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The Physical Development And Clinical Course Of Celiac Disease In Children Depending On Adherence To Diet Therapy

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Abstract: To assess the clinical features of the typical form of celiac disease and the physical development of children depending on adherence to a gluten-free diet.

Keywords: Celiac disease, gluten-free diet, children.

Introduction: Celiac disease is one of the most common autoimmune disorders worldwide, affecting approximately 1% of the population and involving not only the small intestine but also various organs of the endocrine and digestive systems (thyroid and pancreas, liver, stomach, and large intestine) [2,10]. Currently, three forms of intolerance to traditional cereal grains are distinguished, among which celiac disease is the most widely known. The clinical picture of celiac disease is characterized, in the active phase of the disease, by the development of protein-energy deficiency (PED) in most patients, caused by maldigestion and malabsorption syndromes. The typical form manifests with a malabsorption syndrome; in childhood, the disease leads to impaired physical, psychomotor, and sexual development [4].

Analysis of anthropometric indicators is an essential stage in the comprehensive assessment of children's health. According to the ESPGHAN 2020 guidelines, when a child presents with growth retardation, celiac disease must be excluded [2]. After establishing the diagnosis, dynamic assessment of anthropometric data—as key health indicators in children with celiac disease—is required at every specialist visit throughout the entire follow-up period. It has been shown that even with adherence to a gluten-free diet, disturbances in physical development may still occur [6].

To date, the only effective method for treating celiac disease is a gluten-free diet (GFD), which allows for normalization of the morphological and functional condition of the small intestine and elimination of the main clinical symptoms of the disease [5]. The GFD is effective in controlling the so-called "major" gastrointestinal symptoms of the typical form of celiac disease. As a rule, patients with celiac disease report a rapid improvement in their general condition after beginning the GFD. It is well established that children with celiac disease who adhere to a long-term gluten-free diet demonstrate normalization of anthropometric indicators. The GFD is still based on the principle of "allowed/not allowed," with little attention paid to the quality of nutrition. Analysis of the nutritional status of children with celiac disease has revealed hypovitaminosis (folic acid, vitamins D, E, B6, and B12) and mineral deficiencies (calcium, zinc, iron, copper). However, available data on nutritional disturbances in children mainly refer to the period of clinical manifestation and are quite limited for the remission period during long-term diet therapy. Insufficient intake of nutrients, as well as impaired intestinal absorption, directly affects children's physical development. Therefore, efforts are being made worldwide to optimize gluten-free nutrition. The frequency and severity of deficiency states decrease

when specialized gluten-free food products are used [5,7].

Aim of the study: To investigate the clinical features of the typical form of celiac disease and the physical development of children depending on adherence to a gluten-free diet.

METHODS

The study included 50 children aged 1 to 14 years who were newly diagnosed and hospitalized in the Gastroenterology Department of the Republican Specialized Scientific-Practical Medical Center of Pediatrics with the diagnosis of "celiac disease," established according to ESPGHAN clinical and laboratory criteria. All children in the main group had the typical form of the disease and had not followed a GFD prior to admission. Depending on the presence of the diagnosis and adherence to the gluten-free diet for 6–9 months, all patients were divided into two groups. Group 1 included 39 patients who strictly adhered to diet therapy, while Group 2 consisted of 11 children who only partially followed the GFD. All children were examined according to a unified research protocol, which included medical history collection, physical examination, and instrumental and laboratory diagnostic methods. During history taking, attention was paid to the health status of parents and close relatives: the presence of allergic background, chronic or hereditary diseases, and harmful habits. Parents were asked about the association between disease manifestation and the introduction of gluten-containing foods, the presence of unexplained anemia, short stature, unexplained abdominal bloating, constipation, or unstable stools. During the physical examination, attention was given to the general condition, presence of specific complaints, timing of symptom onset, the condition of internal organs and systems, and changes in stool characteristics. Serological testing was performed for all children, including measurement of IgA and IgG antibodies to tissue transglutaminase to confirm celiac disease. Antibody levels were determined in arbitrary units, with normal values <20 U/mL and measurable levels ranging from 2 to 200 U/mL.

Assessment of physical development was carried out according to the WHO standards (2006). The parameters evaluated included length/height-for-age, weight-for-age, and body mass index-for-age.

Statistical analysis was performed using the IBM SPSS Statistics 23 software package. For pairwise comparisons, Fisher's exact test and Student's t-test were used, with statistical significance (two-sided) set at $p<0.05$.

RESULTS

A total of 50 children with a newly diagnosed celiac disease who had not previously adhered to a GFD were observed. Clinical features and physical development were analyzed in three age categories. Among the examined children with celiac disease, 18 (36.0%) were aged 1 to 3 years; 23 (40%) were aged 4 to 7 years; and 10 (20.0%) were aged 8 to 14 years. Regarding gender distribution, the number of girls was 1.5 times higher than that of boys. Among children with celiac disease, the majority were between 1 and 3 years of age—18 (36.0%)—and between 4 and 7 years of age—23 (40%). This indicates an increased intake of gluten-containing foods in children's diets during this age period.

Analysis of the clinical manifestations of celiac disease revealed a wide variety of symptoms. One of the cardinal signs is abnormal stool characteristics in children—profuse, foul-smelling, pale or multicolored, loose, foamy or clay-like stools, difficult to wash off, occurring three or more times per day. Diarrhea, abdominal bloating, abdominal pain, decreased appetite, vomiting, weight loss or poor weight gain, and disturbances in neuropsychological status (irritability, aggressive behavior, restless sleep) were also noted, along with various manifestations of metabolic disorders.

Table 1. Clinical manifestations of celiac disease in children at admission according to age

Symptoms	1-3 years n=18		4-7 years n=22		8-14 years n=10		Total n=50	
	n	%	n	%	n	%	n	%
Abdominal pain	6	33,0	18	78,0	8	80,0	32	64,0
Foul-smelling mushy stool	3	16,67	8	36,7	2	20,0	13	26,0

Polyfecalia (frequent, bulky stools)	12	66,67	14	61,0	8	80,0	34	68,0
Abdominal bloating	8	44,4	9	40,9	3	30,0	20	40,0
Audible bowel sounds from a distance	12	55,5	18	78,2	9	90,0	39	78,0
Intermittent vomiting	18	100	19	86,2	7	70,0	44	88,0
Bone pain	6	33,3	7	31,8	4	40,0	17	34,0
Bone deformities	4	22,2	9	39,1	0	0	13	26,0
Polyvitaminosis	3	11,0	9	39,0	3	30,0	15	30,0
Recurrent aphthous stomatitis	7	38,8	14	60,8	3	30,0	24	48,0
Hair loss / Alopecia	8	44,4	12	52,0	4	40,0	24	48,0
Atopic dermatitis	6	33,3	10	43,4	2	20,0	18	36,0
Muscle weakness	8	44,4	18	78,2	5	50	31	62,0
Tearfulness / Crying tendency	7	38,8	12	52,0	3	30,0	22	44,0
Lethargy / Fatigue	6	33,3	11	47,8	2	20,0	19	38,0
Height-for-age SDS	16	88,9	12	52,7	3	30,0	31	62,0
• -1 SD	13	72,2	20	87,0	8	80,0	41	92,0
• -2 SD	4	22,22	6	27,27	14	14,0	24	48,0
• -3 SD	9	50	8	36,36	3	30	20	40,0
Short stature	3	16,7	2	9,09	1	10	6	12,0
Weight loss / Reduced body mass	0	0	4	18,8	8	80	12	24,0
Stool more than 3 times per day	17	94,4	8	36,7	1	10	26	52,0

As shown in Table 1, the leading clinical manifestations of the disease were symptoms of intestinal dyspepsia. The frequency of stools in children with celiac disease exceeded three times per day in 6 (33.0%) children aged 1–3 years, 18 (78.0%) aged 4–7 years, and 8 (80.0%) aged 8–14 years. Polyfecalia was one of the main symptoms observed, with profuse stools recorded in children aged 1–3 years—12 (55.5%), 4–7 years—18 (78.2%), and 8–14 years—9 (90.0%).

Abdominal pain, a primary symptom of celiac disease, was noted in children aged 1–3 years—6 (33.0%), 4–7 years—14 (61.0%), and 8–14 years—8 (80.0%), mainly located in the mesogastric region, which is characteristic of the disease. The intensity of pain typically increased several hours after meals or immediately before defecation. Abnormal stool characteristics were most frequently observed in children aged 4–7 years—19 (86.2%). Abdominal bloating was noted in all children aged 1–3 years—18 (100%), in 4–7 years—17 (65.2%), and in older children—7 (70.0%). Vomiting was more common in children aged 4–7 years—9 (39.1%)—and absent in the 8–14 age group.

Bone system involvement is a significant aspect of the clinical picture of celiac disease, often caused by disturbances in phosphorus-calcium metabolism. Symptoms included bone and joint pain, most often in the lower extremities, in 15 (30.0%) children, primarily aged 4–7 years—9 (39.0%). Clinically observable bone deformities (thoracic cage, lower limbs, skull) were most common in children aged 4–7 years—14 (60.8%). Polyvitaminosis, in its classical form, appears somewhat delayed and is accompanied by B-vitamin deficiencies, leading to glossitis, stomatitis, gingivitis, and malabsorption of fat-soluble vitamins A, D, E, K, with impaired skin trophicity such as dryness, scaling, and reduced turgor—observed in 24 (48.0%) children, most frequently in the 4–7-year age group—12 (52.0%). Recurrent aphthous stomatitis was recorded in 18 (36.0%) children. Hair loss, up to alopecia, was identified in 31 (62.0%) patients. Atopic dermatitis was diagnosed in every second child with typical celiac disease—22 (44.0%), $p<0.01$.

Neurological symptoms were observed in 31 (62.0%) children, most commonly presenting as tearfulness, muscle weakness, and lethargy.

Anthropometric indicators are key characteristics of nutritional status. Reduced body weight is a sensitive parameter responding to disease and nutritional deficiencies, representing a significant symptom of celiac disease and reflecting the severity of nutritional disorders. Assessment of physical development according to international criteria (Table 1) revealed abnormalities in both height and weight.

In addition to enteral syndrome, children with celiac disease exhibited impaired physical development. Children whose height/length and body weight relative to age fell within -2 SD to +2 SD were considered to have normal physical development. Values below -2 SD down to -3 SD, and above +2 SD up to +3 SD, were considered low and high, respectively, requiring attention to prevent malnutrition or obesity. Values below -3 SD and above +3 SD were classified as “abnormal,” representing extremely low or high height and weight. Nutritional status was assessed using BMI. A BMI below -3 SD was considered severe protein-energy malnutrition (PEM), between -3 SD and -2 SD as moderate PEM requiring urgent intervention, and between -2 SD and -1 SD as mild PEM risk, requiring ongoing monitoring. BMI values between -1 SD and +1 SD were considered normal.

Growth retardation was observed in all age groups. Weight loss occurred in 26 (52.0%) children, and stunted growth was found in 12 (24.0%) children ($p<0.001$). Reduced BMI was diagnosed in 26 (52.0%) children. Normal weight and height-for-age (SDS ±1.0) at diagnosis were observed in 24 (48.0%) children. Growth delay was noted in 11 (22.0%), short stature in 1 (2%), and weight loss in 14 (28.0%) children. Anthropometric analysis shows that children under 3 years primarily lose weight with minimal growth delay, with about half of them having height within average ranges. In children aged 4–7 years, slowed growth velocity with concurrent weight deficit becomes noticeable. In children aged 8–14 years, growth delay predominates over weight relative to height. Linear growth dynamics vary by age: growth retardation in the first three years is minor but progressively increases in children aged 4–7 years ($p<0.05$) and 8–14 years ($p<0.001$). This progressive slowing of growth despite decreasing diarrheal syndrome reflects not only malabsorption of macro- and micronutrients but also somatotropic deficiency and reduced thyroid hormone levels, leading to hypothyroidism.

Moderate protein-energy malnutrition (BMI -2 SD) was observed in one-third of children with the classical form—50.0%. Children with normal SDS prevailed in preschool and school age groups. Reduced BMI was diagnosed in 43.2%, with 16.2% low and 27.0% moderately reduced.

The only proven effective treatment for gluten intolerance is lifelong exclusion of gluten. In children on a GFD, bone mineralization improves, and bone resorption decreases. Children treated exclusively with a GFD maintain normal bone mineral density, while late diagnosis and dietary noncompliance reduce this

parameter. Despite strict adherence being the only treatment, in our study, noncompliance occurred. Good adherence was observed in 39 (78.0%) children, while poor adherence, associated with symptom recurrence and elevated specific antibodies, was noted in 11 (22.0%). Among these, frequent diet violations occurred in 5 (45.5%), occasional in 4 (36.0%), and single violations in 2 (18.0%) children. Based on this, we divided children into two groups: strict adherence to GFD—39 (78.0%) and partial adherence—11 (22.0%).

Significant difficulties in strictly adhering to a gluten-free diet (GFD) reported by parents included the child's unwillingness to follow the prescribed diet, the inability to maintain dietary compliance while attending kindergarten or school, and the challenge of identifying products containing hidden gluten.

Analysis of the disease's clinical course dynamics demonstrated that strict adherence to a GFD leads to a fairly rapid, though not always complete, alleviation of symptoms (Table 2). In particular, after 6 months of following a GFD, the frequency of gastrointestinal symptoms significantly decreased: stool abnormalities reduced by 3.6 times ($p<0.001$), vomiting by 9.8 times ($p<0.001$), abdominal pain by 3.8 times ($p<0.001$), abdominal distension was absent in the group adhering to the diet for 6 months, constipation decreased by 2.1 times ($p<0.001$), and polyfecalia decreased by 16.1 times ($p<0.001$).

The frequency of extraintestinal symptoms also decreased with the diet, but at a slower pace. Over time, these differences became even more pronounced. Extraintestinal symptoms—such as bone deformities, bone pain, muscle weakness, and hair loss—persisted in most children who only partially adhered to the GFD, although the intensity of these manifestations could be somewhat reduced. Normal growth indicators were observed in 41 (82.0%) children. Normal body weight was noted in 28 (56.0%) children. Growth retardation was detected in 9 (18.0%) children ($p<0.001$), and weight reduction in 22 (44.0%) children. Normal BMI values were observed in 30 (60.0%) children, while 20 (40.0%) children had BMI below the normal range.

Analysis of adherence to the gluten-free diet (GFD) demonstrated a significant improvement in physical development indicators, particularly in the group of children strictly adhering to the diet. Thus, adherence to a gluten-free diet (GFD) leads to a fairly rapid, although not always complete, alleviation of symptoms. At the same time, lapses in dietary compliance are accompanied by recurrence of gastrointestinal symptoms and persistence of extraintestinal manifestations of celiac disease. n addition to normalizing stool consistency in our patients, strict adherence to a gluten-free diet (GFD) led to the resolution of most gastrointestinal symptoms in the majority of children: abdominal bloating, abdominal pain, and vomiting disappeared, appetite improved, bone pain and fractures due to minor trauma ceased, and neurological symptoms became less pronounced. In children who only partially adhered to the GFD, these improvements were less pronounced, though still significantly better than before starting the diet.

Thus, improvement in the clinical course of celiac disease and physical development in children on a GFD demonstrated significant positive trends in the overwhelming majority of patients. This is attributable to strict adherence to the diet, which results in improved intestinal absorption and better micronutrient status.

CONCLUSIONS

In the typical form of the disease, diagnosis is most often verified at the age of 1–3 years. Dyspeptic disorders and disturbances in physical development are the most prominent clinical features. Strict adherence to a GFD for 6–12 months leads to rapid alleviation of gastrointestinal symptoms and positively affects anthropometric parameters. Partial adherence improves clinical manifestations, although they remain significantly lower than in the group of children on strict GFD; deviations in physical development persist. Adherence to strict GFD among children reaches 78.0% of patients.

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