



A Study of the Relationship Between Age, Gender, and Some Immunological Parameters in Patients with Celiac Disease in Karbala Province

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Abstract

Celiac Disease (CD) is a public hereditary, autoimmune and multifactorial gastro-intestinal disorder in children and adults defined as a permanent gluten-sensitive enteropathy. The current study aimed to investigate the effect of age and gender factors on the incidence of celiac disease and to evaluate some immunological parameters in the diagnosis of wheat allergy, through a sample of 303 persons suspected of being infected with celiac disease who attended Imam Al-Hassan Al-Mujtaba Hospital in Karbala Governorate for the period from 1/ 2/2022 to 1/9/2022. The questionnaire was prepared and filled with information about celiac disease. The results of the current study showed that the number of infections with celiac disease is 65 out of 188 in females, while in males was 42 out of 115. The number of infected males was 23 out of 42, while the number of females was 30 out of 65 within children category of celiac disease. The results also showed that there were significant differences in the level of TTG IgA, and TTG IgG between males and females.

1. Introduction

Celiac disease (CD) is a systemic immune-mediated illness characterized by enteropathy after exposure to gluten [1]. It affects between 0.5%–1% of the United States and European population [2,3,4]. There is a female predominance of diagnosed disease (2:1 to 10:1) [5,6,7]. CD can affect women's health by decreasing bone mineral density and fertility, increasing risk of concurrent autoimmune disease, and negatively impacting quality of life [8,9,10,11]. Gender-related differences in clinical presentation of CD have been suggested [12,13,14]. Women are more likely to experience abdominal pain and iron deficiency anemia [13,14,15]. Elevations in liver enzymes, weight loss, and the presence of dermatitis herpetiformis appear more common in men [15]. Women reportedly struggle more with persistent symptoms and poorer health-related quality of life even while adhering to a gluten-free diet [11].

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Celiac disease is an intestinal disorder with multifactorial etiology. HLA and non-HLA genes together with gluten and possibly additional environmental factors are involved in disease development. Evidence suggests that CD4⁺ T cells are central in controlling an immune response to gluten that causes the immunopathology, but the actual mechanisms responsible for the tissue damage are as yet only partly characterized [16].

Celiac disease develops in patients who have ingested gluten, which is present in wheat, rye and barley [16–17]. Gluten proteins are grouped into high molecular weight (HMW) glutenins, low molecular weight (LMW) glutenins and alpha-, gamma- and omega-gliadins (based on their differential N-terminal sequence, electrophoresis size and mobility) [18]. Until recently it was thought that the toxic proteins causing CD are not present in the HMW glutenins. In consequence, development of non-toxic HMW glutenins-containing food products was proposed (*e.g.* transgenic food). However, recent evidence showed that there is no group of gluten proteins safe for patients with CD [18]. Interestingly, gluten extracted from several ancient wheat species was reported incapable to stimulate T cell lines (previously shown to be responsive to toxic gliadin fragments) [19]. These findings raise the prospect of identifying bred wheat species with low or absent levels of harmful gluten proteins.

Based on the high association between human leukocyte antigens (HLA) and celiac disease (over 95%) [20], it is thought that HLA-DQ2 positive antigen-presenting cells have gliadin peptides toxic to CD4⁺ T cells. CD4⁺ T cells drive the immune response and damage the mucosa [21–26]. Tissue transglutaminase (tTG) was identified as the autoantigen, which is recognized by the endomysial antibodies [57, 27].

Tissue transglutaminase, an enzyme essential in wound healing for all individuals, was shown to be able to deamidate gliadin peptides *in vitro* [22–25]. The modified gliadin peptides bind much better to HLA-DQ2 and elicit a stronger T cell response. Furthermore, gliadin is one of the main substrates of tTG. It was reported that several peptides can be cross-linked and that tTG itself can be incorporated into HMW complexes. These newly generated molecules are potential "neo"-autoantigens, which might be responsible for the induction of a destructive immune response.

Gliadin-reactive CD4⁺ T cells were isolated from the intestinal mucosa of patients with celiac disease [21]. These T cells can elicit a B cell response with production of autoreactive antibodies against gliadin peptides or tTG. However, whether the role of these antibodies is significant [28] or whether they have a pathogenic role in celiac disease remains unknown [29]. It also remains unknown why tTG or gliadin complexes are recognized only by T cells from celiac patients and not by those from healthy HLA-DQ2 positive subjects. In addition, the increase in CD8⁺ T cells in the epithelium of the mucosa (IEL) cannot be explained by HLA-DQ2 positive cells, which only activate CD4⁺ T cells. Additional factors like infections, which damage the mucosa may trigger the onset of the disease in predisposed individuals [26].

2. Methods

For the purpose of this study, a special form was prepared to contain information including the age, gender, and number of people who attended Imam Al-Hassan Al-Mujtaba Hospital in Karbala Governorate for the period from 1/ 2/2022 to 1/9/2022 who had symptoms of wheat allergy. The celiac disease was diagnosed based on the results of some immunological tests and clinical examination by a specialist doctor.

3. Results and discussion

The results of the current study showed that the number of people with celiac disease was 107 out of 303 person who attended Imam Al-Hassan Al-Mujtaba Hospital, who suffer from symptoms similar to wheat allergy. The number of infected males was 42, while the number of females was 65, as shown in Figure 1.

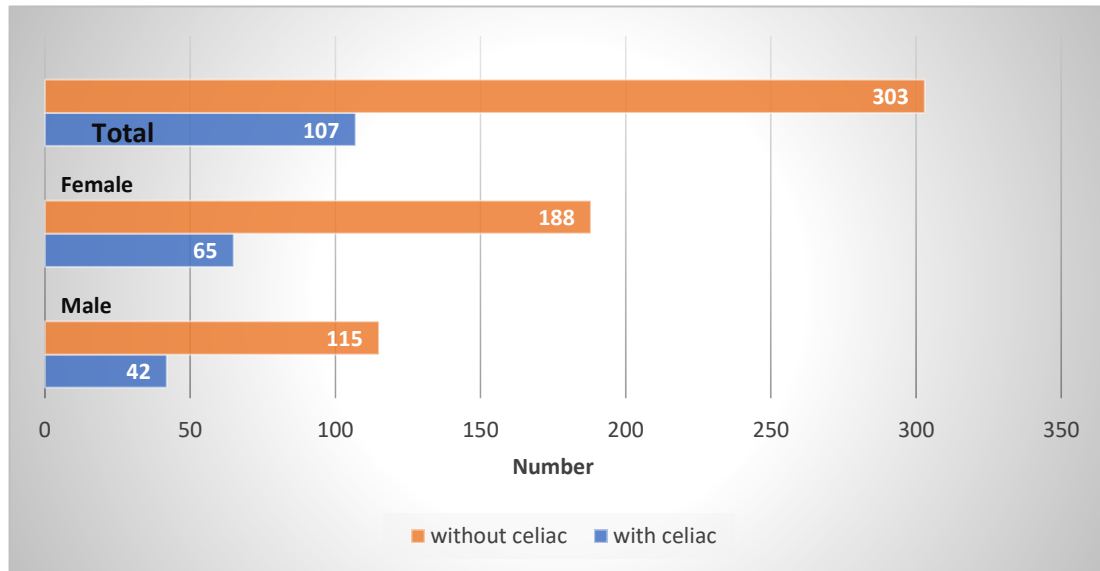


Fig.1. Distribution of people with and without celiac disease in the current study

Males and females with celiac disease were divided into five age groups: babies, children, young adults, middle aged adults and old adults. The results showed that the category of children in both males and females, whose ages range from 3 to 16 years, are the most affected by wheat allergy. The number of infected males was 23 out of 42, while the number of females was 30 out of 65 within children category as shown in figure 2 and 3.

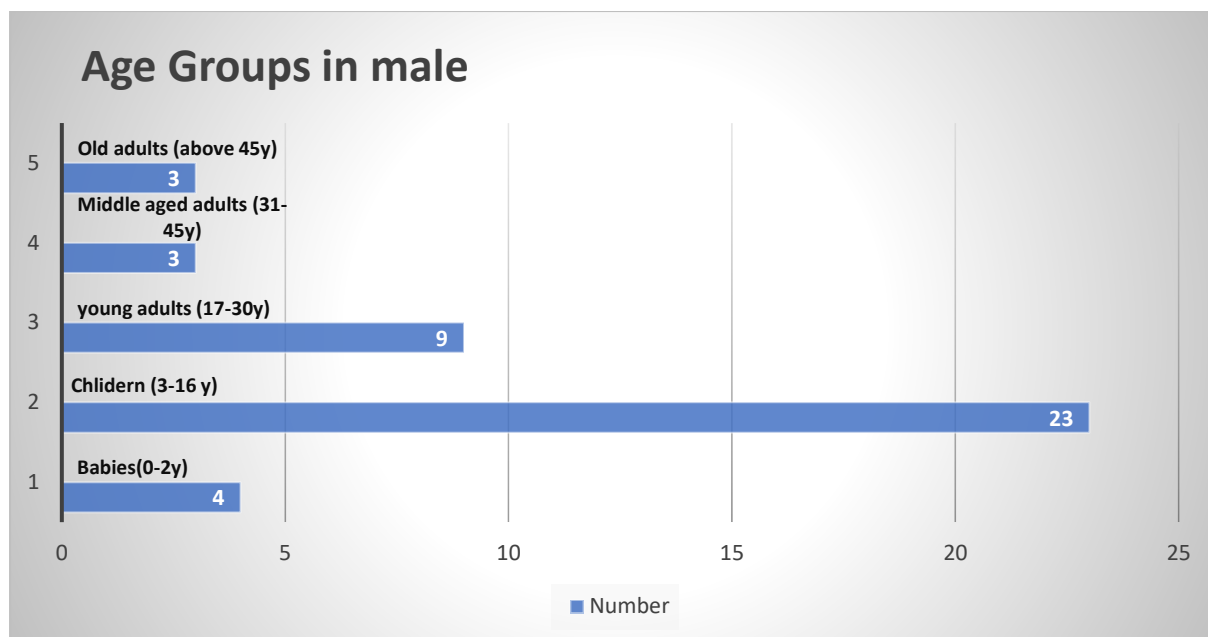


Fig.2. Distribution of age groups in males with celiac disease

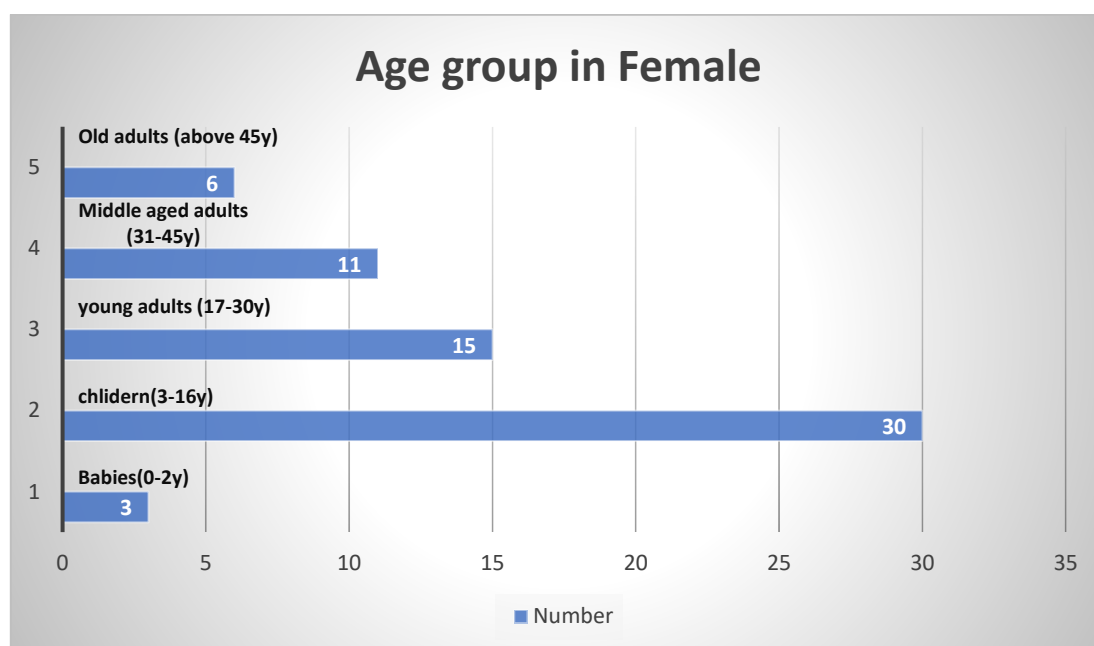


Fig.3. Distribution of age groups in females with celiac disease

The results in Table 1 showed that there were significant differences ($P \leq 0.05$) in the levels of anti-TTG IgA, anti-TTG IgG in the serum between person with and without celiac disease. However, there were significant differences ($P \leq 0.05$) in the levels of anti-TTG IgA, anti-TTG IgG in the serum in between male and female. Also, there were significant differences ($P \leq 0.05$) in level of antigliadin IgA between the between person with and without celiac disease,

while there were no significant differences ($P \leq 0.05$) in level of antigliadin IgA between male and female with celiac disease.

Table 1: Serum immunological parameters of patients with celiac diseases

| Parameter | | | N | Mean± Std. Error |
|------------------------|-------------------|--------|-----|-----------------------------|
| TTG IgA | With celiac | male | 42 | B 49.3095± 14.97866 |
| | | Female | 65 | C 117.1339± 20.12777 |
| | Without celiac | male | 115 | A 3.7757±0.43279 |
| | | Female | 188 | A 3.6183± 0.26607 |
| TTG IgG | With celiac | male | 42 | B 27.6690± 5.30671 |
| | | Female | 65 | C 39.3682± 5.76428 |
| | Without celiac | male | 115 | A 5.6463± 0.73579 |
| | | Female | 188 | A 4.0323± 0.29784 |
| Gliadin IgA | With celiac | male | 42 | B 14.6357± 7.07164 |
| | | Female | 65 | B 23.7015± 7.31330 |
| | Without celiac | male | 115 | A 2.9301± 0.36827 |
| | | Female | 188 | A 3.4622± 0.29959 |

Means having the different letters in the same column differed significantly ($*P \leq 0.05$); SE: Standard Error, TTG: Tissue transglutaminase.

Our study shows that 65 out of 107 (60.7%) patients were female, the majority of female patients. Researches regarding the gender of the CD patients show a female predominance in certain [30],[31], and males in the others [32]. The results of our current study agree with a study conducted by [33] show that the female predominance in diagnosed CD as 65% of the sample was female (1.85:1 ratio). Although there is no known cause for the increased occurrence in women, research indicate that in general, women are more susceptible to autoimmune disorders [34]. Additionally, it is thought that those who already have one autoimmune disease, such as type 1 diabetes, lupus, or rheumatoid arthritis, are predisposed to developing additional autoimmune diseases. For instance, type 1 diabetes and celiac disease usually co-occur. another idea holds that women are more likely than men to experience intestinal issues as a result of hormonal influences and are more willing to inform their doctors about it, leading to a diagnosis [35].

According to the findings of our study, children between the ages of 3 and 16 years made up the majority of the patients with celiac disease, both male (54.7%) and female (46.2%). These results are consistent with a Catalan epidemiological study that used serology to examine the prevalence and found that CD prevalence was five times higher in children (1/71) than in adults (1/357) [36]. Children have twice as many CDs as adults, according to comparable studies from Brazil and India [37,38]. Multiple studies have demonstrated that whereas traditional symptoms only appear in less than 25% of adult cases, the typical clinical malabsorption pattern is frequently observed during diagnosis in children [39]. As a person becomes older, there is a tendency toward less severe clinical manifestations [40]. Only minor symptoms, which frequently include an increase in stool volume or intestinal gas caused by lactose malabsorption or bacterial overgrowth, are common in older children and adults. In fact, in an adult with celiac disease, constipation could be the only symptom.

Also, the results of our current study showed high levels of TTG IgG and TTG IgA in the serum of females compared with males, which indicates the severity of the infection depending on the immunological parameters used in the diagnosis of celiac disease. These findings are supported by a study [41] that found a Marsh grade of more than two is substantially related to an anti-tTG antibody titer greater than 10 times the upper limit of normal (84 U/ml).

4. Conclusion

The current study concluded that the largest number of infections with wheat allergy was in females and that the age group of children was the most affected by wheat allergy in both males and females. The current study also showed that the severity of infection in females is higher than that of males, depending on the values of immunological parameters.

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