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Vitamin and mineral deficiency in children newly diagnosed with celiac disease

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Background/aim: To establish the frequency of vitamin and mineral deficiency in children newly diagnosed with celiac disease.

Materials and methods: The files of patients diagnosed with celiac disease in our Pediatric Gastroenterology Clinic from June 2008 to June 2013 were reviewed retrospectively.

Results: A total of 52 pediatric patients diagnosed with celiac disease via serology and duodenal biopsy and who fulfilled the study criteria were enrolled in the study. The mean diagnosis age of the patients was 8.5 ± 3.9 years and 33 (63.5%) of the patients were female. Vitamin D, vitamin A, vitamin E, zinc, and iron deficiencies were determined in 27 (51.9%), 4 (7.7%), 7 (13.5%), 35 (67.3%), and 18 (34.6%) patients, respectively, at the time of diagnosis. Vitamin D deficiency was observed more frequently in patients with growth retardation at the time of application (P = 0.02).

Conclusion: Vitamin D, zinc, and iron deficiency are frequently observed in pediatric patients with celiac disease at the time of diagnosis. Therefore, serum vitamin D, zinc, and iron levels should be checked in all children diagnosed with celiac disease.

Key words: Celiac, iron, vitamin A, vitamin D, vitamin E, zinc

1. Introduction

Celiac disease is a chronic autoimmune disease that particularly affects the proximal small bowel (1). An autoimmune-mediated mechanism plays a part in the pathophysiology of the disease, and small bowel mucosal injury and malabsorption occur due to the hypersensitivity to gluten in prone individuals. Vitamin and mineral deficiency may also be seen depending upon malabsorption. Consequently, the clinical symptoms of the disease are not limited to the gastrointestinal system and may appear with a heterogeneous clinical spectrum involving the extraintestinal system. The typical symptoms of the disease include chronic diarrhea, abdominal distention, and growth retardation (2,3). However, the disease may also manifest itself with extraintestinal findings related to the hematologic, endocrine, and autoimmune systems. Anemia is the most frequently seen disorder in the hematologic system that often develops due to iron deficiency (4-9). Hypocalcemia and osteopenia may also occur due to vitamin D deficiency (10,11). No extensive study has been conducted regarding the vitamin and mineral deficiencies of pediatric patients diagnosed with celiac disease up to the present. Accordingly, it is the objective of this study to determine the frequency of vitamin A, D, and E deficiency, as well as zinc and mineral deficiencies, in pediatric patients diagnosed with celiac disease at the time of application to our clinic.

2. Materials and methods

The files of the patients diagnosed with celiac disease and followed in our Pediatric Gastroenterology, Hepatology, and Nutrition Clinic from June 2008 to June 2013 were reviewed retrospectively. Patients with complete file records and vitamin and mineral levels checked at the time of application were enrolled in the study. The demographic characteristics, complaints at the time of application, findings of duodenal biopsy, and serum 25 OH vitamin D, vitamin A, vitamin E, iron, and zinc levels of the patients were taken from the file records. The study was approved by the Ethics Committee of İnönü University (approval number 162/2013).

The diagnosis of celiac disease was established in accordance with the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition's guidelines

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for patients who were admitted to our clinic (12). The duodenal biopsy material obtained for the diagnosis was examined by experienced pathologists in this field. The severity of the histopathological findings identified in the biopsy material was determined in accordance with the Marsh classification as modified by Oberhuber et al. (13) in our clinic. Based on this classification, an increased number of intraepithelial lymphocytes (Marsh I) is inadequate for diagnosis. However, the presence of crypt hyperplasia and villous atrophy (Marsh III) in addition to the Marsh I lesion is enough to establish the diagnosis of celiac disease. Serum 25 OH vitamin D, vitamin E, vitamin A, iron, and zinc levels were checked in patients diagnosed with celiac disease in our clinic.

2.1. Definitions

2.1.1. Vitamin D deficiency

Defined as serum 25-OH vitamin D level of <20 mg/dL (14).

2.1.2. Vitamin A deficiency

Defined as serum vitamin A level of <20 μg/dL in patients <6 years old and <26 μg/dL in patients ≥6 years old (15).

2.1.3. Vitamin E deficiency

Defined as serum vitamin E level of <3 mg/L in patients <6 years old, <4.3 mg/L in patients 7–12 years old, and <5.6 mg/L in patients >12 years old (15).

2.1.4. Zinc deficiency

Defined as serum zinc level of <67 μg/dL in patients younger than 5 years old, <77 μg/dL in patients 6–9 years old, <76 μg/dL for male and <79 μg/dL for female patients 10–14 years old, and <64 μg/dL for male and <60 μg/dL for female patients >14 years old (15).

2.1.5. Iron deficiency

Defined as serum iron level of <22 μg/dL in patients younger than 5 years old, <39 μg/dL in patients 6–9 years old, <28 μg/dL for male and <45 μg/dL for female patients 10–14 years old, and <34 μg/dL for male and <28 μg/dL for female patients >14 years old (15).

2.2. Exclusion criteria

Patients with chronic liver disease, chronic kidney disease, hematologic diseases, vitamin D metabolism disorder, or inflammatory bowel disease were not enrolled in the study.

2.3. Data analysis

The statistical evaluation was performed using SPSS 15.0 for Windows (SPSS Inc., USA). The variables were provided in numbers and percentages for qualitative data and as means ± SD for quantitative data. The categorical data were compared by using a chi-square test. $P < 0.05$ was considered statistically significant.

3. Results

A total of 52 pediatric patients with celiac disease proven by duodenal biopsy and who fulfilled the study criteria were enrolled in the study. The mean diagnosis age of the patients was 8.5 ± 3.9 years and 33 (63.5%) of the patients were female. The most common complaints were abdominal pain and growth retardation (Table 1). Two patients (3.8%) presented with diabetes mellitus and 3 patients (5.7%) presented with gastritis. Vitamin D, vitamin A, vitamin E, zinc, and iron deficiency were determined in 27 (51.9%), 4 (7.7%), 7 (13.5%), 35 (67.3%), and 18 (34.6%) patients, respectively, at the time of diagnosis (Table 2). Vitamin D deficiency was observed more frequently in patients with growth retardation at the time of application ($P = 0.02$) (Table 3).

4. Discussion

Malabsorption is a common condition in patients presenting with the symptoms of classic celiac disease (16). Vitamin and mineral deficiencies may also be seen depending on malabsorption. The limited number of studies performed regarding the frequency of vitamin and mineral deficiencies in adult patients with celiac disease reported the frequency of vitamin and mineral deficiencies in varying rates up until now (11,14,17). A recent study

Table 1. Symptoms and signs of pediatric patients with newly diagnosed celiac disease at the time of application (n = 52).

Symptoms and signs	n (%)
Abdominal pain	30 (57.7)
Failure to thrive	28 (53.8)
Diarrhea	10 (19.2)
Anorexia	9 (17.3)
Abdominal distention	7 (13.5)
Vomiting	5 (9.6)
Constipation	4 (7.7)
Asymptomatic	2 (3.8)

Table 2. The frequency of vitamin A, E, D, zinc, and iron deficiency in pediatric patients with newly diagnosed celiac disease (n = 52).

Symptoms and signs	n (%)
Vitamin D deficiency	27 (51.9)
Vitamin A deficiency	4 (7.7)
Vitamin E deficiency	7 (13.5)
Zinc deficiency	35 (67.3)
Iron deficiency	18 (34.6)

Table 3. Association between the symptoms and signs of pediatric patients with newly diagnosed celiac disease and vitamin D deficiency (n = 52).

Variable	D vitamin ≤20 mg/dL	D vitamin >20 mg/dL	P
Failure to thrive	18 (72)	10 (37)	0.02
Abdominal pain	19 (70.4)	11 (44)	0.10
Diarrhea	5 (72)	5 (72)	1
Anorexia	4 (14.8)	5 (20)	0.72
Abdominal distention	2 (7.4)	5 (20)	0.24
Vomiting	4 (14.8)	1 (4)	0.35

performed by Wierdsma et al. (11) demonstrated the presence of at least one vitamin or mineral deficiency in 67% of patients newly diagnosed with celiac disease. Our particular study has revealed the presence of zinc deficiency in two-thirds of the patients with celiac disease at the time of diagnosis and vitamin D deficiency in more than half.

Patients with celiac disease experience metabolic bone diseases, including osteoporosis, osteopenia, and bone fractures (10,17–21). There are several factors that affect the development of metabolic bone disease in patients with celiac disease. Villous atrophy developing in the proximal portion of the small bowel under the influence of the disease affects the absorption of active calcium. Additionally, intraluminal fatty acids are increased due to malabsorption and bind calcium. The amount of vitamin D-dependent calcium-binding protein is reduced on the intestinal wall during the active disease period (22). As a result, calcium absorption declines. In patients with celiac disease, low levels of vitamin D based on malabsorption is another reason for the development of metabolic bone disease. Therefore, early identification and treatment of vitamin D deficiency will prevent the development of metabolic bone disease in patients with celiac disease. Vitamin D deficiency was identified in more than half of the patients in our study. Tavakkoli et al. (14) reported vitamin D deficiency in 25% and vitamin D insufficiency in 34% of patients with celiac disease. Therefore, all patients should be evaluated for vitamin D deficiency at the time of diagnosis.

Fat-soluble vitamins A and E can be stored in the body. That is why vitamin A and E deficiencies are rarely seen in healthy individuals, even if these vitamins are not taken daily. However, vitamin A and E deficiency can be seen in celiac patients (23,24). We determined that 7.7% and 13.5% of patients with celiac disease presented with vitamin A deficiency and vitamin E deficiency, respectively, at the time of application. Similarly, Wierdsma et al. (11) reported vitamin A deficiency in 7.5% of adult patients newly diagnosed with celiac disease. Hozyasz et al. (25) investigated red blood cell tocopherol levels in 18 patients diagnosed with untreated celiac disease and reported lower than normal levels of tocopherol in all of the patients.

Anemia is one of the most common extraintestinal symptoms in patients with celiac disease and it is often related with iron deficiency. The frequency of iron deficiency anemia varies from 12% to 69% in patients with celiac disease (4–9). We have also determined low serum iron levels in one-third of the patients. Similarly, Harper et al. (26) examined the serum iron levels of 405 patients with celiac disease. Iron deficiency was reported in 33% of male patients and in 19% of female patients.

Zinc deficiency in patients with celiac disease is considered as being related with endogenous loss, rather than malabsorption (27). Several skin lesions are possible in zinc deficiency. The dermatological findings encountered in celiac disease may partially be associated with zinc deficiency. Our study has revealed zinc deficiency in two-thirds of the patients at the time of diagnosis. Likewise, Wierdsma et al. (11) previously reported zinc deficiency in 67% of adult patients with celiac disease.

Our study had a few limitations. First, the study was retrospective in nature and patients with incomplete file records were excluded from the study. The second limitation was that no control group consisting of healthy children of the same age was used in the study.

In conclusion, vitamin D deficiency and low levels of serum zinc and iron are substantially frequent in pediatric patients with celiac disease. Therefore, serum vitamin D, zinc, and iron levels should be checked in all children diagnosed with celiac disease.

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