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BRIEF REPORT

Assessment of iron status and iron deficiency anemia in patients with celiac, a single center experience

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ABSTRACT

Aim: This study aimed to assess the status of iron stores and the frequency of iron deficiency anemia in Celiac disease (CD) patients referred to the Golestan Research Center of Gastroenterology and Hepatology, Gorgan, Iran.

Background: Studies have shown that nutritional deficiencies affect 20-38% of patients with CD due to malabsorption and as a result of a gluten-free diet.

Methods: In this study, 59 out of 100 CD patients were assessed. The presence and severity of anemia were determined using the concentration of serum hemoglobin according to WHO criteria. The status of body iron stores was also assessed based on serum ferritin levels.

Results: Mean and SD of age, duration of disease, serum hemoglobin, ferritin, TIBC, and serum iron were 39.9±11.9 years, 69.8±45.4 months, 12.6±1.99 g/dl, 54.3±55.3 mg/dL, 365.9±49.1 µg/dL, and 84.1±37.1 µg/dL, respectively. 68.42% had no anemia, 19.3% had mild anemia, 8.77% had moderate anemia, and 3.51% had severe anemia. 25.42% of patients had depleted iron stores, 71.19% had normal iron stores, and 3.39% were exposed to iron overload. There was a statistically significant correlation between serum hemoglobin and the duration of disease diagnosis (P=0.037, r=0.302).

Conclusion: In this study, 31.58% of CD patients on a gluten-free diet had some degree of anemia. In addition, 25.42% of patients had depleted iron stores. These results suggest that CD patients should be evaluated for iron status, even with a gluten-free diet.

Keywords: Celiac disease, Iron deficiencies, Anemia, Iron-deficiency, Ferritins, Diet, Gluten-free, Nutrition assessment.

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Introduction

Celiac disease (CD) is a type of enteropathy with a systemic disorder that is mediated by the immune system and occurs during contact with gluten with intestinal mucosa in genetically predisposed individuals. It is characterized by a wide range of gastrointestinal and systemic clinical signs and varying degrees of damage to the small intestinal mucosa (1, 2). Currently, the only known treatment for controlling the symptoms and complications of this disease is a gluten-free diet (2).

Untreated CD is associated with an increased risk of many complications associated with the impaired nutritional status of patients (3-6). Studies have shown that nutritional deficiencies affect 20-38% of these patients (7-11). Nutritional deficiencies in celiac disease may be due to malabsorption due to the intestinal effects of the disease or as a result of a gluten-free diet (GFD). The severity of these deficiencies may be influenced by the time elapsed before the CD diagnosis or treatment, the location and extent of small bowel injury, and the degree of

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malabsorption (11, 12). Some studies have reported that GFD may also cause nutritional imbalances and some micronutrient deficiencies (11).

Anemia, which occurs in 5 to 40 percent of patients in the West and more than 80 percent of patients in developing countries, is one of the most common extraintestinal manifestations of CD. Although studies have shown that anemia in CD is multifactorial (nutritional or non-nutritional) (13, 14), in a study in which 93% of patients with CD had anemia, the most common cause was iron deficiency (81.5%) (15). Nutritional anemia can occur for a variety of reasons, including iron deficiency, B12 or folic acid deficiency, or even copper and zinc deficiency, although the most common causes of nutritional anemia are iron, folic acid, and vitamin B12 deficiency (13).

There is a relationship between the severity of anemia and the severity of villi atrophy. In this regard, studies have shown that even after the healing of the small intestinal mucosa, the recovery of iron stores may take a relatively long time. Thus, iron deficiency may be an important nutritional problem in CD patients (2, 15). In addition, although mandatory wheat flour fortification has been applied on a global scale, these rules do not apply to gluten-free flour. This means that the risk of iron deficiency is higher in patients with celiac disease (16).

This study aimed to assess the status of iron stores and the frequency of iron deficiency anemia in patients with celiac disease referred to the Golestan Research Center of Gastroenterology and Hepatology, Gorgan, Iran.

Methods

In this analytical cross-sectional study, 59 out of 100 referred patients with a definite diagnosis of celiac disease (based on biopsy and serological tests) to the Gastroenterology and Liver Research Center of Golestan University of Medical Sciences located in Sayyad Shirazi Hospital in Gorgan in 2020 were entered into the study.

One ml of blood containing anticoagulant and 5 ml of blood in a tube without anticoagulation were taken from all patients, and after half an hour of incubation at 37 ° C, serum was isolated using a centrifuge and was maintained until tests at -70 ° C. Blood containing anticoagulants was used for the CBC test. The tests were performed using a laboratory kit according to the kit instructions in the Kavosh laboratory.

The presence and severity of anemia were determined using the concentration of serum hemoglobin according to the criteria of the World Health Organization (17). In addition, the status of body iron stores was assessed based on serum ferritin levels and according to the criteria of the World Health Organization (18). Data analysis was performed descriptively using STATA.15 software.

This study was performed after approval by the

Table 1. Comparison of age, disease duration, hemoglobin, ferritin, TIBC, and serum iron between men and women with celiac disease (n=57)

		Mean	SD	Min	Max	P-value
Age	Women	36.5	10.3	16	63	0.046
	Men	43.1	13.5	16	66	
	Total	39	11.9	16	66	
Duration of disease	Women	56.3	37.1	10	181	0.009
	Men	90	50.1	20	192	
	Total	69.8	45.4	10	192	
Hemoglobin	Women	11.91	1.9	5	14.3	0.0002
	Men	13.92	1.46	10.6	16	
	Total	12.6	1.99	5	16	
Ferritin	Women	54	62.9	1.5	296	0.964
	Men	54.7	39.6	2.57	170	
	Total	54.3	55.3	1.5	296	
TIBC	Women	363.1	48.9	276	464	0.605
	Men	370.1	50.3	284	505	
	Total	365.9	49.1	276	505	
Serum Iron	Women	74.1	35.1	17	179	0.005
	Men	101.9	34.4	34	197	
	Total	84.1	37.1	17	197	

TIBC: total iron-binding capacity

ethics committee of Golestan University of Medical Sciences (ethic code: IR.GOUMS.REC.1399.246). Study details were described for all the patients and informed written consent was taken before entering the study.

Results

Mean and standard deviation (SD) of age, duration of disease, serum hemoglobin, ferritin, TIBC, and serum iron were 39.9±11.9 years, 69.8±45.4 months, 12.6±1.99 g/dl, 54.3±55.3 mg/dL, 365.9±49.1 µg/dL, and 84.1±37.1 µg/dL, respectively. The difference between age, duration of disease, serum hemoglobin, and serum iron in men and women was statistically significant, but there was no statistically significant difference between men and women in terms of ferritin and TIBC levels (Table 1).

According to the WHO criteria (17), out of 57 patients for whom hemoglobin level information was available, 68.42% (39 patients) had no anemia, 19.3% (11 patients) had mild anemia, 8.77% (5 patients) had moderate anemia, and 3.51% (2 patients) had severe anemia. There was no statistically significant difference between men and women in terms of the severity of anemia (Table 2).

Categorizing disease duration in three sections was performed based on 25 (36 months), 50 (55 months), and 75 (93 months) percentiles. There was no statistically significant difference between the rate and degree of anemia in the mentioned age categories (P=0.427).

According to the WHO criteria (18), 25.42% of patients (15 patients) had depleted iron stores, 71.19% of patients (42 patients) had normal iron stores, and 3.39% of patients (2 patients) were exposed to iron overload. There was no statistically significant difference between men and women in terms of iron stores (P=0.233).

Although there was no statistical correlation between age and serum hemoglobin level, there was a statistically significant correlation between serum hemoglobin and the duration of disease diagnosis (P=0.037, r=0.302).

Discussion

The results of this study showed that 31.58% of CD patients on a gluten-free diet had some degree of anemia. In addition, 25.42% of patients had depleted iron stores. Although the accurate interpretation of ferritin levels to assess iron stores requires simultaneous examination of inflammatory markers, the present study was performed in patients on a gluten-free diet, although the adherence to the diet and clinical or serological and histological symptoms was not evaluated.

In a study of newly diagnosed CD patients in the Netherlands, 80 patients with a mean age of 42.8 years were studied. Serum levels of folic acid, vitamin B12, hemoglobin, and ferritin were measured. Twenty percent of the patients were vitamin B9 deficient, 19% were vitamin B12 deficient, 46.2% were deficient in iron stores, and 32.4% had iron deficiency anemia (5). In another study, 39 newly diagnosed CD patients (32 females and 7 males) with a mean age of 48 years were evaluated for some nutrients. 41% of patients had B12 deficiency, 31% had folate deficiency and 41% had anemia. In addition, serum vitamin B12 levels returned to normal without supplementation and over 4 months after starting a gluten-free diet (4).

Anemia is associated with iron deficiency, often due to increased blood loss, or impaired iron absorption. Iron deficiency anemia is more common in patients with CD who have recently been diagnosed (19, 20) and may persist for varying periods after starting a gluten-free diet (15). Iron deficiency anemia in children and adults may also be a clinical feature of CD and even the only finding (21, 22). Although accurate epidemiological data on iron deficiency in CD are limited, some recent studies indicate that iron deficiency is significant in both children (23) and adults

Table 2. Comparison of anemia regarding gender (n=57)

	Women	Men	Total
Without anemia	25	14	39
Mild anemia	7	4	11
Moderate anemia	4	1	5
Severe anemia	2	0	2
P-value			0.833

(24) with celiac disease. As shown in the present study, about a quarter of patients had depleted iron stores, which indicates that these patients need a periodic evaluation of iron status not only at the beginning of diagnosis but also when they are on a gluten-free diet. However, studies show that iron deficiency may still occur despite iron supplementation (25).

Studies have shown that the mRNA of the DMT1 receptor, ferroportin, hephaestin, and transferrin increased in people with CD compared to healthy controls while the body's iron stores decreased in celiac disease. These iron-regulating proteins are also enhanced by iron deficiency (not related to celiac disease), indicating that the re-regulation of iron absorption capacity that appears to occur in CD is primarily due to iron deficiency (26). In contrast, a recent study found that DMT1 and ferroportin mRNA expression increased in celiac disease with or without iron deficiency. In addition, ferritin mRNA expression in celiac disease increases only in those with iron deficiency (27).

The diagnosis of iron deficiency anemia in CD, even considering its high prevalence, should be made after careful consideration of other common causes such as colon cancer (21). In addition to malabsorption problems caused by the disease, in some studies, gastrointestinal occult bleeding has been reported as a cause of iron deficiency anemia in celiac disease (28).

There were two limitations in this study. First, 41 out of 100 registered patients declined to participate. Second, the sample size of the study is low.

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Conflict of interests

The authors declare that they have no competing interests.

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