.2%)	0.001

n – number; *p* – level of statistical significance.

n – liczba; *p* – istotność statystyczna.

Table 2. Frequencies of gastrointestinal symptoms in the children with celiac disease

Tabela 2. Częstotliwość występowania objawów żołądkowo-jelitowych u dzieci z chorobą trzewną

Number (Lp.)	Name of symptom (Objaw)	Frequency (Częstotliwość)				*p*
		group 1 (n = 59)		group 2 (n = 52)		
		n	%	n	%	
1.	abdominalgia	35	59.3	34	65.4	ns
2.	flatulence	10	16.9	40	76.9	<0.001
3.	chronic diarrhea	0	0	31	59.6	<0.001
4.	recurrent diarrhea	23	39.0	11	21.1	0.03
5.	constipation	1	1.7	0	0	–
6.	vomiting	1	1.7	3	5.8	ns
7.	failure to thrive	10	16.9	5	9.6	ns
8.	recurrent stomatitis	0		3	5.8	ns

ns – not significant.

ns – nieistotne statystycznie.

Table 3. General symptoms of celiac disease in the children and adults

Tabela 3. Ogólne objawy choroby trzewnej u dzieci i dorosłych

Number (Lp.)	Name of symptom (Objaw)	Frequency (Częstotliwość)				*p*
		group 1 (n = 59)		group 2 (n = 52)		
		n	%	n	%	
1.	body mass and/or height deficiency	41	69.5	38	73.1	ns
2.	bone/vertebral column pain	2	3.4	bd		
3.	bone fractures in the past	1	1.7	7	13.5	ns
4.	retardation of sexual development	2	3.4	–	–	–
5.	menstrual cycle disturbances (17 girls aged 14–18 years and 41 women)	2/17	11.8	14/41	34.1	0.04
6.	emotional disturbances (pertains to 23 children assessed by a psychologist)	3/23	13.0	–	–	–
7.	tetany	0	0	3	5.8	–
8.	epileptic seizures	0	0	1	1.9	–

bd – lack of data.

bd – brak danych.

Table 4. Occurrence of coexisting diseases in celiac diseases

Tabela 4. Choroby współistniejące z chorobą trzewną

Number (Lp.)	Name of disease (Choroba)	Frequency (Częstotliwość)				*p*
		group 1 (n = 59)		group 2 (n = 52)		
		n	%	n	%	
1.	iron deficiency anemia	17	28.8	42	80.7	0.001
2.	increased aminotransferase activity	2	3.4	38	73.1	0001
3.	diabetes mellitus type 1	8	13.4	2	3.8	ns
4.	thyroid gland disorder	3	5.1	8	15.4	ns
5.	bronchial asthma	3	5.1	2	3.8	ns
6.	rash	1	1.7	5	9.6	ns
7.	atopic dermatitis	7	11.9	4	7.7	ns
8.	herpetiform dermatitis (Dühring's disease)	1	1.7	2	3.8	ns
9.	Down's syndrome	2	3.4	0	0	–
10.	autoimmune hepatitis	0	0	1	1.9	–
11.	psoriasis	0	0	2	3.8	ns
12.	Leśniowski-Crohn disease	1	1.7	0	0	–
13.	IgA deficiency	4	6.8			–

Among the coexisting diseases in adults, iron deficiency anemia (28.8% in children vs. 80.7% in adults) and increased activity of ALT and AST (3.4% vs. 73.1%) were statistically more frequent than in the children. Diabetes mellitus type 1 was diagnosed in 13.4% of the children and atopic dermatitis in 11.9%. Autoimmune thyroid gland inflammation was observed in 15.4% of the adults. Other immunological disorders were present in single cases.

Discussion

In the last decades, the clinical picture of celiac disease has changed in both children and adults. The frequency of the classical form of the disease, which manifests with steatorrhea, cachexia, a large distended abdomen, and edema, is decreasing and the number of atypical forms is increasing [11–20]. In a study comprising 131 newly diagnosed cases of celiac disease in Poland in the years 1990–2001 it was observed that the number of diagnosed cases of the classical form of celiac disease decreased by a factor of five, while the detection of atypical forms, silent and latent, increased by a factor of three. In the present authors' earlier study conducted in 2001–2006 in 109 children aged 8 months to 18 years, full-blown symptoms were observed in only five children under two years old [21]. In preschoolers and school-children, atypical symptoms of the disease, such as chronic abdominalgia, short stature, and deficiency of body mass, as well as anemia were observed. In adults the classical form of celiac disease or late-onset celiac disease is observed in single cases. In the present study the oldest patient was 75 years old and was admitted to the clinic in poor general condition with celiac disease with cachexia, general edema, abdominal ascites, hypoproteinemia, anemia, and dyselectrolytemia.

The increased severity of the symptoms of the disease and laboratory abnormalities in the adult patient group could be connected with the duration of the disease process. Full-blown enteropathic syndrome was also observed in two adult female patients in whom celiac disease was diagnosed during puerperium. Only in one adult patient was celiac disease diagnosed during childhood; she stopped adhering to a gluten-free diet while a university student and did not associate typical celiac symptoms with the earlier diagnosed disease. In the analyzed children aged 7 to 18 years, celiac disease had not been diagnosed earlier in any of them and the most frequent reason for referral to the clinic was deficit height and/or body mass or chronic abdominal pains. In the present study, celiac disease was significantly more frequently diagnosed in female patients, which is in accord with the findings of other authors [1, 15]. The most frequent symptoms of celiac disease in both groups, adults and children, were low body mass and chronic abdominalgia, and in adults also flatulence and chronic diarrhea. In Szaflarska-Szczepanik's study, among the most frequent symptoms in silent celiac disease were also low body mass and short stature, which occurred at similar rates, as well as chronic abdominal pain [15]. In the present study

only 30% of the children and 27% of the adults were properly nourished. Chronic diarrhea with loss of body mass and recurrent diarrhea were prominent among the symptoms in the adults, and from this study it can be inferred that this is a significant symptom indicative of celiac disease in this age group. In 34.1% of the woman, disturbances of the menstrual cycle were also observed. This may also influence fertility and this effect is more pronounced in women than in adolescent girls [22].

Of the concomitant diseases in the adults, hypochromic anemia (80.7%) and increased aminotransferase activity (73.1%) were very frequent. This may be indicative of the long-term disease process, since increased ALT and AST was observed in children in only 2 cases (3.4%) and anemia in 17 (28.8%). These results are close to those of other authors, who observed hypochromic anemia in 10–22% of children and 10–90% of adults. This was microcytic anemia due to iron deficiency [2, 6, 7, 11, 12, 15]. According to the American Gastroenterology Association (AGA), celiac disease may be the cause of unexplained hypochromic anemia in adult patients [20]. A similar frequency of celiac disease among patients with hypochromic anemia was observed in the European population [23].

In many reports a higher frequency of autoimmune disease among patients with celiac disease is stressed. More frequent occurrence of diabetes, autoimmune hepatitis, thyroiditis, Down's syndrome, Turner's syndrome, IgA deficiency, and others has been described [1, 3, 12, 24–26]. According to some studies, in 30% of celiac disease patients at least one autoimmune disease is present and the overall frequency of such diseases is 10 times higher than in whole population [3]. In the present study at least one autoimmune disease was present in 28.8% of the adults and 22% of the children. In the children, diabetes mellitus of type 1 was diagnosed the most frequently and in the adults thyreoiditis and other autoimmune diseases. In the course of celiac disease, malabsorption may lead to disturbances in bone mineralization in the form of osteopenia and osteoporosis [17, 28]. Symptoms of these disturbances may be bone pain, pain of the vertebral column, and more frequent fractures caused by slight injuries. Examination of mineral bone density by Krzesiek and Iwańczak [27] showed that 40.5% of children aged 5 to 17 years with celiac disease had decreased bone density. These changes were most often present in children with newly recognized disease. Decreased bone density correlated with the patients' nutritional status and with atrophy of the intestinal villi demonstrated in histological examination. In the present study, 13.5% of the patients with celiac disease reported bone fractures in the past which could be a result of low bone mineralization. In another study, very frequent osteoporosis and osteopenia in celiac disease in adults were observed [28]. Evaluation of mineral bone density, calcium metabolism, and parathyroid gland function in 20 adult patients with celiac disease (mean age: 47.5 ± 11.5 years) demonstrated osteopenia in 11 patients and in 7 patients osteoporosis of the lumbar spine, femoral neck, and the whole body. In adult patients with celiac disease a negative calcium balance and a secondary increase in parathyroid hormone (PTH) have been observed. According to the authors of the study, elimination of gluten from the diet was not sufficient for regression of these pathologies and the patients required supplementation of calcium and vitamin D [28, 29]. According to the AGA, celiac disease is diagnosed in 1.5 to 3% of patients with osteoporosis [11, 12].

Increased in ALT and AST activity was observed in 73.1% of the adults and 3.4% of the children with celiac disease. The difference was statistically significant. These results confirm those of other authors, according to whom aminotransferase activity may be increased in 32% of children with celiac disease [12, 20]. They also indicate that the number of patients with aminotransferase activity increases with the age of patient and the time of untreated disease.

This study shows differences in clinical symptoms between adults and schoolchildren with celiac disease. The most frequent symptoms among the children were body mass deficiency, short stature, abdominalgia, recurrent diarrhea, and anemia. In adults the most common were iron deficiency anemia, chronic diarrhea, flatulence, abdominalgia, and increased aminotransferase activity. Statistical differences between the adults and children were observed in the cases of flatulence, chronic and recurrent diarrhea, increased aminotransferase activity, and disturbances of the menstrual cycle. Diseases of the thyroid gland, rash, atopic dermatitis, Dühring's disease, bronchial asthma, and psoriasis were the most frequent among the coexisting diseases. These diseases were mostly observed in the adults, while in the children the most frequent was diabetes mellitus type 1. It was shown that the number of coexisting diseases and the frequency of some clinical symptoms increased with patient age.

References

[1] Guideline for the diagnosis and treatment of celiac disease in children. Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. J Ped Gastroent Nutr 2005, 40, 1–19.

[2] Rewers M: Epidemiology of celiac disease: what are the prevalence, incidence and progression of celiac disease. Gastroenterology 2005, 128, S47–S51.

[3] Green PHR: The many faces of celiac disease: clinical presentation of celiac disease in adult population. Gastroenterology 2005, 128, S74–S78.

[4] Dubè C, Rostom A, Sy R: The prevalence of celiac disease in average-risk and at-risk western European populations: A systemic review. Gastroenterology 2006, 128, 557–567.

[5] Catassi C, Fabiani E, Ratsch IM: The coeliac iceberg in Italy. A multicentre antigliadin antibodies screening for coeliac disease in school-age subject. Acta Paediatrica 1996, (suppl.) 412, 29–35.

[6] Marsh MN: Gluten major histocompatibility complex, and the small intestine. Gastroenterology 1992, 102, 330–354.

[7] Marsh MN, Crowe PT: Morphology of the mucosal lesion in gluten sensitivity. Bailleres Clin Gastroenterol 1995, 9, 273–293.

[8] Rostom A, Dubè C, Cranney A: The diagnostic accuracy of serologic tests for celiac disease: A systematic review. Gastroenterology 2005, 128, S36–S46.

[9] Matusiewicz K, Iwańczak B, Iwańczak F: Anti-tissue transglutaminase antibodies in dependence on villous atrophy in children with celiac disease. Gastroenterol Pol 2002, 9, 109–115.

[10] Palczewska I, Niedźwiecka Z: Percentile scale of somatic development of children and youngsters. Instytut Matki i Dziecka, Warsaw, 1999.

[11] O'Leary C, Wieneke P, Healy M: Celiac disease and the transition from childhood to adulthood: A 28-Year Follow-Up. Am J Gastroenterol 2004, 99, 2437–2441.

[12] Fasano A: Clinical presentation of celiac disease in the pediatric population. Gastroenterology 2005, 128, S68–S73.

[13] Dewar DH, Ciclitira PJ: Clinical features and diagnosis of celiac disease Gastroenterology 2005, 128, S19–S24.

[14] Green PHR, Stavropoulos SN, Panagi SG: Characteristics of adult celiac disease in the USA: results of a national survey. Am J Gastroenterol 2001, 96, 126–31.

[15] Szaflarska-Szczepanik A: Changing clinical picture of coeliac disease in children own investigation. Pediatr Pol 2003, 78, 45–51.

[16] Grzybowska-Chlebowczyk U, Woś H, Więcek S, Kajor M, Szymańska M, Staszewska-Kwak A, Piątkowska M, Gałka M: The contemporary clinical picture of the celiac disease in children. Pol Merk Lek 2005, 103, 49–53.

[17] Fasano A, Catasii C: Coeliac disease in children. Best Pract Res Clin Gastroenterol 2005, 19, 467-478.

[18] Green PHR: The many faces of celiac disease: Clinical presentation of celiac disease in the adult population. Gastroenterology, 2005, 12, 574–578.

[19] Ravikumara M, Tuthill DP, Jenkins HR: The changing clinical presentation of coeliac disease. Arch Dis Child 2006; 91, 969–971.

[20] AGA Institute medical position statement on diagnosis and management of celiac disease. Gastroenterology 2006, 131, 1977–1980.

[21] Mowszet K, Piasecka A, Reich M, Iwańczak B: Appearance of coeliac disease in childhood depending on feeding mode. Pediatr Współcz Gastroenterol Hepatol Żywienie Dziecka 2007, 9, 17–21.

[22] Waszczuk E, Homola W: Reproductive disorders and celiac disease. Adv Clin Exp Med 2006, 15, 6, 1093–1098.

[23] Urbanowicz A: Hematologic features in coeliac disease. Gastroenterol Pol 2008, 15, 115–118.

[24] Murray JA: Celiac disease in patients with an affected member, type 1 diabetes, iron-deficiency or osteoporosis? Gastroenterology 2005, 128, S52–S56.

[25] Rujner J, Piontek E, Breet Chruściel J: Prevalence of type 1 diabetes in children with celiac disease. Przegl Pediatr 1996, suppl. 1/3, 191–197.

[26] Waszczuk E, Kosiara M, Dobosz T, Paradowski L: Celiac disease and diabetes mellitus. Adv Clin Exp Med 2007, 16, 2, 297–301.

[27] Krzesiek E, Iwańczak B: Assessment of bone mineral density in children with celiac disease. Pol Merk Lek 2008, 24, 141, 219–226.

[28] Szymczak J, Bohdanowicz-Pawlak, Waszczuk E, Bednarek-Tupikowska G: Bone mineral density and secondary hyperparathyroidism in adult celiac diseases patients. Endokrynol Pol 2006, 56, 4, 676–677.

[29] Mora S, Barera G, Beccio S: A prospective, longitudinal study of the long-term effect of treatment on bone density in children with celiac disease. J Pediatr 2001, 139, 516–521.

Address for correspondence:

Barbara Iwańczak
Department of Pediatrics, Gastroenterology and Nutrition,
Wroclaw Medical University
M. Skłodowskiej-Curie 50/52
50-369 Wrocław
Poland
E-mail: barbara@iwanczak.com
Tel.: +48 71 733 12 50

Conflict of interest: None declared

Received: 13.01.2009
Revised: 9.02.2009
Accepted: 23.04.2009