

Original Research Article

Frequency of celiac disease in patients with vitiligo

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ABSTRACT

Background: Celiac disease (CD) is an autoimmune and inflammatory disease that occurs in the small intestine as a result of gluten intake in individuals. Vitiligo, in which autoimmune factors play an essential role, is associated with depigmentation due to the loss of epidermal melanocytes. Many autoimmune diseases are known to be associated with vitiligo. This study aims to determine the frequency of CD in vitiligo cases.

Methods: Out of 61 vitiligo patients, 32 (52.4%) are women, and 29 (47.6%) are men; of the 119 healthy volunteers, 58 (48.7%) are women, and 61 (51.3%) are men. Serum levels of tissue transglutaminase (tTG) IgA and tTG IgG antibodies were measured in all participants. If at least one of these two antibodies are positive, mucosal biopsies were taken from the second section of the duodenum by endoscopy.

Results: There is no significant difference between the study group and the control group in terms of age and body mass index (BMI) ($p=0.16$, $p=0.80$, respectively). tTG IgA and tTG IgG were positive in one patient in each group. In both patients, the results of the duodenal biopsy were histopathological compatible with CD. There was no difference between the vitiligo group and the control group in terms of CD frequency ($p=0.56$).

Conclusion: The frequency of CD in vitiligo patients is similar to the control group. However, it should be kept in mind that the frequency of CD in patients with vitiligo may be higher than the rates assumed incidental, and necessary research should be carried out for early diagnosis in such patients.

Keywords: CD, Vitiligo, Prevalence

INTRODUCTION

CD occurs as a result of intolerance to gluten in cereals such as wheat, barley, oats and rye. The disease progresses with characteristic histopathological findings such as inflammation in small intestine and villus atrophy, and recovery is observed with a gluten-free diet.¹ In most of the CD cases, patients are asymptomatic, or the disease progresses with minor symptoms, and these patients are often undiagnosed. Accordingly, true prevalence of disease in community is unknown.²⁻⁵ The prevalence of the disease in a screening study conducted with healthy blood donors in Turkey was found to be 1.3%.⁶ In a screening study conducted in European countries, a high prevalence was observed between 1/80-1/300 in both healthy children and adults.⁷⁻¹⁰

The use of serological tests with high specificity and sensitivity is beneficial in detecting atypical patients. The most commonly used serological screening tests are based on tTG antibodies (IgA and IgG) and anti-endomysial (EMA) antibodies. The sensitivity and specificity of tTG antibody assays are above 95%, while anti-endomysial (EMA) antibody assays have 100% sensitivity and specificity.^{5,11} There are also reports claiming that the sensitivity of tTG antibodies is somewhat higher than that of anti-endomysial antibodies.¹² The definitive diagnosis of CD is made by duodenal or jejunal biopsy.^{1,11}

In the classic form of CD, diarrhea, abdominal pain, iron, folate, calcium, and vitamin D deficiency, and weight loss are observed. However, it can also be presented by

the presence of a wide variety of extraintestinal manifestations, including anemia, persistent hypertransaminasemia, osteopenia, neurological-psychiatric disorders, signs of hyposplenism, and autoimmune diseases. In some studies, published in recent years, it is stated that there may be skin diseases among extraintestinal findings of CD.¹³ The most well-known and proven one among these skin diseases is dermatitis herpetiformis.¹⁴ According to several case reports, CD serological markers and/or improvement with a gluten-free diet are observed in conditions such as alopecia areata, dermatomyositis, and cutaneous vasculitis. There are also sporadic cases showing that CD is associated with diseases such as vitiligo, IgA dermatosis, lupus erythematosus, and lichen sclerosis.¹⁵

Vitiligo is an acquired depigmentation disease. White macules and patches of various sizes and forms are observed on the skin, and melanocytes are not present in these areas. The spread of the disease can be symmetrical or segmental. Although the cause of pigment cell damage is not fully known, autoimmunity is thought to play a role in the pathogenesis of vitiligo, as it is seen with diseases such as thyroiditis, Addison's disease, pernicious anemia, and diabetes mellitus.^{16,17} The existence of the relationship between vitiligo and gluten intolerance remains controversial.¹⁵ In a study conducted with vitiligo patients, no correlation was found between these two immunological disorders according to serological tests for CD; however, the presence of vitiligo in CD patients has been reported in some studies. According to these data, sporadic cases should be considered.¹³ Both CD and vitiligo are autoimmune diseases. There are few studies in the literature regarding the relationship between these two diseases, and their results are also controversial.^{13,18-20} In this study, aimed to determine the frequency of CD in vitiligo patients.

METHODS

Sixty-one patients (32 females, 29 males) who were admitted to the Kırıkkale University Faculty of Medicine outpatient dermatology clinics between May 2009 and March 2010 were included in the study. One hundred nineteen blood donors (58 females, 61 males) were selected as the control group. Necessary information was provided to all participants in the patient and control groups, written and verbal consent was obtained from all participants. This study was approved by the decision of Kırıkkale university faculty of medicine ethics committee dated 11.05.2009 and numbered 2009/074.

Inclusion criteria included the characteristics of the patients in the study were as: diagnosed with vitiligo, who are informed about the study and consent to the study, who have not previously been diagnosed with CD, without medical examination for CD, without any malignancies and patients between the age of 16-80.

Exclusion criteria included the patients who are not with the characteristics were: under the age of 16, over 80 years old, previously diagnosed with CD, previously investigated with CD pre-diagnosis, pregnancy, malignancies and who do not agree to participate in the study.

The cases were questioned in terms of weakness, weight loss, nausea, vomiting, diarrhoea, constipation, bloating, abdominal pain, family history of similar illness, and other chronic diseases. Body mass indexes (kg/m²) were calculated by measuring body weight and height.

In the patient group and control group, venous blood samples were taken from all individuals following fasting for at least 10 hours. These samples were tested with the enzyme-linked immunosorbent assay (ELISA) method, using the μ -Quant Biotec instruments spectrophotometer and E1x50 auto strip washer devices, with Immco Diagnostic Inc. Immu Lisa anti hum tTG IgA and Immu Lisa anti hum tTG IgG antibody-ELISA test kits. For both antibodies, values above 25 IU/ml considered positive. In patients with positive serum tTG IgG and negative tTG IgA, serum IgA level was also measured to detect IgA deficiency.

In cases where at least one of the anti-tTG IgA and anti-tTG IgG antibodies is positive, the upper gastrointestinal system endoscopy was performed with Fujinon EG-450 HR video endoscope. At least three biopsy samples were taken from the second section of the duodenum. All histological examinations were performed by a single pathologist in KU faculty of medicine pathology department, and biopsy samples were classified according to the modified Marsh classification. Patients diagnosed with CD were treated and followed up in the gastroenterology outpatient clinic.

Statistical Analysis carried out with SPSS 10.0 for windows software. Age and BMI averages were compared between the patient group and the control group using the t-test method. Frequency comparisons of tTG IgA, tTG IgG, and CD between the patient and control groups were performed with the chi-square test. $P \leq 0.05$ were considered statistically significant.

RESULTS

The demographic characteristics of the patient and control groups are given in Table 1. There were 32 females (52.5%), and 29 males (47.5%) in the patient group and 58 females (48.7%) and 61 males (51.3%) in the control group (Table 1). There is no difference between the two groups in terms of gender ($p=0.64$).

The age and BMI of the individuals included in the study are given in Table 1 as mean and standard deviation (SD). The mean age of the vitiligo group is 34.63 ± 13.28 years, and the mean BMI is 25.88 ± 4.65 ; the mean age of the control group is 37.20 ± 7.22 years, and the mean BMI

is 25.69 ± 4.64 . There is no difference between the vitiligo group and the control group in terms of age and BMI (respectively, $p=0.16$, $p=0.8$).

Table 1: Age and BMI of the study participants.

Variables	Vitiligo group (mean \pm SD)	Control group (mean \pm SD)	P
Gender (F/M)	32/29	58/61	0.64
Age (years)	34.63 ± 13.28	37.20 ± 7.22	0.16
BMI (kg/m²)	25.88 ± 4.65	25.69 ± 4.64	0.80

In the vitiligo group, two patients (3.2%) have type 1 DM, four patients (6.5%) have type 2 DM, 17 patients (27.8%) have autoimmune thyroiditis, one patient (1.6%) has both type 2 DM and autoimmune thyroiditis, and one patient (1.6%) has polyglandular syndrome (Table 2).

Table 2: Other accompanying diseases of patients in the vitiligo group.

Diseases	No. of patients	Percentage (%)
Type 1 DM	2	3.2
Type 2 DM	4	6.5
Thyroiditis	17	27.8
PGS	1	1.6

Both tTG IgA and tTG IgG antibodies were positive in one female patient (1.63%) in the vitiligo group; similarly, both tTG IgA and tTG IgG antibodies were positive in one female participant (0.84%) in the control group. There was no significant difference between the two groups in terms of tTG IgA and tTG IgG antibody positivity ($p=0.56$ for both tTG IgA and tTG IgG antibodies) (Table 3).

Table 3: tTG IgA and tTG IgG antibodies.

Antibodies	Vitiligo group	Control group	P
tTG IgA/tTG IgG antibodies	1/61 (1.63)	1/119 (0.84)	0.56

In the duodenal biopsy of the tTG antibody-positive patient in the vitiligo group, results were consistent with CD (Marsh IIIb). Similarly, the duodenal biopsy findings of the tTG antibody-positive participant in the control group were also consistent with CD (Marsh I). There was no difference between the vitiligo group and the control group in terms of CD frequency ($p=0.56$).

DISCUSSION

In this study, investigated the frequency of CD in patients with vitiligo and the frequency of CD was found to be

1.63%, which is similar to the control group ($p=0.56$). Because CD is mostly atypical, attention has been focused on extraintestinal signs and symptoms of CD in recent years. In some studies, published recently, it is stated that there may be skin diseases among extraintestinal findings of CD.¹³ The most well-known and proven one among these skin diseases is dermatitis herpetiformis.¹⁴ According to several case reports, CD serological markers and/or improvement with a gluten-free diet are observed in conditions such as alopecia areata, dermatomyositis, and cutaneous vasculitis. There are also sporadic cases showing that CD is associated with diseases such as vitiligo, IgA dermatosis, lupus erythematosus, and lichen sclerosus.^{15,21} There are also studies showing the relationship between autoimmune diseases and CD. Early diagnosis is important due to increased malignancy and mortality in CD.²²

Vitiligo is an acquired depigmentation disease. Although the cause of pigment cell damage is not fully known, autoimmunity is thought to play a role in the pathogenesis of vitiligo, as it is seen with diseases such as thyroiditis, Addison's disease, pernicious anemia, and diabetes mellitus.^{16,17} The existence of the relationship between vitiligo and gluten intolerance remains controversial.¹⁵

Although some patients with CD have vitiligo disease, in a study investigating the serological markers of CD in patients with vitiligo, no correlation was found between these two immunological diseases.¹⁹ Therefore, it was emphasized that cases with CD could be coincidental.¹³

Petaros et al investigated autoimmune diseases in 125 Italian children with CD. According to this study, dermatitis herpetiformis in 4 cases, autoimmune hepatitis in 2 cases, psoriasis in 1 case, vitiligo in 1 case, and lichen sclerosus in 1 case were detected. In relatives of the same patient group consisting of 1352 people, vitiligo was detected in 2 people. When the CD group and the control group were compared in terms of autoimmune diseases, the difference was shown to be statistically significant.¹⁸

In another study investigating autoimmunity and CD and involving 57 celiac patients, thyrotoxicosis in 3 patients, Type 1 DM in 2 patients, fibrosing alveolitis in 3 patients, vitiligo in one patient, rheumatoid arthritis in one patient and cryptogenic cirrhosis in one patient were detected.^{23,24}

In a study conducted in Turkey, 55 pediatric patients with CD (ages ranged from 2 to 19) were investigated, and five patients (9.1%) were diagnosed with vitiligo.²⁵ Due to the existing relationship between vitiligo and autoimmune diseases, attention is drawn to the consideration of autoimmunity theory and genetic linkage. Similar to this study, in another study conducted in our country, the vitiligo group comprised of 80 patients and a control group consisting of 88 people were

compared in terms of CD frequency. IgA-tTG and IgA EMA values were found high in one patient in both the study group and the control group. There was no statistical difference between the two groups in terms of IgA-tTG and IgA EMA values. These two cases with abnormal serological test results were evaluated endoscopically, and CD in the patient in the vitiligo group was diagnosed after the intestinal biopsy, in contrast, the biopsy result in the patient in the control group was negative. As a result, it was shown in the study that there is no significant relationship between vitiligo and CD; however, there are few studies conducted in the literature with different populations, and similar results are obtained. Also, it should be taken into consideration that the study includes the control group.^{17,21}

In this study, where we investigated the frequency of CD in 61 patients with vitiligo disease, we found CD in one patient (1.63%). Although the number of cases in our study is small, the frequency of CD that we found in patients with vitiligo is compatible with the literature.

The frequency of CD in vitiligo patients was similar to the control group. Although the sample size in our study is small, it should be taken into consideration that the frequency of CD in vitiligo patients may be higher compared to the incidental CD cases in society. Due to the importance of early diagnosis, it will be appropriate to investigate CD in such cases.

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