ORIGINAL ARTICLE

Evaluation and treatment of celiac disease in the central and south of Iraq

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ABSTRACT

Aim: To estimate the differences between patients with celiac disease based on symptoms, diagnosis, treatment, and follow-up.

Materials and Methods: A retrospective cross-sectional study carried out between July 1, 2022 and April 2023, enrolling 200 patients from different provinces of central and south Iraq with Celia disease, whose diagnosis depended on a specialized physician according to WHO guidelines with long-term follow-up. Participants were following up for three to six months in private clinics. Survey was written in English, and the questionnaire form contains 13 fields divided into three sections. Diagnosis of Celia before and after treatment parameters: Tissue Transglutaminase Antibody, IgG, Serum (tTg-Ig G), and tTg-IgA levels the fourth part included a glutin-free diet and symptomatic treatment.

Results: Females and ages below 20 were most affected. 176(88%) patients had detectable tTG levels; after 3 months, 72(36.0%) patients had an increase in their body weight but less than 5 kg, while 14(7.0%) of the patients showed an increase of more than 5 kg. But after 6 months, 73(36.5%) patients had an increase in their body weight less than 5 kg, while 45(22.5%) of patients showed an increase of more than 5 kg.

Conclusions: Celiac patient profile in central Iraq is not different from that in other parts of the world, with typical patient being female and under 30 years of age. The study highlighted to a certain degree that a gluten-free diet can have a modest and promising positive impact on BMI in some patients.

KEY WORDS: gluten, celiac disease, and tissue transglutaminase antibody

INTRODUCTION

Coeliac disease (CD) is a persistent immune-mediated enteropathy affecting the small intestine, which is triggered by the consumption of gluten in those who possess genetic susceptibility, and the genetic vulnerability plays a significant impact, as a clear majority of patients >95% exhibit the HLA-DQ2 gene, whereas approximately 5% exhibit the HLA-DQ8 gene [1]. Coeliac disease is a prevalent hereditary condition worldwide and it affects about 1 in 100 persons in the world. The prevalence of the disease is higher in females compared to males, with a ratio of 3 to 1 [2]. Despite of the clear rise in the occurrence of sickness, one frequently encountered obstacle in the process of diagnosis is occasionally associated with the variability observed in the manifestation of certain features across different patients. Clinically CD showed a highly diverse range of symptoms, from the standard (gastrointestinal) aspects to unusual (extra intestinal) ones [3]. Celiac disease is characterized by a diverse range of clinical manifestations related to gluten, specific antibodies, and the presence of HLA-DQ2 or HLA-DQ8. This condition is associated with a distinct pattern of intestinal damage, including inflammatory cell infiltration, crypt hyperplasia, and ultimately villous atrophy. Following a gluten-free diet (GFD) can lead to both clinical and serologic remission, which are considered key features of CD [4]. In light of the multiple extraintestinal symptoms of the disease, celiac disease may be more appropriately viewed as a systemic issue than only a gastrointestinal disorder [5]. Extraintestinal symptoms are typical in both children and adults. Iron deficiency microcytic anaemia is a prevalent condition that can be detected in approximately 40% of patients (by the underlying factor causing iron malabsorption or chronic inflammation) [6] or, less frequently, macrocytic anemia brought on by a vitamin B12 and/or folic acid deficiency (more common in Europe than the US). Affected calcium and vitamin D3 absorption is the occurrence of alterations

in bone mineral density, such as osteopenia or osteoporosis, has been observed in approximately 70% of patients upon diagnosis [7]. The presence of growth retardation and small stature in children may indicate a possible underlying CD. Defects in the enamel of the teeth and aphthous stomatitis (seen in roughly 20% of CD patients who are undiagnosed) are additional symptoms [8]. The most frequent clinical signs of CD typically involve recurrent episodes of disturbed bowel habits (diarrhea and/or constipation), presence of gastro-esophageal reflux (GERD), and weight loss [9]. The clinical signs and disease-specific antibodies are used to make a diagnosis. The gold standard for confirming a diagnosis is duodenal mucosal biopsies. Before following a gluten free diet, the serology and biopsy should both be completed (GFD) [10]. HLADQ2/DQ8 genotyping is possible in certain situations. The HLA gene DQ2 genotype predominates among celiac patients in Iraq [11]. The detection of celiac disease can be achieved through the use of anti-endomysial (EMA) antibodies of the immunoglobulin A (IgA) type, which exhibit a sensitivity of 90% and a specificity of 99% in patients with villous atrophy. Initial reports claimed that anti-transglutaminase antibody serology had a higher specificity of >90% and a sensitivity of 99% than other methods. However, it is currently believed to share traits with anti-endomysial antibodies [12].

AIM
The aim of the study is to determine the variability within a specific population-based cohort of individuals diagnosed with celiac disease with regard to age, gender, haemoglobin, body weight, diagnosis tests, treatment, and follow-up.

MATERIALS AND METHODS
A retrospective cross section study carried out between July 1, 2022 and April 2023 that enrolling 250 patients from different provinces of central and south Iraq (Babylon, Karbala, Al Najaf, Al Muthanna, and Diwaniya) with celiac disease that diagnosis depended on specialized physician according to WHO guidelines, and excluded 50 patients due to the lack of diagnostic evidence, insufficient lab results and inability to follow up for 6 months with them for different causes, and the study was completed on 200 patients in detail and with long-term follow-up. The participants were following up for three and six months in private clinics. The research form contained 13 fields divided into five sections. The first section contains social information such as age, gender, and education.

The second part includes signs and symptoms, which included epigastric pain, loose motion, oral ulcers, weight loss, severe pallor, nausea, vomiting, diarrhea, anemia, and anorexia and other chronic disease. The third part consists of diagnosis which included the body weight, hemoglobin, tissue transglutaminase antibody, IgG, serum tTg-Ig G, and tTg-IgA levels. The fourth part included gluten free diet (GFD) and symptomatic treatment. In addition, for the final part it included the patient follow up after 3 months and 6 months of treatment and the responsiveness of the approach. After that, we collect the obtained data in Microsoft Excel program tables and then statistically analyzed it as shown in the results using IBM SPSS Statistics version 26.

STATISTICAL ANALYSIS
The data analysis was conducted using SPSS® version 26, a statistical tool developed by IBM Inc. in Chicago, IL, USA. The standard deviation was used to express the numerical variables. When the Kolmogorov-Smirnov test failed to reveal a normal distribution, the variables were examined using the nonparametric Kruskal-Wallis test to evaluate the mean differences between groups. Bivariate correlation analysis was also carried out to evaluate the relationship between markers. Statistics were deemed significant at P < 0.05.

RESULTS
During the study period, 200 patients with celiac disease were included, 44 (22.0%) were males and 156 (78.0%) were females (χ^2=42.440, P-value=0.000). The mode age of the participants was in age group of 20-29 years, where was 76 (38.0%) of participants (χ^2=62.72, P-value=0.000), however, 119 (59.5%) of patients with university education was consider significant when compared with other educations (χ^2=150.52, P-value=0.000), 75 (37.5%) patients had more than three symptoms (χ^2=58.75, P-value=0.000). On other hands, the 107 (53.5%) patients had low hemoglobin level; also, the frequency and percentage of the subtypes are shown in Table 1.

ASSOCIATION OF DETECTABLE TTGG IGA AND TTG-IG G WITH GENDER, EDUCATION, HB, AND BODY WEIGHT
Out of the total sample size of a 176 patients, 88% exhibited detectable tTg levels, while the remaining 12% showed undetected tTg levels. The current study reveals a notable negative correlation between the

Table 1. Frequencies and percentages of the variant's subtypes in the study

		Frequency	Percent	SD	Chi-Square	P value
Age	<20	45	22.5	1.623	42.440	0.000
	20-29	76	38.0			
	40-49	15	7.5			
	≥ 50	64	32.0			
	Total	200	100.0			
Gender	Male	44	22.0	0.415	62.72	0.000
	Female	156	78.0			
	Total	200	100.0			
Education	Illiteracy	7	3.5	0.811	150.52	0.000
	Primary	20	10.0			
	Secondary	54	27.0			
	University	119	59.5			
	Total	200	100.0			
	Total	200	100.0			
Total no. of symptoms	None	12	6.0	1.240	58.75	0.000
	One	23	11.5			
	Two	44	22.0			
	Three	46	23.0			
	More than three	75	37.5			
	Total	200	100.0			
Hb	Normal	93	46.5	0.50003	0.98	0.322
	Low	107	53.5			
	Total	200	100.0			
		tTg-Ig G	tTg-Ig A	Gender	education	Hb

measured tTgG IgA and tTg-IgG and hemoglobin levels. This indicates that when the level of HB is high or close to normal in individuals with celiac disease, there is a corresponding decrease in these stereological tests and vice versa. This pattern is also observed in patients with levels of education, also these seen with gender that may be due to most cases in present study from female patients (Table 2).

The statistical analysis using the chi-square test yielded a χ2 value of 115.52, with a corresponding P-value of 0.000, indicating a significant association between tTg levels and the patient group. At the time of the study, the average duration of adherence to a gluten-free diet ranged from 3 to 6 months. After 3 months, 72 (36.0%) patients had an increase in body weight, but less than 5 kg, and 14 (7.0%) patients had an increase in body weight of more than 5 kg. However, after 6 month, 73 (36.5%) patients with increased in their body weight less than 5 kg while 45 (22.5%) of the patients showed increased more than 5 kg (Table 3).

DISCUSSION

An autoimmune enteropathy caused by food gluten sensitivity in people with certain genetic predispositions is called celiac disease [13]. It covers a wide range, from overt malabsorption or common gastrointestinal symptoms to disorders that are clinically quiet [14]. Due to the advancement of diagnostic techniques for identifying CD, the loss of iron in the intestine enterocytes, malabsorption of daily iron, and very infrequently gastrointestinal hemorrhage may cause the pathogenesis of CD [15]. Studies using small-bowel biopsies and serologic assays in patients referred for IDA investigation have revealed CD in 1.8 percent to 14.6 percent of patients [16]. This study examines the prevalence of celiac disease in patients using a very sensitive screening test (the tTG antibody test). Our study showed that the Iraqi patients of with celiac disease with symptoms in the Center and South area of Iraq had 88.0% to tTG (IgA and IgG) positive titer. On other hands, our study showed there was a significant gender difference between the participants; the majority of them, specifically 156 (78.0%), were female

Table 2. Frequencies of the serological tests and gender, education, and Hb

		tTg-Ig G	tTg-Ig A	Gender	Education	Hb
tTg-Ig G	Pearson Correlation	-	.148[*]	-0.354[**]	-0.134[*]	-0.357[**]
	Sig. (2-tailed)	-	0.087	0.001	0.016	0.006
	N	200	200	200	200	200
tTg-Ig A	Pearson Correlation	0.148[*]	-	-0.414[**]	-0.139[*]	-0.288[**]
	Sig. (2-tailed)	0.087	-	0.011	0.013	0.017[**]
	N	200	200	200	200	200

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 3. Frequencies and percentages of the serological and follow-up in the study

		Frequency	Percent	SD	Chi-Square	P value
tTg-Ig G	Negative	24	12.0			
	Positive	176	88.0	0.326	115.52	0.000
	Total	200	100.0			
tTg-Ig A	Negative	24	12.0	0.326		
	Positive	176	88.0		115.52	0.000
	Total	200	100.0			
Follow up 3 months						
Weight < 5kg	Yes	72	36.0			
	No	128	64.0	0.483	15.68	0.000
	Total	200	100.0			
Weight > 5kg	Yes	14	7.0			
	No	186	93.0	0.256	147.92	0.000
	Total	200	100.0			
Follow up 6 months						
Weight < 5kg	Yes	73	36.5			
	No	127	63.5	0.483	14.58	0.000
	Total	200	100.0			
Weight > 5kg	Yes	45	22.5			0.000
	No	155	77.5	0.419	60.5	
	Total	200	100.0			

while only 44 (22.0%) were male. This is in accordance with general established research stating that more women get diagnosed with celiac disease than men [2, 17]. This may be due to the fact that women are thought to be predisposed to autoimmune disease and the reason for which is not yet completely understood [18]. In regards to symptoms, 75 (37.5%) of the participant reported having more than 3 symptoms at the time of diagnosis while the rest of the patients 125 (62.5%) reported having three or less symptoms. Recent research has found that the number of patients presenting with mild symptoms has been increasing in the recent years [19], the most common of these symptoms is chronic diarrhoea, weight loss and abdominal distension. Also, a significant portion of the participants 107 (53.5%) had low haemoglobin levels indicating a tangible correlation between anaemia and celiac disease. Since iron is a vital micronutrient, a lack of it in CD is typically caused by malabsorption owing to destruction to the intestinal mucosa's villi. However, the diminished expression of many regulatory proteins may also contribute to iron shortage in CD [20]. Serology tests of the patients showed that 176(88%) patients had detectable tTG levels and 24(12%) patients had undetectable tTG levels. This demonstrates the accuracy and sensitivity of these tests making them an important and significant biomarker in the diagnosis process, a process which previously relayed on histological assessment of intestinal mucosa but since the 1980s of the last century serological tests became the first step when there is a suspicion of celiac disease [21]. At the

time of the study, a gluten free diet lasted three to six months on average. After 3 months, 72 (36.0%) patients with an increase in their body weight but less than 5 kg while 14 (7.0%) of the patients showed increased more than 5 kg. However, after 6 month, 73 (36.5%) patients with increased in their body weight less than 5 kg while 45 (22.5%) of the patients showed increased more than 5 kg. This data illustrates that a significant portion representing the majority did not have an increase in their body weight. A possible explanation for this might be refectory celiac disease due to non-completely adherence to diet (GFD) or they use food that they think is free of gluten, as in some cereals, biscuits, and pastries, but they contain gluten. Even though it's uncommon, RCD should be considered in those with a confirmed diagnosis of CD who don't improve after trying a rigorous gluten-free diet, especially if they have severe weight loss or no weight gain [22]. For the remaining patients who did gain weight the majority of them experienced it on a small scale, that is <5 kg this could be an indication of the ineffectiveness of the gluten free diet in improving the clinical manifestation of weight loss in celiac patients but it can also be attributed to the relatively short time frame in which the follow ups occurred. This proposes the idea that the slight increase in weight was a reflection of the duration of the study rather than the effectiveness of the GFD diet. To further support this claim, other studies with a longer duration of follow-ups showed better results in regards to weight gain an example for which, when compared to the control group, A prospective research with 39 CD patients and 39 controls the study shown that individuals who were initially diagnosed with a body mass index (BMI) within the normal range 18.5-24.9 Kg/m2 had weight gain over time. Conversely, it was seen that 50% of patients who had an underweight BMI 18.5 Kg/m2 at diagnosis transitioned to the normal weight category following a two-year follow-up period [23]. Furthermore, a variety of retrospective studies involving 679 individuals diagnosed with celiac disease and adhering to a gluten-free diet (GFD) revealed that 22% of overweight patients experienced weight gain following the initiation of a GFD. Additionally, 15.8% of these individuals transitioned from a normal or low body mass index (BMI) category to an overweight classification BMI>25 kg/m2 subsequent to commencing a GFD. The duration of these studies ranged from 1 to 345 months, with a mean duration of 39.5 months. In general, there was a significant increase in the average body mass index (BMI) following adherence to a gluten-free diet (GFD). Specifically, among the participants who initially had a BMI within the normal range, 21.8 percent had weight gain, resulting in a BMI increase over two units [24].

CONCLUSIONS

The study data demonstrated that the celiac patient profile in central Iraq is not different to that in other parts of the world with the typical patient being female and under 30 years of age. More importantly the study highlighted to a certain degree that gluten free diet can have a modest and promising positive impact on BMI in some patients. However, the total majority did not gain any weight in the first place and for the ones that did experience and improvement in weight they gained less than 5 kg total. This can lead to the understanding that for patients of celiac disease who are following the gluten free diet, it might take a significant amount of time to see benefits and improvements at least regarding weight. A possible limitation of this study was the personal adherence of patients to GFD.

RECOMMENDATIONS

Since GFD can be beneficial to a significant portion of celiac disease patients in Iraq, it is safe to say that is should be considered for all patients as part of the main management strategy. Also, efforts should be made by government and even private stores or markets to make gluten free options more available and accessible. Finally, all patients should be urged to adhere to the diet in spite of the social, economic and personal burdens that may accompany it since, to this day it remains the only true management method. Or if can introduce drugs that decrease the absorption of gluten from GIT.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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