Original Article

Gastrointestinal and Non-gastrointestinal Presentation in Patients with Celiac Disease

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Abstract

Background: Celiac disease (CD) may have a variety of different presentations. This study has aimed to explore the prevalence of gastrointestinal (GI) and non-GI symptoms in patients with CD according to data collected in Italy and Romania (Europe) and Iran (Middle East).

Methods: This is a retrospective cross-sectional study conducted in Iran, Romania and Italy with data collection during the period from May 2009 – May 2011. For each center we included only patients with CD that was confirmed by endoscopy, small bowel biopsies and positive serology. GI symptoms such as abdominal pain, diarrhea, constipation, nausea and vomiting, weight loss and flatulence, as well as additional signs and symptoms of iron deficiency anemia (IDA), osteoporosis, hypertransaminasemia, and other related abnormalities were collected.

Results: Overall, 323 women and 127 men, whose mean age at diagnosis was 34.2 ± 16.47 years were included in this study. Of these, 157 subjects (34.9%) reported at least one GI symptom. The majority of cases had the following primary presenting GI symptoms: diarrhea (13.6%), dyspepsia and constipation (4.0%). Other disease symptoms were reported by 168 (37.3%) patients. The most presenting non-GI symptoms in the majority of cases were anemia (20.7%) and osteopenia (6%). There were statistically significant differences between the majority of symptoms when we compared the reported clinical symptoms from different countries.

Conclusion: This study indicated that upper abdominal disorders such as abdominal pain and dyspepsia were the most common primary complaints among European patients, whereas Iranian patients had complaints of diarrhea and bloating as the classic presentations of CD. For non-GI symptoms, anemia was the most frequent complaint for both Iranian and Italian patients; however it was significantly higher in Iranians.

Keywords: Celiac disease, clinical presentation, gastrointestinal, non-GI symptoms

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Introduction

Celiac disease (CD) is the result of intestinal mucosal damage caused in susceptible subjects by the gluten content of some cereals. CD is often atypical or subclinical, thus numerous cases remain undiagnosed with increased risk of autoimmune disease.[1] The highest incidence (1 in 100 to 1 in 300) of CD is observed in European countries,[1–3] and there is a prevalence of 1 in 166 among apparently healthy blood donors in the Iranian population.[4]

CD might present with either gastrointestinal (GI) or non-GI symptoms. Asymptomatic patients with positive serologic test and villous atrophy on biopsy are usually diagnosed when screened for associated conditions such as diabetes mellitus type 1, epilepsy, iron deficiency anemia (IDA), or a family history of CD.[5,6]

The frequency of CD in Iraqi type 1 diabetic patients is 11.2%.[7] In another study from Kuwait, CD accounts for 18.5% of cases of chronic diarrhea in children.[8] Celiac disease may present in a variety of different ways such as recurrent abdominal pain and bloating, chronic diarrhea, constipation in a few patients, excessive rectal gas, weight loss, mouth sores, fatigue, anemia (iron deficiency), osteopenia (osteomalacia, osteoporosis), swelling, fluid in the abdomen, behavior changes, mood disorders, and growth retardation. Others may have few or no apparent symptoms.[9] This may have important health consequences since dietary avoidance of gluten results in complete remission of the disease, which avoids the two major complications of malignancy and osteoporosis[10] and results in decreased mortality of CD patients.[11] The majority of celiac patients are asymptomatic members of high-risk groups, such as those with diabetes mellitus or thyroid disease and

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close relatives of CD patients.[12]

The recognition that there is a high prevalence of subclinical CD in Western populations and Iran has prompted some experts to call for universal screening.[13,14] Diverse faces of this disease have been observed in the presentation pattern of diagnosed CD in different countries. These studies suggest that histopathological damage is more pronounced in patients presenting with GI symptoms, however the percentage of patients presenting with non-GI symptoms have been increasing over the last decade.

The aim of this study is to explore the prevalence of GI and non-GI symptoms in patients with CD from two regions of the world, Europe (Italy and Romania) and the Middle East (Iran).

Materials and Methods

Patients and settings

This is part of a retrospective cross-sectional study that abstracted data from patients' documents during the period May 2009 – May 2011 in Iran, Italy and Romania. The Iranian component of the study consisted of 100 patients from the Gastroenterology and Liver Diseases Research Center at Taleghani Hospital in Tehran, Iran. This study included 100 Romanian patients from Fundeni Clinical Institute at the Clinical of Gastroenterology and Hepatology in Bucharest. Included were patients from five different areas in Italy: 50 patients from Spedali Civili Brescia in Brescia; 50 patients from St. Orsola-Malpighi Hospital at the University of Bologna in Bologna; 50 patients from the Regional Celiac Center at the University Hospital ''G. Martino'' in Messina; 50 patients from the Gastroenterology and Hepatology Section, Department of Clinical and Experimental Medicine, University of Perugia; and 50 patients from Milan. For each center, we included only confirmed CD cases with endoscopic procedures, small bowel biopsies, and positive serologies. Patients' symptoms were the leading cause for referral to the clinics.

Diagnosis of celiac disease (CD)

All centers used the modified Marsh classification for the diagnosis of celiac disease: Marsh 1 (>25 intraepithelial lymphocytes per 100 enterocytes); Marsh 2 (increased intraepithelial lymphocytes accompanied by crypt hyperplasia); Marsh 3A (partial), Marsh 3B (subtotal), and Marsh 3C (total villous atrophy) as described by Rostami et al.[14] The final diagnosis of CD was established when patients with abnormal mucosal findings were serologically positive for human anti-tissue transglutaminase (tTGA) and/or anti-endomysial antibody (EMA).

In Bologna, Italy, IgA-EMA was investigated by indirect immunofluorescence that used human umbilical cord cryostat sections. Sera were tested at the initial dilution of 1:5 and, when positive, titrated up to the end point. In Iran, IgA-tTG antibody and immunoglobulin A were measured using a commercially available kit (AESKULISA tTG, Germany) and an enzyme-linked immunosorbent assay (ELISA) method. The result was considered positive when a value higher than 15.0 U/ml was recorded. In Bucharest, Romania, the IgA-tTG was determined by ELISA (Inova Diagnostics, Inc.) and IgA-EMA by indirect immunofluorescence.

Assessments

During the same period, we compared the number of biopsy samples taken from each center and their clinical data. For each specimen, the following information was available: sex and age of the patient, location and sample provider, summary of the clinical history, serology, genetic and histopathological findings.

GI symptoms of abdominal pain, diarrhea, constipation, nausea and vomiting, weight loss and flatulence in addition to signs and symptoms such as IDA, osteoporosis, hypertransaminasemia, and other related abnormalities were collected.

Statistical analysis

Information about non-GI symptoms for Romanian patients was not completed and excluded from further analysis. Contingency tables, chi-square and Fisher's exact tests were employed to assess the association between the patient's country of residence and GI or non-GI symptoms. The *t*-test was used to compare the numeric variables. For comparison of continuous data among the groups, we used the ANOVA test.

Results

Overall, there were 323 (71.8%) women and 127 men whose mean age at diagnosis was 34.2 ± 16.47 years (range: 1–87 years) included in this study from Italy, Romania and Iran. Romanian patients were the oldest, with a mean age of 38.9 ± 12.3 years whereas Iranian patients were the youngest (31 ± 13.6 years). In all participating countries, there were more females (Table 1). There was a statistically significant difference between the studied populations according to age ($P = 0.002$).

A total of 157 (34.9%) patients reported at least one GI disease symptom. The main presenting GI symptoms were chronic diarrhea (13.6%), abdominal pain (10.5%), dyspepsia and constipation (4.0%). There were 62% of Iranian patients who reported GI symptoms; the most frequent was abdominal pain (33%), followed by chronic diarrhea (32%), bloating (11%), and constipation (8%). In Italian patients approximately 32% had GI symptoms of which abdominal pain (32%) was predominant followed by dyspepsia (14%) and chronic diarrhea (8.4%). As seen in Table 2, in the 15% of Romanian patients who reported GI symptoms, chronic diarrhea (8%) was observed more frequently followed by abdominal pain (6%) and weight loss (5%).

There were 168 (37.3%) patients who reported other symptoms or diseases. The most presenting non-GI symptoms in the majority of cases were anemia (20.7%) and osteopenia (6%). Iranian patients reported up to 79% of any type of non-GI symptoms that included anemia (55%), osteopenia (25%), neurological (21%), and menstrual abnormalities (14%). In Italian patients, the 34.8% who reported non-GI symptoms had complaints of anemia (15.2%), osteopenia (4%), and thyroiditis (4%). Among Romanians, only the non-GI symptom of asthenia (2.0%) was reported (Table 3). Additionally, 79 (17.9%) patients had the combination of at least one GI and non-GI symptom (Table 3).

There were statistically significant differences observed between most symptoms when we compared the reported clinical symptoms from different countries ($P < 0.05$; Tables 2 and 3).

Marsh 1 and 2 lesions were noted in 26.4% of patients, Marsh 3A was found in 21.8%, Marsh 3B was found in 19.3%, and Marsh 3C in 32.4% of patients. There was a statistically difference for Marsh Classification across the countries (Table 1).

There were 29 (6.4%) patients who reported a family history of CD. However, in Romanian data no reports of family history were registered.

Table 1. Demographics and Modified Marsh Classification in the study countries.

Demographic factors	Country			Total	*P*-value
	Iran	Italy	Romania		
Age (years)	*31 ± 13.6	33.6 ± 18.6	38.9 ± 12.3	34.2 ± 16.4	0.002
Sex					
Male	†36 (36)	70 (38)	21 (21)	127 (28.2)	0.06
Marsh Classification					
1	21 (21)	35 (14)	7 (7)	63 (14)	
2	19 (19)	34 (13.6)	3 (3)	56 (12.4)	
3A	27 (27)	52 (20.8)	19 (19)	98 (21.8)	
3B	13 (13)	49 (19.6)	25 (25)	87 (19.3)	< 0.001
3C	20 (20)	80 (32)	46 (46)	146 (32.4)	
Family history of celiac disease (CD)	1 (1)	28 (11.2)	0	29 (6.4)	< 0.001

*Mean ± SD; †Number (%)

Table 2. Gastrointestinal (GI) symptoms and disorders according to country.

GI symptoms, signs and diagnoses	Country			Total	*P*-value
	Iran	Italy	Romania		
	No. (%)	No. (%)	No. (%)		
Abdominal pain	33 (33)	8 (32)	6 (6)	47 (10.5)	0.41
Chronic diarrhea	32 (32)	21 (8.4)	8 (8)	61 (13.6)	< 0.001
Constipation	8 (8)	9 (3.6)	1 (1)	18 (4)	0.04
Weight loss	5 (5)	6 (2.4)	5 (5)	16 (3.6)	0.33
Bloating	11 (11)	1 (0.4)	0	12 (2.7)	< 0.001
Dyspepsia	3 (3)	36 (14.0)	0	39 (8.7)	< 0.001
Any GI symptoms	62 (62)	80 (32.0)	15 (15)	157 (34.9)	< 0.001
Malabsorption*	0	4 (1.6)	2 (2)	6 (1.3)	0.4

*Malabsorption = a state arising from abnormality in absorption of food nutrients across the GI tract.

Table 3. Non-gastrointestinal (non-GI) symptoms according to country.

Non-GI signs or symptoms	Country *			*P*-value
	Iran	Italy	Total	
	No (%)	No (%)	No (%)	
Anemia	55 (55)	38 (15.2)	93 (20.7)	< 0.001
Dermatitis herpetiformis	3 (3)	4 (1.6)	7 (1.6)	0.23
Osteoporosis	2 (2)	10 (4)	12 (2.7)	0.1
Osteopenia	25 (25)	2 (0.8)	27 (6)	< 0.001
Hypertransaminasemia	4 (4)	7 (2.8)	11 (2.4)	0.16
Thyroiditis	1 (1)	10 (4)	11 (2.4)	0.52
Aftosis	3 (3)	7 (2.8)	10 (2.2)	0.23
Diabetes	0	4 (1.6)	4 (0.9)	0.2
Food allergy	1 (1)	1 (0.4)	2 (0.4)	0.56
IgA deficiency	0	3 (1.2)	3 (0.7)	0.3
Neurological symptoms	21 (21)	2 (0.8)	23 (5.1)	< 0.001
Menstrual abnormality	14 (14)	0	14 (3.1)	< 0.001
Asthenia	0	4 (1.6)	4 (1.6)	0.4
Failure to thrive	7 (7)	4 (1.6)	11 (2.4)	0.003
Low B12/folic acid	0	3 (1.2)	3 (1.2)	0.29
Any non-GI symptoms	70 (79)	87 (34.8)	168 (37.3)	< 0.001
Combination of GI and non-GI symptoms	46 (46)	33 (12.8)	79 (17.6)	< 0.001

*Information about non-GI symptoms for Romanian patients was not completed and therefore excluded from analysis.

Despite the variability in symptoms among different countries shown in this study, no statistical correlation was found between total GI or non-GI symptoms and their combination with demographic factors that included sex and age. Additionally, this correlation was not significant for histology type (Table 4).

Discussion

The results of this study indicated that upper abdominal disorders such as abdominal pain and dyspepsia were the most common primary complaints in Italian or Romanian patients, which was similar to other European countries.[16,17] However, for Iranian patients, abdominal pain, chronic diarrhea and bloating were considered classic presentations. Studies have shown that CD is the most common cause of adult chronic non-bloody diarrhea in Tehran and atypical symptoms in Isfahan[18,19]; this is a common presentation for CD in the Middle East.[6,20]

In study by Emami et al., typical symptoms were the most common symptoms in patients with malabsorption. Therefore these patients should undergo duodenal biopsy, irrespective of serology. These researchers proposed that when endoscopic evaluation is indicated because of symptoms, a routine duodenal biopsy should be performed.[19]

In another study the prevalence of CD was determined in patients with unexplained IDA. The authors recommended that CD should be considered in any adult patient with unexplained IDA, irrespective of GI symptoms.[21]

In our study females comprised 72% of all patients, which was

Table 4. Comparison of demographic factors and pathological classification of celiac disease (CD) among patients with and without gastrointestinal (GI) symptoms.*

	GI symptoms No (%)	*P*-value	Non-GI symptoms No (%)	*P*-value	Combination No (%)	*P*-value
Age group (years)						
< 15	15 (26.3)	0.32	22 (38.6)	0.97	6 (10.5)	0.24
15–30	47 (37.6)		46 (36.8)		26 (20.8)	
> 30	95 (35.4)		100 (37.3)		47 (17.5)	
Sex						
Male	46 (36.2)	0.74	43 (33.9)	0.39	21 (16.5)	0.78
Female	111 (35.4)		125 (38.7)		58 (18)	
Marsh Classification						
1	20 (31.7)	0.58	22 (34.9)	0.71	10 (15.9)	0.78
2	24 (42.9)		24 (42.9)		13 (23.2)	
3A	37 (37.8)		39 (39.8)		18 (18.4)	
3B	27 (31)		34 (39.1)		15 (17.2)	
3C	49 (33.6)		49 (33.6)		23 (15.8)	

* CD patients without GI or non-GI symptoms were not included for analysis in this table.

similar to the United States, Europe and the Middle East, all of which have a female predominance.[22–24] The reason behind this female predominance is unknown, but could be explained by the fact that the prevalence of immune-mediated diseases in general is higher in women.[15] In this study we observed no difference among males and females according to GI or non-GI symptoms, whereas some studies presented more GI symptoms for males and more non-GI symptoms for females.[15,24]

Wheat and barley comprise a major portion of the Middle Eastern diet for most of the population; there are very few alternative diets to gluten-containing crops.[4] Therefore the severity of CD in the form of anemia or osteopenia may be higher in this area compared to Western countries.[20] Anemia was the highest non-GI symptom reported for both Iranian and Italian patients; however, it was significantly higher in Iranian data. A total of 25% of the Iranian patients reported osteopenia.

Some studies reported a high number of neurological disorders in patients with CD.[25,26] In contrast to Italian and Romanian patients, neurological symptoms were the third highest non-GI presentation in the Iranian database. The link between CD and neurological disorders might be attributed to the genetic background, most importantly the HLA region and other markers.[26]

This multicenter study has been performed in different populations where CD is very common and shows that the clinical picture of CD might be variable. In conclusion, we have found that lower GI symptoms and anemia were higher in the Middle Eastern population whereas upper abdominal symptoms (abdominal pain and dyspepsia) were the most common primary complaints among European patients. We have observed a significant association with non-GI conditions such as diabetes type I, abnormal liver enzymes and other autoimmune conditions in Italian patients. It is likely that a significant number of patients who undergo endoscopies for GI and non-GI symptoms, such as diarrhea, dyspepsia and anemia, might have CD.

Limitations to this study were the retrospective design; data were collected according to non-standardized patient's documents; some of the information pertaining to symptoms in Romanian patients was not completed; and we did not have access to socioeconomic or racial data. Since we included CD patients from only one center in Iran, thus our results were not representative of the entire picture for CD in Iran.

This study has suggested that a high index of suspicion for CD would be required to detect CD in Iranian patients with atypical presentation. Similarly anemia, dyspepsia and other upper GI symptoms are more likely to be consistent with CD in European countries and may warrant screening for CD.

Conflicts of interest

The authors declare that there is no conflict of interest.

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References

1. Rostami Nejad M, Rostami K, Emami MH, Zali MR, Malekzadeh R. Epidemiology of celiac disease in Iran: a review. *Middle East J Dig Dis*. 2011; **3:** 5 – 12.
2. Rostami Nejad M, Hogg-Kollars S, Ishaq S, Rostami K. Subclinical celiac disease and gluten sensitivity. *Gastroenterol Hepatol Bed Bench*. 2011; **4:** 102 – 108.
3. Barada K, Abu Daya H, Rostami K, Catassi C. Celiac disease in the developing world. *Gastrointest Endosc Clin N Am*. 2012; **22**:773 – 796.
4. Shahbazkhani B, Malekzadeh R, Sotoudeh M, Moghadam KF, Farhadi M, Ansari R, et al. High prevalence of coeliac disease in apparently healthy Iranian blood donors. *Eur J Gastroenterol Hepatol*. 2003; **15:** 475 – 478.
5. Emami MH, Karimi S, Kouhestani S. Is routine duodenal biopsy necessary for the detection of celiac disease in patients presenting with iron deficiency anemia? *Int J Prev Med*. 2012; **3:** 273 – 277.
6. Emami MH, Taheri H, Kohestani S, Chitsaz A, Etemadifar M, Karimi S, et al. How frequent is celiac disease among epileptic patients? *J Gastrointestin Liver Dis*. 2008; **17:** 379 – 382
7. Mansour AA, Najeeb AA. Coeliac disease in Iraqi type 1 diabetic patients. *Arab J Gastroenterol*. 2011; **12:** 103 – 105.
8. Shaltout AA, Khuffash FA, Hilal AA, el Ghanem MM. Pattern of protracted diarrhoea among children in Kuwait. *Ann Trop Pediatr*. 1989;

9: 30 – 32.
9. Bethesda. Celiac disease. National Institutes of Health Consensus Development Panel on Celiac Disease; 2004.
10. Feighery C. Coeliac disease. *BMJ*. 1999; **319:** 236 – 239.
11. Corrao G, Corazza GR, Bagnardi V, Brusco G, Ciacci C, Cottone M, et al. Mortality in patients with celiac disease and their relatives: a cohort study. *Lancet*. 2001; **358:** 356 – 36112.
12. Fasano A, Catassi C. Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology*. 2001; **120:** 636 – 651.
13. Ventura A, Magazzù G, Greco L. Duration of exposure to gluten and risk for autoimmune disorders in patients with celiac disease. *Gastroenterology*. 1999; **117:** 297 – 303.
14. Rostami K, Kerckhaert J, Tiemessen R, von Blomberg BM, Meijer JW, Mulder CJ. Sensitivity of antiendomysium and antigliadin antibodies in untreated celiac disease: disappointing in clinical practice. *Am J Gastroenterol*. 1999; **94:** 888 – 894.
15. Tajuddin T, Razif S, Dhar R, Thorne J, Murray FE. Clinical presentation of adult coeliac disease. *Ir Med J*. 2011; **104:** 20 – 22.
16. Collin P, Huhtala H, Virta L, Kekkonen L, Reunala T. Diagnosis of celiac disease in clinical practice: physician's alertness to the condition essential. *J Clin Gastroenterol*. 2007; **41:** 152 – 156.
17. Shahbazkhani B, Mohamadnejad M, Malekzadeh R, Akbari MR, Esfahani MM, Nasseri-Moghaddam S, et al. Coeliac disease is the most common cause of chronic diarrhoea in Iran. *Eur J Gastroenterol Hepatol*. 2004; **16:** 665 – 668.
18. Al-Bayatti SM. Etiology of chronic diarrhea. *Saudi Med J*. 2002; **23:** 675 – 679.
19. Emami MH, Kouhestani S, Karimi S, Baghaei A, Janghorbani M, Jamali N, et al. Frequency of celiac disease in adult patients with typical or atypical malabsorption symptoms in Isfahan, Iran. *Gastroenterol Res Pract*. 2012; **2012:** 106965.
20. Masjedizadeh R, Hajiani E, Hashemi J, Shayesteh AA, Moula K, Rajabi T. Celiac disease in South-West of Iran. *World J Gastroenterol*. 2006; **12:** 4416 – 4419.
21. Emami MH, Karimi S, Kouhestani S. Is routine duodenal biopsy necessary for the detection of celiac disease in patients presenting with iron deficiency anemia? *Int J Prev Med*. 2012; **3:** 273 – 277.
22. Green P, Stavropoulos S, Panagi S, Goldstein S, McMahon D, Absan H, et al. Characteristics of adult celiac disease in the USA: results of a national survey. *Am J Gastroenterol*. 2001; **96:** 126 – 131.
23. Ciacci C, Cirillo M, Sollazzo R, Savino G, Sabbatini F, Mazzacca G. Gender and clinical presentation in adult celiac disease. *Scand J Gastroenterol*. 1995; **30:** 1077 – 1081.
24. Rostami Nejad M, Rostami K, Pourhoseingholi MA, Nazemalhosseini Mojarad E, Habibi M, et al. Atypical presentation is dominant and typical for coeliac disease. *J Gastrointestin Liver Dis*. 2009; **18:** 285 – 291.
25. Luostarinen L, Himanen SL, Luostarinen M, Collin P, Pirttilä T. Neuromuscular and sensory disturbances in patients with well treated coeliac disease. *J Neurol Neurosurg Psychiatry*. 2003; **74:** 490 – 494.
26. Taddeucci G, Bonuccelli A, Polacco P. Diagnosis of coeliac disease in patients with isolated neuropsychological symptoms. *Pediatr Med Chir*. 2005; **27:** 43 – 45.