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**Columns:** **PROSPECTIVE STUDY**

**Seroprevalence of celiac disease among United Arab Emirates healthy adult nationals: A gender disparity**

Abu-Zeid YA *et al*. Seroprevalence of CD among Emiratis

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**Abstract:**

**AIM:** To determine the celiac disease (CD) prevalence and associated manifestations or risk factors in healthy adult Emiratis.

**METHODS**: It is a cross-sectional prospective study, recruiting 1197 (573 women and 624 men) of healthy Emiratis between September 2007 and April 2008 among those who went to Al Ain Hospital to undertake the prenuptial examination. Test for anti-tissue transglutaminase (tTG) IgA antibodies was used for CD diagnosis. Any subject positive in the anti tTG antibodies assay, was also tested for anti-endomysial (EMA) IgA antibodies. A structured interview was used to collect basic demographic and clinical recall data including: information on name, contact address, age, gender, education status, previously diagnosed as celiac disease patient, diagnosis of celiac disease in 1st degree relatives and history of “chronic diarrhea, anemia, headache, hepatitis, diabetes, tumor, and thyroid disorder”.

**RESULTS**: Fourteen blood samples (1.17%; 14/1197) were seropositive for celiac disease. The 14 latent CD seropositive patients were 13 women and 1 man and therefore the seroprevalence of celiac disease was 1:86 (14/1197) for adult Emiratis: 1:44 (13/573) for women and 1:624 for men. Binary logistic regression revealed that history of chronic anemia (crude OR = 7.09; 95%CI: 2.32-21.61; *P* = 0.003) and being a woman [OR = 14.46; 95%CI: 1.89-110.91; *P* = 0.001] were associated with CD seropositivity. Whereas, the thyroid disorder showed a positive association with celiac disease seropositivity that approach statistical significance [OR = 11.30; 95%CI: 1.32-96.95; *P* = 0.09] and therefore was included in the multiple logistic regression analysis, which showed that CD seropositivity is independently associated only with history of chronic anemia [OR = 4.58; 95%CI: 1.45-14.48; *P* = 0.01] and being a woman person [OR = 10.47; 95%CI: 1.33-82.14; *P* = 0.026].

**CONCLUSION**: Compared to men the CD seroprevalence among women was remarkably higher. The CD association with women and chronic anemia is of importance from a public health perspective.

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**Key words:** Celiac disease; Epidemiology; Serology; Prevalence; Gender; United Arab Emirates

**Core tip:** Celiac disease (CD) prevalence is unknown in United Arab Emirates. Screening for CD among adult Emiratis from Al Ain city was done by anti TtG antibodies and anti-endomysial antibodies (EMA) confirmed those positive. A structured interview used to collect demographic data and clinical history. Eleven hundred ninety seven were included in the study; the seroprevalence was 1:86 for all adults; 1:44 for women; 1: 624 for men. Chronic anemia and being a woman independently associated significantly with CD seropositivity. To our knowledge, this is the first study on CD prevalence among Emiratis; reporting the highest gender difference in celiac disease seroprevalence worldwide.

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**INTRODUCTION**

Celiac disease is a chronic inflammatory condition in the small intestine, as a response to eating gluten in genetically susceptible individuals. Many symptoms are associated with celiac disease including chronic diarrhea, anemia, and iron/vitamins deficiencies; but what is called as silent or latent celiac disease is also common. Therefore, celiac disease is considered as one of the less diagnosed diseases and affected persons are mostly unaware of having the disease. Moreover, diagnosis of celiac disease often is required for extra-intestinal manifestations, including psychiatric[1], skin[2], and autoimmune diseases[3]. Those who remain undiagnosed are at risk of many long-term complications including but not limited to infertility, osteoporosis, and lymphoma. The basis of treatment of celiac disease is abiding to a diet free of gluten[4]. Therefore, timely diagnosis is essential not just to enable proper treatment of symptoms but also to avoid possible complications[5].

The early epidemiological studies of celiac disease in Europe were based on clinical presentation followed by intestinal biopsies led to undervaluing the prevalence of the disease. Development of highly sensitive and specific serological tests on which subsequent epidemiological studies were based upon, resulted in reporting higher celiac disease prevalence and revealing many clinical features of the disease[6].Although intestinal biopsy is considered as the gold standard in diagnosis, serological tests are needed for screening to determine who needs the biopsy. Serology is also useful in distinguishing between the disease and the other causes of intestinal villi atrophy. The recommended test for celiac disease screening is anti-tissue transglutaminase (tTG) antibodies. The test detects both IgA and IgG antibodies. The sensitivity of anti tTG antibodies test is more than 90% but the specificity is less compared with anti-endomysial antibody (EMA) test[7]. The tTG test is based on ELISA which is from a cost and time perspective superior to EMA test[8].

Celiac disease affects all ages and races worldwide and its prevalence varies from 0.5%-3%. Initially the disease was thought to be largely confined to northern Europe and Australasia and not common in North America and the Middle East, but celiac disease is now known to be prevalent in all those regions[9]. The published prevalence for celiac disease varies between 1:150-1:300 in UK and 1:80-1:122 in Ireland[4], while it was 1:200 among Italian school children which is much more than earlier prevalence based on clinical findings[10]. Hotmeier and Caspary reported that; for each diagnosed celiac disease patient there are approximately 7-10 undiagnosed patients[11]. The above-mentioned findings suggested an analogy to what is called celiac disease iceberg. A study reported a prevalence of 1:96 in north India and the study concluded that celiac disease is more common than expected[12], while the prevalence was 1:50 in Shiraz, Iran[13]. There are few reports from the Middle East and the Gulf on the prevalence of celiac disease, and to our knowledge no study exists on the prevalence of celiac disease in UAE nationals. Therefore, this study aims at estimating the prevalence of celiac disease among healthy adult Emiratis.

**MATERIALS AND METHODS**

***Study design***

This study was a prospective cross sectional concerning celiac disease prevalence in Al Ain city among adult Emiratis who were undergoing the tests of prenuptial examination. Sample size calculation was based on an estimated celiac disease prevalence of 1%, and a lower 95% confidence limit of 0.58%. The estimated minimum number of subjects to be included was 1150; and was adjusted to around 1200 to include about 4% more than the required number.

***Study area***

Al Ain is the second largest city in the Emirate of Abu Dhabi, it is located inland on the country's eastern border with Oman about 165 km from Abu Dhabi and about 140 km from Dubai. The area of this city covers over 1.17 million hectares mostly of sand dunes, the temperature during the year ranges between 10°C up to 48°C. Al Ain city is the country hub for learning, harboring the UAE University and is famous as a tourist destination. The city is divided into 35 districts with a total population of 0.63 million, 30.8% of whom were Emiratis (estimation of mid 2012).

Al Ain Hospital is one of two major governmental hospitals in Al Ain city and at the time of sampling, it was the only place in the city performing the prenuptial examination tests for UAE nationals.

***Study population and blood sampling***

The study population is Emiratis who visited Al Ain Hospital for the prenuptial examination between September 2007 and April 2008. The inclusion criteria were: being an adult (16 year of age or more), not previously diagnosed as a celiac disease patient and willing to participate in the study. The exclusion criteria were: Emiratis less than 16 years of age, Emiratis who were diagnosed as having celiac disease, Emiratis with serological equivocal results for celiac disease diagnosis and all non-Emiratis. Blood sampling was carried out at Al Ain Hospital; 5 mL was obtained from each subject. Sera were separated on the same day and stored at -80°C. Sera were tested for anti-tissue transglutaminase **(**tTG) IgA antibodies, total IgA measurement was carried out for sera which were negative in tTG IgA. Seropositive sera in anti tTG IgA antibodies were tested for anti EMA IgA antibodies and the following criteria were used to define a serum as celiac disease positive: positive in both anti tTG IgA and anti EMA IgA antibody tests; or in sera with total IgA deficiency, positive in both anti tTG IgG and anti EMA IgG antibodies. The criteria for a serum sample to be designated as CD seronegative were if sufficient in total IgA to be negative in anti tTG IgA, or if deficient in total IgA to be negative in anti tTG IgG.

***Demographic and clinical recall data***

For each subject a structured interview was done including information on name, contact address, age, gender, education status, knowledge about celiac disease, if he/she was previously diagnosed as celiac disease patient, diagnosis of celiac disease in 1st degree relatives, history of: chronic diarrhea, anemia, headache, diabetes, tumor, hepatitis and thyroid disorder.

***Anti tTG IgA antibodies***

Anti tTG IgA antibodies were measured using an ELISA method based on human recombinant transglutaminase (IBL International, Hamburg, Germany). The test was carried out according to the manufacturer instruction. Interpreting the results for tTG IgA qualitatively was based on OD cutoff ratio values as described in the footnote of Table 1.

***Total human serum IgA***

Quantitative determination of human IgA in serum was carried out using an ELISA method. The test was carried out according to the manufacturer recommendation (XEMA, Medica Co., Moscow, Russia). Sera with IgA level < 0.05 g/L are considered IgA deficient.

***Anti-endomysial IgA antibody***

The test is based on indirect immunofluorescence assay for semi-quantitative assessment of endomysial antibodies. The test was carried out according to the manufacturer instruction (Immco diagnostics, New York, USA).

***Ethical aspects***

Al Ain Medical District Human Research Ethics Committee approved the ethical application in July 2007. Upon fully explaining the objectives and the expected benefits from participating in the study, each subject included in the study gave his/her consent for the blood sample and to provide the required information for the structured interview.

***Statistical analyses***

Data analysis was carried out on personal computer using SPSS (version 15, SPSS Inc., Chicago, IL, USA). The difference in age between “men and women” and between “diabetics and non-diabetics” was assessed by the student’s *t* test. The linear by linear (for ordinal variables), the Pearson chi-square test and the Fisher exact test were used to compare dichotomous nominal variables between women and men. Binary and multiple logistic regressions were used to analyze the association between the variables obtained from the structured interview with celiac disease serology.

**RESULTS**

***Study population attributes***

Fourteen hundred and thirty persons were requested to participate in the study and 1211 (84.7%) approved. Fourteen were excluded due to grossly hemolyzed samples (11) or equivocal CD serology (3). Therefore, 1197 Emiratis (573 women and 624 men) were included in the study. The age range was 16-70 years with a mean ± SD of 24.87 ± 6.35. The mean age for men 26.36 ± 7.413 was higher (*P* <0.001) compared to women 23.247 ± 4.427. The distribution according to age of the study population into 6 groups (16-20, 21-25, 26-30, 31-35, 36-40 and > 40 years of age) and according to gender, showed that most men and women (87.4%) were between 16 and 30 years and there were more men in all the age groups except in the age group 16-20 years (data not shown).

***Serological data***

All sera tested for total IgA antibodies were IgA sufficient (data not shown). Fourteen blood samples (1.17%; 14/1197) were seropositive for anti tTG IgA and anti EMA IgA and fulfilled the celiac disease seropositive definition and therefore their donors were considered serologically as celiac disease patients (Table 1). The 14 seropositive patients were 13 women and 1 man and therefore the seroprevalence of celiac disease was 1:86 (14/1197) for adult Emiratis: 1:44 (13/573) for women and 1: 624 for men.

***Association of variables with celiac disease serology***

In order to test for any association between variables obtained through the structured interview and celiac disease serology, results of binary logistic regression analyses are presented in Table 2. The History of chronic anemia (OR = 7.09, 95%CI: 2.32-21.61, *P* = 0.003) and being a woman (OR = 14.46; 95%CI: 1.89-110.91, *P* < 0.001) were associated with celiac disease seropositivity. Whereas, the thyroid disorder showed a positive association with celiac disease serology that approach statistical significance (OR = 11.30; 95%CI: 1.32-96.95, *P* = 0.09) and therefore was included in the multiple logistic regression analysis. Using multiple logistic regressions (for the statistically significant variables in binary logistic regression in addition to the variable thyroid disorder) revealed that only history of chronic anemia and being a woman were independently associated with celiac disease serology (Table 2). Five out of the 14 CD patients reported a history of chronic anemia and one patient reported a thyroid disorder. None of the remaining eight CD patients complained from diarrhea or any symptoms or signs of any disease (Table 1).

***CD serology and structural interview variables in men and women***

The distribution of gender in relation to celiac disease serology and the structural interview data was analyzed. Most of the CD seropositive were women (*P* = 0.0006) and most of the anemic persons were women (*P* < 0.001). Whereas, most of the diabetics were men (*P* < 0.005). The difference in diabetes between the two sexes is most likely due age. Diabetics (mostly men) had significantly higher (*P* < 0.001) age (35.76 ± 12.454) than non-diabetics (24.67 ± 6.028). No other significant difference in the studied variables was found between the two sexes (Table 3).

**DISCUSSION**

The epidemiological pattern of celiac disease in the world has changed due to many factors *e.g.*, more awareness to the wide variation in the clinical presentations of celiac disease and discovering new serological tests which are simpler, inexpensive and led to increase in the power of detection and hence increase in the reported prevalence of celiac disease[6]. The new serological tests have helped in diagnosis of celiac disease and reporting a higher disease prevalence (1:133) in some countries[14]. However, the actual prevalence of celiac disease is still not clear in spite of these efforts to detect the disease.

In the Middle East, there are few studies on the prevalence of celiac disease in the general population, most of the studies focus on populations at risk, such as those having autoimmune disease *e.g.* diabetes mellitus type I and autoimmune thyroiditis[15]. Generally celiac disease prevalence undervalued and its clinical features have not been fully determined due to small sample size, selection bias, limited knowledge about celiac disease and insufficient research funds[6,16]. In Libya, as an example of a Middle East country, celiac disease prevalence among school students was (1:41) much higher than those reported in Europe or North America[17].In Saudi Arabia, celiac disease prevalence among healthy adolescents was (1:45) for both sexes; (1:33) for females and (1:68) for males. The investigators concluded that the celiac disease prevalence in their study may be among the highest worldwide[18].

To our knowledge, this is the first study on celiac disease prevalence in UAE. This study is prospective cross-sectional concerning celiac disease prevalence among adult UAE nationals who were in the course of undertaking the prenuptial examination. The prenuptial tests include screening for HIV, hepatitis B, syphilis and anemia. The only targeted population was men and women who were apparently healthy at time of recruitment. Choosing this population is satisfactory because the aim of the study is to detect silent/latent celiac disease in healthy adult UAE nationals. Furthermore, from logistic point of view, those Emiratis were in the process of giving blood for the prenuptial tests, therefore, there was no need for much effort to persuade them to participate in the study. Moreover, the study population choice may be reason for the nearly equal gender ratio in this study. The more men in our study can be explained in part that women refused more to participate in the study compared with men; also, some men came alone because their intention was to marry foreigners and the prenuptial tests for foreigners is not carried at the test center at Al Ain Hospital.

In this study, the overall prevalence of celiac disease is 1:86 among UAE nationals of Al Ain city is higher than the celiac disease prevalence in the general population of Western Europe; in Denmark (1:330), Finland (1:130), Germany (1:500), Italy (1:184) and Netherland (1:198)[8]. The celiac disease high prevalence among healthy adult Emiratis emphasize the celiac disease iceberg terminology (that refers to many undiagnosed celiac disease patients in the general population).

Chronic anemia is a major manifestation of CD; it was shown to be associated with seropositivity for celiac disease. Five seropositive subjects have a history of chronic anemia. Several studies reported anemia as the most common sign of celiac disease among adults. In a study of 200 celiac disease patients, 5% of them were anemic due to nutritional deficiency[19]. Thus, it is suggested that all patients who have anemia or iron deficiency should be examined for celiac disease. Iron deficiency usually affects 2%-5% of adolescents, adult girls and women[20]. Most of the anemic subjects in this study were women, which is in agreement with the fact that anemia is more common in women compared with men.

The women-to-men ratio of those who are seropositive for celiac disease in this study (13:1) is much higher than that reported in Finland (11:21)[21],Sweden (7:3)[22],and Argentina (2:1)[23] but comparable to the ratio reported from eastern Switzerland (10:1)[24]. In this study, the seroprevalence of celiac disease in Emirati women was considerably higher compared with men; this dichotomy in gender-related celiac disease prevalence was more remarkable compared to studies from other countries. Most of our subjects (87.4%) were in the young age category (16-30) which agrees with the conclusion of Dixit and coworkers[25] that “gender disparity was most marked in young adults between the ages 18 and 29 years of whom only 18% of the patients diagnosed with celiac disease were males”. There are unknown factors that contribute to the high prevalence of latent celiac disease among women; two obvious factors are the amount of gluten consumption and the extent of intestinal damage[26]. There is no study comparing the consumption of wheat in women and men in UAE and this study didn't include this variable in the structured interview. There are indications that autoimmune diseases have common genetic risk factors and many of these are gender-predisposed[27]. Possibly women are genetically more susceptible to environmental exposure factors that affect the immunological processes leading to celiac disease. Smoking may be protective against celiac disease and in UAE men constitute the bulk of smokers[28,29], also some endoscopy-confirmed CD patients who were smokers had negative CD serology[30]. Therefore, smoking may partly explain why men in this study have much less celiac disease compared with women. In support of this interpretation a retrospective study, from Sheikh Khalifa Medical City, Abu Dhabi, UAE, reported that only 48% of celiac disease children patients were females[31]. Therefore, on the assumption that those children were nonsmokers at the time of study, it is imperative to interpret the difference in celiac disease prevalence between women and men in this study on epigenetic or environmental factors *e.g.* smoking rather than on inherent genetic susceptibility between the genders. On the other hand, the gender discrepancy may be related to the failure of the serological test to detect the disease in young men due to hormonal or environmental factors. Therefore, one may suggest that for young men with clinical symptoms suggestive of the disease, endoscopy and biopsy should be the basis for diagnosis with less emphasis on the serological tests.

There are some limitations in this study; most of the study population were at the age range of 16-30 years; therefore, compared to the general population older age groups were less represented. The diagnosis relied only on highly specific serological tests but not proved by biopsy. There was no information on the diet of the sampled population, but it is well known that due to the modern lifestyle, the consumption of fast food (wheat-based diets) among Emiratis has increased considerably during the last decades[32]. Finally, the study includes only the major risk factors for celiac disease and does not include factors that may be protective against celiac disease such as smoking.

In conclusion, as anemia is a major manifestation rather than a risk factor of celiac disease, gender is the most important risk factor associated with celiac disease seropositivity in this study, with much higher prevalence in women (1:44) compared with men (1:624). These findings are of importance from a public health perspective and should be conveyed to the health authority for raising the awareness of the disease among the health workers and the population. Health workers should know that there are many undiagnosed celiac disease women patients among UAE nationals. Therefore, they should refer any patient with vague symptoms, complications or signs suggestive of celiac disease for investigation. Among the measures to diagnose latent/silent or unrecognized celiac disease in the general population is the screening of all women who suffer from chronic anemia.

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**COMMENTS**

***Background***

celiac disease (CD) can be easily mistaken for many other diseases due to its vast clinical symptoms and presentations. CD is a chronic inflammatory condition in the small intestine, in response to eating gluten in genetically susceptible individuals. It is a lifelong disease and the only treatment up-to-date is the complete abiding to a gluten-free diet. The highest prevalence of the disease worldwide has been reported in the Middle East. The aim of this study is to determine CD prevalence and associated manifestations or risk factors in healthy adult Emiratis.

***Research frontiers***

The lack of information on the prevalence of the disease from many countries is hindering the effort to draw a worldwide prevalence map of the disease. There is no previous report on the prevalence of CD in the United Arab Emirates.

***Innovations and breakthroughs***

We have reported for the first time the prevalence of celiac disease among Emiratis. Furthermore, from public health perspective our findings of the highest gender disparity in the celiac disease prevalence worldwide is interesting, the prevalence in women was 1:44 compared with 1:624 in men. The study points to the importance of considering celiac disease as an etiological agent particularly in Emiratis women who suffer from chronic anemia.

***Applications***

The results suggest that celiac disease is common among young Emiratis women in Al Ain; therefore, further studies on celiac disease in UAE are warranted to determine the actual celiac disease prevalence in UAE.

***Peer review***

CD prevalence is unknown in UAE and Screening for CD is very important. This is the first study on CD prevalence among Emiratis and it reports the highest gender difference in celiac disease seroprevalence worldwide.

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**P-Reviewers:** Abenavoli L **S-Editor:** Ding Y **L-Editor: E-Editor:**

**Table 1 Demographic, serology and clinical history data in adult Emiratis diagnosed serologically with celiac disease**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Subject** | **Gender** | **Age** | **tTG IgA1**  | **EMA****IgA** | **Clinical2****history** |
| 1 | M | 24 | 7.6 | +++ | a |
| 2 | F | 28 | 1.27 | + | t |
| 3 | F | 22 | 2.42 | +++ | n |
| 4 | F | 24 | 3.6 | ++ | n |
| 5 | F | 23 | 8.25 | +++ | a |
| 6 | F | 20 | 3.15 | ++ | n |
| 7 | F | 20 | 6.6 | +++ | n |
| 8 | F | 22 | 4.87 | +++ | a |
| 9 | F | 25 | 9.1 | +++ | n |
| 10 | F | 18 | 9.89 | + | a |
| 11 | F | 24 | 9.13 | +++ | n |
| 12 | F | 27 | 7.6 | + | n |
| 13 | F | 24 | 4.25 | +++ | n |
| 14 | F | 22 | 6.78 | ++ | a |

**1**Using qualitative evaluation ratio for tTG IgA the cutoff for the positive >1.2, equivocal 0.85-1.2, and negative subjects <0.85. **2**a: Anemia; t: Thyroid disorder; n: No complain. M: Male; F: Female; EMA: Anti-endomysial antibodies.

**Table 2 Distribution and association of variables according to celiac disease serology in Emiratis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variable** | **CD –ve** | **CD +ve** |  |  |
| ***n* (%)** | ***n* (%)** | **1OR (95%CI)****[*P*]** | **2OR (95%CI)****[*P*]** |
|
| CD in family  | No‡ | 1181 (99.8) | 14 (100) | 0.998 (0.99-1.00) | - |
|  | Yes | 2 (0.2) | 0 (0.0) | [0.828] |  |
| Anemia | No‡ | 1097 (92.7) | 9 (64.3) | 7.09 (2.32-21.61) | 4.58 (1.45-14.48) |
|  | Yes | 86 (7.3) | 5 (35.7) | [0.003] | [0.01] |
| Headache | No‡ | 1171 (99.0) | 14 (100) | 0.997 (0.99-1.00) | - |
|  | Yes | 12 (1.0) | 0 (0.0) | [0.594] |
| Diarrhea | No‡ | 1178 (99.6) | 14 (100) | 0.99 (0.98-1.00) | - |
|  | Yes | 5 (0.4) | 0 (0.0) | [0.731] |
| Diabetes | No‡ | 1162 (98.2) | 14 (100) | 0.996 (0.99-1.00) | - |
|  | Yes | 21 (1.7) | 0 (0.0) | [0.480] |
| Tumor | No‡ | 1182 (99.9) | 14 (100) | 0.98 (0.97-0.99) | - |
|  | Yes | 1 (0.1) | 0 (0.0) | [0.878] |
| Thyroid disorder | No‡ | 1175 (99.3) | 13 (92.9) | 11.30 (1.32-96.95) | - |
|  | Yes | 8 (0.7) | 1 (7.1) | [0.09] |
| Hepatitis | No3 | 1172 (99.1) | 14 (100) | 0.998 (0.99-1.00) | - |
|  | Yes | 11 (0.9) | 0 (0.0) | [0.610] |
| Sex | Man**3** | 623 (52.7) | 1 (7.1) | 14.46 (1.89-110.91) | 10.47 (1.33-82.14) |
|  | Woman | 560 (47.3) | 13 (92.9) | [0.001] | [0.026] |

**1**Crude odd ratio; **2**Adjusted odd ratio; **3**Reference group. CD: Celiac disease; CI: Confidence interval; OR: Odd ratio.

**Table 3 Distribution of celiac disease serology and structural interview data in adult Emiratis men and women**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Parameter** | **Frequency*****n* (%)** | **Men*****n* (%)** | **Women*****n* (%)** | ***P*** |
| CD Serology  | -ve | 1183 (98.8) | 623 (99.8) | 560 (97.7) | 0.00061 |
|   | +ve |  14 (1.2) |  1 (0.2) |  13 (2.3) |
| CD in family  | No | 1195 (99.8) | 624 (100) | 571 (99.7) | 0.2291 |
|   | Yes |  2 (0.2) |  0 (0.0) |  2 (0.3) |
| Anemia  | No | 1106 (92.4) | 601 (96.3) | 505 (88.1) | <0.001**2** |
|  | Yes |  91 (7.6) |  23 (3.7) |  68 (11.9) |
| Headache  | No | 1185 (99.0) | 618 (99.0) | 567 (99.0) | 1.000**†** |
|  | Yes |  12 (1.0) |  6 (1.0) |  6 (1.0) |
| Diarrhea  | No | 1192 (99.6) | 621 (99.5) | 571 (99.7) | 1.01 |
|  | Yes |  5 (4.4) |  3 (0.5) |  2 (0.3) |
| Diabetes  | No | 1176 (98.2) | 606 (97.1) | 570 (99.5) | <0.005**2** |
|  | Yes |  21 (1.8) |  18 (2.9) |  3 (0.5) |
| Tumor  | No | 1196 (99.9) | 623(99.8) | 573 (100) | 1.01 |
|  | Yes |  1 (0.1) |  1 (0.2) |  0 (0.0) |
| Thyroid disorder  | No | 1188 (99.2) | 622 (99.7) | 566 (98.8) | 0.0961 |
|  | Yes |  9 (0.8) |  2 (0.3) |  7 (1.2) |
| Hepatitis  | No | 1186 (99.1) | 617 (98.9) | 569 (99.3) | 0.642**2** |
|  | Yes |  11 (0.9) |  7 (1.1) |  4 (0.7) |

1Fisher's Exact Test; **2**χ2 with continuity correction. CD: Celiac disease.