

Epidemiologic and Demographic Survey of Celiac Disease in Khuzestan Province

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ABSTRACT

BACKGROUND

Celiac disease presents with a wide spectrum of symptoms. This study clarifies different aspects of celiac disease along with the most common patterns of celiac presentation in Khuzestan Province, Iran.

METHODS

Patients' information was obtained by evaluation of their files from the archives of the Khuzestan Celiac Society and records at gastroenterologists' offices in this province.

RESULTS

Overall, there were 103 (40 males, 63 females) patients included in this study. Patients' mean ages were 33 ± 11 years (males) and 31.6 ± 11.7 years (females). In terms of geographic distribution, 54.1% resided in the center of the province followed by 26.5% who were residents of the northern area. The rate of employment among men was 70.6% whereas it was 8.3% for women. In terms of education, 21.9% of men and 33.3% of women had academic educations. The rate of matrimony was 80.6% (n=29) for men, 65.4% (n=38) for women and 3.4% (n=2) who were divorced. Mean height was 164 ± 14 cm in men and 157.5 ± 10 cm in women. Mean BMI at the time of presentation was 22.7 in men and 22.6 in women. The most common gastrointestinal (GI) complaints in male patients were diarrhea (35%), reflux (20%), bloating (17.5%), abdominal pain (15%), vomiting (15%) and constipation (7.5%). Female patients experienced diarrhea (49.2%), abdominal pain (31.7%), bloating (31.7%), vomiting (19%), constipation (9.5%) and reflux (7.9%). The most common concomitant non-GI disorders among male patients were anemia (17.1%), thyroid disease (14.3%), and weight loss (14.3%); women experienced anemia (33.9%), thyroid disease (12.5%), and weight loss (7.1%). Approximately half of the patients exhibited symptoms for more than five years prior to diagnosis and 90% were diagnosed by gastroenterologists. Of these, 43% had normal endoscopy results. The most common serologic markers were anti-TTG (69.9%), anti-EMA (27.7%).

CONCLUSION

Physicians, prior to attributing patients' symptoms to irritable bowel syndrome (IBS), should be aware that patients who present with long-term non-specific symptoms might possibly have celiac disease. During endoscopy, the threshold for obtaining biopsies should be low.

KEYWORDS

Celiac disease; Diarrhea; Anemia; Endoscopy; Khuzestan; Iran

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INTRODUCTION

Celiac disease, also known as celiac sprue, non-tropical sprue or gluten sensitive enteropathy, is a chronic autoimmune disorder that involves genetically susceptible persons who consume gluten.¹⁻³ Gliadin, the soluble part of gluten, plays a main role in the pathogenesis of this disorder and can result in villous atrophy and crypt hyperplasia.⁴⁻⁶

In recent years the prevalence of celiac has increased and it is estimated that approximately 1% of the general population has this disorder.^{7,8} In Iran the prevalence of celiac disease is reported to be approximately 1 per 166 persons.⁹⁻¹¹ For many years celiac disease or gluten sensitive enteropathy was presumed to be exclusive in European nations, however today it is clear that this disorder involves all races worldwide.^{10,12-15} Epidemiologic estimates of the prevalence of this disorder is less than the real prevalence which is assimilated to the iceberg model. In this model, the apex represents patients with classic symptoms whereas the major area belongs to patients who have no obvious signs or symptoms of typical presentation and remain undetected.^{4,16-18} Approximately⁸ remain unidentified instead of every patient diagnosis as the result of symptoms.¹⁹ The main reason for this increase in prevalence is not clear however as the time period for genetic changes is too short, it may possibly be the result of environmental and life style changes.²⁰ On the other hand, the age for celiac presentation has changed tremendously during the past 30 to 40 years; in the past it has been presumed to be a disease of children with the majority of cases diagnosed before age 2. However today many newly diagnosed celiac cases are adults^{21,22} which may be due to increased medical personnel awareness of atypical forms of this disease. Clinical presentation of celiac includes a wide spectrum from that range from asymptomatic cases to apparent malabsorption, multiple organ involve-

ment and even malignancies.²³ Delays in diagnosis, particularly among patients with severe involvement can result in increased mortality due to the risk of malignancy, in particular non-Hodgkin's lymphoma which has a six-time higher risk compared with the general population.^{7,24,25}

Gastrointestinal (GI) symptoms are less prevalent among older people who suffer from celiac disease in comparison with younger patients. Instead, signs of micronutrient deficiencies may be the first or only symptom of this disease.²⁶ In this group celiac can present as iron deficiency anemia, osteoporosis, herpetic-like skin lesions, elevated liver enzymes or neurologic disorders²⁷ because the small intestine can potentially compensate for minimal degrees of involvement. Up to 38% of patients are asymptomatic.^{28,29} Detection of various aspects of this disease and determination of its prevalence in different regions can increase community awareness, in particular among family physicians with regards to this disease and its most common forms of presentation. This will assist with early diagnosis of celiac patients. The current study attempts to identify the most common signs and patterns of celiac disease presentation in Khuzestan Province, Iran.

MATERIALS AND METHODS

This cross-sectional epidemiologic study evaluated patients' profiles retrieved from the archives of Khuzestan Celiac Society and records from gastroenterologists' offices in this province. Patients' information was recorded as a check list. In case of incompleteness of any file, we contacted the patient by phone. Obtained information included signs and symptoms before diagnosis, duration of involvement before diagnosis, level and specialty of the managing physician, age and weight of patient at the time of diagnosis, comorbidities and patient's family history. Additionally, the geographic origin of patients in this province and the level of patients' education were determined.

After data collection, statistical analysis was performed by descriptive statistics and included the average, standard deviation, absolute and relative

frequency and t-test for qualitative and quantitative variables. We used SPSS software version 19.

RESULTS

Overall, in a six-month period until the end of March 2013, we gathered information on 127 patients based on the results of duodenal biopsies and in cases of normal pathology (Marsh 0), based on positive serology and symptoms. Because of incompleteness of a number of files (Marsh 0 with uncertain serology) or patient inaccessibility, we omitted 24 patients from this study. We obtained information from 103 patients who referred for final analyses. Among these, 40 (38.8%) were male and 63 (61.2%) were female. Mean age of males was 33 ± 11 years and for females, it was 31.6 ± 11.7 years. In terms of geographic distribution, 53 (54.1%) resided in Ahvaz and the central part of the province. The rest were from the south (12.2%), west (3.1%), east (4.1%) and north (26.5%) areas of Khuzestan Province (Figure 1). The rate of employment and occupation among males was 70.6%, for females it was 8.3%. The remaining participants were either housewives or students.

In terms of education in males, 9.4% (3) were illiterate, 31.2% (10) had a preliminary education up to high school, 37.5% (12) had diplomas and 21.9% (7) had an academic education. For females, 5% (3) were illiterate, 36.7% (22) had less than a diploma, 25% (15) had a diploma and 33.3% (20) had an academic education. The level of education of 11 patients was unknown. The rate of matrimony was 80.6% (29) in males, 65.4% (38) in females and 3.4% (2) patients were divorced.

Mean height was 164 ± 14 cm in men and 157.5 ± 10 cm in women. Mean BMI at the time of presentation was 22.7 in men and 22.6 in women (Table 1). The most common GI complaints in male patients in descending order were diarrhea (35%), reflux (20%), bloating (17.5%), abdominal pain (15%) and vomiting (15%). These complaints in female patients included diarrhea (49.2%), abdominal pain (31.7%), bloating (31.7%), and vomiting (19%; Table 2). The most common concomitant

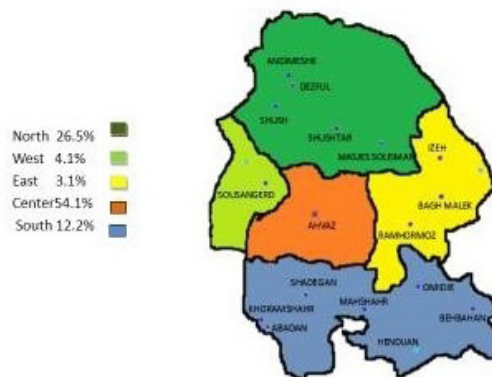


Fig. 1: Geographic distribution of celiac patients in Khuzestan province

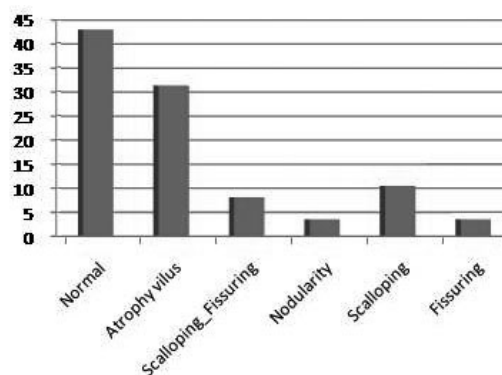


Fig. 2: Endoscopic findings

non-GI disorders among male patients were anemia (17.1%), thyroid disease (14.3%), weight loss (14.3%) and diabetes mellitus (5.7%). Non-GI disorders among females included anemia (33.9%), thyroid disease (12.5%), weight loss (7.1%), asthma (5.4%), diabetes mellitus (3.6%), osteoporosis (3.6%), and infertility (3.6%; Table 3). A total of 17 patients (7 males and 10 females) had nonspecific increased liver enzymes that were less than 3 times more than the upper limit of normal. Approximately 47.3% males and 45.5% females were symptomatic for more than five years before diagnosis. In almost 90% of cases the diagnosing physician was a gastroenterologist. In 8.8% of cases the diagnosing physician was a specialist and 1.1% of cases were diagnosed by a general or family physician (Table 4).

During upper endoscopy the most common find-

Table 1: Patient characteristics.

Variable	Male	Female
Number	40 (38.8%)	63 (61.2%)
Age (average) years	33(±11)	31.6 (±11.7)
Higher education	21.9%	33.3%
Matrimony rate	80.6%	65.4%
Height (average) cm	164.6 ± 14	157.5 ± 10
BMI (average) kg/m ²	22.7	22.6

Table 2: Gastrointestinal (GI) symptoms and complaints*.

GI complaint	Male (%)	Female (%)	Overall (%)
Diarrhea	35	49.2	43.7
Reflux	20	7.9	11.7
Bloating	17.5	31.7	26.2
Abdominal pain	15	31.7	25.2
Vomiting	15	19	17.5
Constipation	7.5	9.5	8.7

*: The sum is more than 100% because some patients had more than one symptom.

Table 3: Concomitant non-gastrointestinal (non-GI) disorders.

Disorder	Male (%)	Female (%)
Anemia	17.1	33.9
Thyroid disorder	14.3	12.5
Weight loss	14.3	7.1
DM	5.7	3.6
Asthma	2.9	5.4
Osteoporosis	0	3.6
Infertility	0	3.6
IBD	0	1.8
Miscellaneous	11.4	19.6

Table 4: Percent of illustrating physicians.

Responsible physician	Percent
Subspecialist (gastroenterologist and endocrinologist)	90
Specialist (internist)	8.8
General or family physician	1.1

ings included duodenal atrophy (31.4%), scalloping (10.5%), scalloping-fissuring (8.1%), fissuring alone (3.5%), duodenal nodularity (3.5%) and normal results in 43% of cases (Figure 2). Pathologic reports were Marsh 0 in 13.2%, Marsh I in 25.3%, Marsh II in 11% and Marsh III in 50.5%. The most

common serologic finding in these patients were anti-TTG (69.9%), anti-EMA (27.7%). In 42 patients, HLA DQ2 was positive.

DISCUSSION

Overall, according to an estimated prevalence the incidence of celiac in society is approximately 1%.^{7,11} According to the results of this study, it is clear that most celiac patients have not been diagnosed and they have undergone nonspecific or symptomatic treatment.

Patients' mean age at the time of diagnosis was 33 years for men and 31.6 years for women. In comparison to a study by Masjedizadeh et al. in Khuzestan Province conducted seven years prior,³⁰ this figure has increased by approximately ten years. This increase has shown that the pattern of celiac diagnosis has changed and the disease does not pertain to the pediatric population per se because a considerable number of individuals were affected by this disease after adolescence.^{21,22} This finding was compatible with a study by Green³ and according to Hauser et al., there was no meaningful relation between age and disease incidence.³¹ The female/male ratio in this study was 1.57 to 1; the disease was more common in women, which supported the results reported by Greco et al. in 2002.³²

In terms of geographic distribution and residence, the results of this study have shown that the central area of Khuzestan Province had the highest numbers diagnosed (54.1%). This area includes the majority of the province's population and also immigrants from other parts of state, followed by patients from the northern area (26.5%). In this region most people are from the Lor ethnic group. These patients have been diagnosed in the center of province (Ahvaz) by gastroenterologists. There were 22% of male patients and 33.3% of female patients who had an academic education who were diagnosed with irritable bowel syndrome (IBS) by general physicians with no specific evaluation. In terms of marital status, 35% of female patients and 20% of male patients were single or divorced which indicated that the impact of this disease decreased

the chances of having a normal, ordinary marriage among these patients.

In this study, mean height for males was 164.6 ± 14 cm and for females it was 157.5 ± 10 cm. Similarly the average BMI among males was 22.7 and for females, it was 22.6 which was similar to the results of a previous study conducted in Shiraz¹¹ and show that for identifying this disease, seeking short and thin persons is not mandatory. The most common disease symptom was diarrhea (35% in males, 49% in females) which supported the results of a study by Masjedizadeh et al. in 2005³⁰ however other GI presentations such as nonspecific, scattered abdominal pain (15% in males, 31% in females), bloating (17.5% in males, 31.7% in females), reflux, vomiting and constipation should not be ignored. In contrast, in this study only 27.7% of cases were positive for anti-EMA, whereas Masjedizadeh reported 85% of cases who tested positive for anti-EMA. The most common serologic marker was anti-TTG (69.9%) which was similar to the study by Hashemi.³³ The exact titers of the serologic markers were not clear because of different laboratories and kits. Pathologic reports in more than 87% of cases reported Marsh I or more advanced stages which was compatible with the results obtained by Masjedizadeh.³⁰ All Marsh 0 patients had positive serology results and celiac related symptoms that responded to a gluten-free regimen before tagging as celiac.

Overall, only 30% of patients involved peculiarly by celiac disease. The most common non-GI concomitant disorders seen in male patients were anemia (17.1%), thyroid disease (14.3%), weight loss (14.3%) and diabetes mellitus (5.7%). These disorders among females included anemia (33.9%), thyroid disease (12.5%), weight loss (7.1%), asthma (5.4%), diabetes mellitus (3.6%), osteoporosis (3.6%) and infertility (3.6%).

Hence, in all patients who suffer from these disorders, particularly those which are unusual and refractory to treatment, the possibility of celiac should be explored. This is especially important prior to making a diagnosis of IBS. As recommend-

ed by Shahbazkhani, all patients suspicious for IBS should be investigated for celiac disease.³⁴

Approximately half of these patients were symptomatic for more than five years prior to diagnosis and in 90% of cases the diagnosis was made by subspecialist physicians and gastroenterologists. Hence, general and family physicians and internists should be made aware of the possibility of celiac disease and its different presentations. This awareness should be emphasized by various educational and post-graduate programs.

On the other hand, during upper endoscopy the macroscopic appearance of duodenum was normal in 43% of cases which indicated that if there was any suspicion celiac disease, the threshold for obtaining a duodenal biopsy during endoscopy should be low.

Celiac disease is a condition that can develop at any age with varied, heterogeneous presentations. In patients who suffer from long-term nonspecific symptoms, prior to a presumed diagnosis of IBS, physicians should be aware of the possibility of celiac disease. Likewise, during an endoscopy, investigations should not be limited to the macroscopic, general appearance of the duodenum. The threshold for obtaining a biopsy should be low.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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