The Canadian Celiac Health Survey

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The Canadian Celiac Health Survey

ABSTRACT

Purpose:

To characterize the diagnostic process, frequency of associated disorders, family history and impact of a gluten-free diet in individuals with celiac disease.

Results:

All members of the Canadian Celiac Association (n=5,240) were surveyed with a questionnaire. Respondents included 2,681 adults with biopsy-proven celiac disease. The mean age was 56 years. Most common presenting symptoms included abdominal pain (83%), diarrhea (76%) and weight loss (69%). The mean delay in diagnosis was 11.7 years. Diagnoses made prior to celiac disease included anemia (40%), stress (31%) and irritable bowel syndrome (29%). Osteoporosis was common. Prior to diagnosis, 27% of respondents consulted three or more doctors about their symptoms.

Conclusions:

Delays in diagnosis of celiac disease remain a problem. Associated medical conditions occur frequently. More accurate food labeling is needed. Improved awareness of celiac disease and greater use of serological screening tests may result in earlier diagnosis and reduced risk of associated conditions.

Key words: Celiac, gluten-free diet, survey

The Canadian Celiac Health Survey

BACKGROUND:

Celiac disease (gluten sensitive enteropathy) is an auto-immune, permanent intolerance to specific peptides of gluten-containing cereals (including wheat, rye and barley), that causes progressive atrophy of the villi of the small intestine in genetically susceptible individuals (1). Malabsorption of iron, folate, calcium and fat-soluble vitamins from the proximal small intestine is common, resulting in anemia and reduced bone density. Diarrhea and reduced absorption of other macro and micronutrients may occur if the disease progresses to the distal small bowel (2). In addition to its impact on the gastrointestinal tract, untreated celiac disease can affect other body systems including the blood, skeletal, endocrine, neurologic and reproductive systems (3).

Celiac disease can manifest with a wide number and variety of symptoms, many of which do not appear to be gut-related. Anemia is common, especially among women (4) and may be the only presenting sign (5). The onset of celiac disease is often silent (6). Celiac disease can also be expressed as a bilateral itchy skin rash, that often presents with mild or no gastrointestinal symptoms even though villous atrophy is present in the majority of patients (7). Long delays in diagnosis of celiac disease are due largely to the lack of awareness of its wide diversity of clinical presentations (5,8,9,10)

For many years celiac disease was regarded as a childhood disease. However, it is now widely recognized that the symptoms can develop at any age in genetically predisposed individuals (8). Acute symptoms in adults are sometimes triggered by gastroenteritis, gastrointestinal surgery and pregnancy (2).

Until recently, celiac disease was considered to be less common in North America than in Europe. However, in a large multi-center study (n = 13,145) in the United States a prevalence of celiac disease of 1 in 133 in the general population was reported (11). Prevalence among first-degree and second-degree relatives of individuals with celiac disease was 1 in 22 and 1 in 39 respectively, and in symptomatic patients 1 in 56. Although celiac disease is now recognized as one of the most common disorders in both Europe and the United States, it remains one of the most under diagnosed. Highly sensitive serological tests, including endomysial antibody (EMA) and tissue transglutaminase antibody (tTG), are now available for more accurate screening of individuals at risk of having celiac disease (12). When more widely used they could help reduce the long delays now reported in its diagnosis.

Untreated, celiac disease is accompanied by an increased risk of osteoporosis (13), reproductive disorders in both females and males (14,15,16), malignancy (17,18,19) and a number of other autoimmune diseases, including Type 1 diabetes (20,21,22) and autoimmune thyroid disease (23,24). Early diagnosis and treatment of celiac disease has been shown to decrease the risk of many of these associated disorders, including osteoporosis (25,26) reproductive disorders (15,16,27,28) and malignancy (17,18,29,30).

Currently, the only treatment for celiac disease is adherence to a strict gluten-free diet for life. Many find this diet complex, expensive and difficult to follow (31). More information is needed on the impact of having to follow a strict gluten-free diet for life by individuals with celiac disease.

OBJECTIVES:

The objectives of this study were:

1. To obtain information about the clinical features and the length and nature of the diagnostic process in individuals with celiac disease.
2. To determine what proportion of individuals and their first-degree relatives had other immune-mediated and associated medical conditions.
3. To evaluate the health-related quality of life of individuals with celiac disease.

MATERIALS AND METHODS:

The Professional Advisory Board of the Canadian Celiac Association (CCA), in collaboration with the University of Ottawa, conducted the Canadian Celiac Health Survey. A comprehensive questionnaire was developed that included 76 different questions in 11 sections including demographics, clinical features and diagnosis. Specific questions were directed to determine whether the diagnosis was confirmed by small bowel biopsy, symptoms prior to diagnosis, misdiagnoses, duration from the onset of symptoms to diagnosis, and associated medical conditions among the respondents and their first-degree relatives. Specific questions on bone disease and reproductive health were included. Quality of life was evaluated with the SF-12 generic health survey, (32) along with a section relating to the impact of a gluten-free diet on quality of life.

The survey questionnaire was reviewed by two international experts in celiac disease, by members of the CCA Professional Advisory Board, and was pre-tested in 14 CCA members for readability and face validity. A pilot survey was conducted on 414 members of the Ottawa Chapter of the CCA in 2001 to confirm the feasibility of a national survey (33). The questionnaire was mailed by the CCA in October 2002 to all its members (n = 5,240). The membership had broad representation from all provinces of Canada. Only one mailing was done. Anonymity was maintained by not coding the questionnaires. Since memberships in the Canadian Celiac Association are family memberships, only one member with celiac disease per household was instructed to complete the questionnaire. Informed consent was obtained from the participants and ethics approval was received from Queen's University, Kingston, Ontario, Canada.

The data was analyzed using SPSS v10 for Windows. Logic checks were done using cross-tabulations for key variables. Frequency distributions and cross-tabulations were conducted for all variables. Chi-square tests for categorical and Student's t-tests for normally distributed continuous variables were performed.

RESULTS:

There was a 65% response rate (n = 3,408). Of the respondents, 504 (15%) individuals were excluded from analysis as they did not have biopsy-proven celiac disease or physician-diagnosed dermatitis herpetiformis. Another 55 respondents were excluded either because the gender was not correctly identified (n = 35) or the questionnaire was not adequately completed (n = 20). For the purpose of this paper, the analysis was confined to adult members (n = 2,681) who had biopsy-proven celiac disease or who had been diagnosed with dermatitis herpetiformis by a

physician. The results of the pediatric population (age <16 years, n = 168) will be published elsewhere.

Of the survey respondents, 74.5% were female. The mean age of participants was 56 years (SD±15, range 16-90 yrs). Most participants (69%) had some post-secondary education. The mean age at diagnosis was 46 (SD±16) years (48 for males and 45 for females) as shown in Figure 1. Two hundred and eighty-three (11%) respondents had been told by a physician that they had dermatitis herpetiformis. The mean duration of disease after diagnosis was 10 years (median duration 7 years). Seven percent had been first diagnosed as a child and of these 57% reported that their symptoms had disappeared and then reoccurred during adulthood. Of those who reported the date of diagnosis (n = 2,611), 62% were diagnosed prior to 1998 and 38% were diagnosed during or after 1998. Only 378 (14%) respondents with biopsy-confirmed disease reported having serological testing performed at the time of diagnosis. Of those individuals diagnosed prior to 1998, 3.8% had a positive serological test, and in those diagnosed in 1998 or later 31.5% had a positive serological test.

Clinical symptoms and recovery from symptoms

The various clinical symptoms in individuals prior to their diagnosis of celiac disease are listed in Table 1. Although bloating and abdominal pain (83%) and diarrhea (75%) were most commonly reported, a wide variety of other more atypical symptoms were reported by a large percentage of the respondents. They included: weight loss, extreme weakness/tiredness, mood swings/depression, migraine, easy bruising, constipation, mouth ulcers, edema of the hands and feet, and others. The clinical presentations reported in this survey did not differ in those individuals diagnosed within the last ten years compared to individuals diagnosed for more than ten years.

Table 1 (Column 2) presents the number and percent of respondents who reported full recovery from each clinical symptom after being on a gluten-free diet. For example, 52% of those presenting with bloating and abdominal pain reported full recovery when on a gluten-free diet.

Prior diagnoses and possible triggers

Diagnoses given to the respondents prior to their confirmation of celiac disease are presented in Table 2. They included anemia (40%), followed by stress, irritable bowel syndrome, vitamin deficiency, peptic ulcer, food allergies, and chronic fatigue syndrome.

In response to a question regarding possible triggers that occurred within six months prior to onset of their clinical symptoms of celiac disease, 23% of respondents (n = 628) identified severe stress, 9% (n = 234) reported a severe gastrointestinal infection, 8% (n = 221) had a pregnancy and 7% (n = 197) had major surgery.

Delays in diagnosis

Prior to diagnosis, 37% of respondents consulted two or more family doctors about their symptoms, 27% consulted three or more physicians and 14% consulted two or more gastroenterologists. The variety of specialists consulted included gastroenterologists, rheumatologists, neurologists, hematologists, dermatologists, and others. In 77% of cases, a gastroenterologist confirmed the final diagnosis. The mean delay in diagnosis after onset of

symptoms was 11.7 years (median delay 5 years). Delays in diagnoses were not shorter in those individuals diagnosed within the last 5 years compared to those diagnosed prior to 1998 (P = 0.38).

Associated medical conditions

Table 3 lists the medical conditions that were diagnosed in the respondents. The most common were iron deficiency anemia, osteoporosis, lactose intolerance, hypothyroidism, rheumatoid arthritis, and type 1 diabetes mellitus.

In response to the questions on bone health, 42% (n = 1,103) reported a history of a previous fracture and 16% had broken at least one wrist. Bone density had been measured in 57% (n = 1,523) of respondents. Thirty five percent (n = 838) of 2,365 respondents said they had been diagnosed with either osteoporosis (26%) or osteopenia (9%). Among this group, 83% (n = 695) reported taking calcium and 77% (n = 645) were taking vitamin D. In addition 18% were taking one anti-osteoporosis medication: alendronate, risedronate, calcitonin, or raloxifene and 9% were taking either estrogen or estrogen/ progesterone.

For malignancies, 2% (n = 53) reported a diagnosis of breast cancer, 1% (n = 30) colon cancer, 0.9% (n = 25) melanoma, 0.7% (n = 19) lymphoma and 0.4% (n = 11) reported having small intestinal cancer.

Reproductive health

Among the 1,939 female respondents, 14.5% (n = 282) reported difficulty conceiving children, 4.7% had been treated for infertility, 31 % (n = 597) had a history of a miscarriage and, of the latter group, 35% had 2 or more miscarriages. The mean age at menarche was 13 years.

Among the 659 males who responded, 46% reported decreased sex drive, 17% had been tested for sperm count and of those 27% had low counts.

Associated medical conditions among first-degree relatives

Fifteen percent of the respondents had one or more first-degree relatives who had been diagnosed with celiac disease. Table 4 lists a number of celiac-associated conditions among the first-degree relatives of the respondents. For example, 13% of respondents had one or more first-degree relatives with hypothyroidism and 9% had one or more first-degree relatives with type I diabetes.

Health Related Quality of Life

The SF-12 scores were used to estimate the overall, generic health-related quality of life (HRQoL) (32). The results were compared to normative Canadian data on the SF-36 (34). The mean summary score for physical function (PCS) was 48 (range 12 to 65) and 50 (range 12 to 68) for mental function (MCS) (n = 2,480). These were similar to the SF-36 summary scores for the Canadian population; PCS of 50 and MCS of 52 (34). However, when analyzed according to gender, the mean PCS and MCS were significantly greater in males than females (PCS of 50 and MCS of 52 in males versus PCS of 47 and MCS of 49 in females, P < 0.001). In addition, individuals who were diagnosed within the last year (N = 398) had a significantly lower HRQoL for the MCS, when compared to those diagnosed over a year or more (P < 0.001).

Impact of gluten-free diet

In response to the question on compliance with gluten-free diet, 90% described their diet as strictly gluten-free. Eighty-one percent of respondents avoided going to restaurants some or most of the time. Thirty-eight percent avoided traveling some or most of the time and 94% brought gluten-free foods with them when traveling.

When asked what two factors would contribute most to improving the lives of individuals with celiac disease, the respondents identified earlier diagnosis (60.5%) and better labeling of gluten-containing foods (52%).

DISCUSSION:

This national survey is the largest of its kind ever conducted in individuals with celiac disease. We had an excellent response to the survey, which included representation from all ten Canadian provinces. The female/male ratio of 3:1 was similar to that observed in a recent U.S. survey (35), and the mean age at diagnosis was slightly lower at 46 years compared to 53 years. Eighty-six percent of respondents had biopsy-proven celiac disease which is similar to the 82% reported on an earlier Canadian survey (36) and slightly higher than the 75% reported in the U.S. survey (35). The results of the national survey were similar to those of the pilot survey, suggesting good accuracy in the data obtained (33).

In this survey and others (35,37), many of the respondents had received one or more different diagnoses before their diagnosis of celiac disease. The most common were anemia, stress, irritable bowel syndrome, and chronic fatigue syndrome. In a recent U.S. survey nearly 40% of the respondents were previously diagnosed with irritable bowel syndrome (35) compared to 29% in the present survey. Some studies have suggested that celiac disease might predispose individuals to irritable bowel syndrome (38,39). Celiac disease should be considered as a diagnostic possibility in individuals with symptoms of irritable bowel syndrome.

Symptoms of celiac disease are sometimes triggered by gastroenteritis, gastrointestinal surgery and pregnancy (2), all of which were reported in this survey. It has been suggested that gastroenteritis or gastrointestinal surgery may cause non-specific up-regulation of the gut immune system, which triggers the onset of symptoms in patients with previously "silent" celiac disease (40).

Bloating, abdominal pain and diarrhea, are regarded as more classic presentations of celiac disease, and were the most commonly reported symptoms. Diarrhea was reported by 76% of respondents, which is slightly lower than the 85% reported in the U.S. survey (35), but much higher than the 50% reported in Scotland where celiac disease is considered to be common. (41). In a recent National Institutes of Health (NIH) consensus statement it was recommended that patients with chronic diarrhea, malabsorption and abdominal distention should be screened for celiac disease (5).

Of interest was the large percentage (32%) of respondents who reported constipation prior to diagnosis. These results are very similar to those of a recent US survey in which 38.6% of their patients with celiac disease had constipation as a pre-diagnosis symptom, and most reported its resolution after 6 months on a gluten-free diet (42).

A large number of other more atypical symptoms were reported that may not be as readily recognized as gut related. They included iron deficiency anemia (49%) followed by extreme

weakness, depression, bone/joint pain, mouth ulcers and migraine (Table 1). All of these are symptoms commonly reported in celiac disease (3,5,40,43).

A high prevalence of celiac disease among patients with lactose intolerance has been reported (44). In our survey 18% of the respondents had lactose intolerance, which can cause similar gastrointestinal discomfort as celiac disease. Limiting lactose intake until the gut has healed may be necessary in some patients.

Although changes over time in the clinical presentation of celiac disease in adults have been reported (41), no differences in clinical presentation of the disease were noted in this survey between individuals diagnosed for longer than ten years, compared to those diagnosed within the last ten years.

Among the 7% of respondents diagnosed with celiac disease as children, more than half reported that their symptoms disappeared, only to reappear in adulthood, which was very similar to the U.S. survey (35). When patients are diagnosed with celiac disease they should be informed that celiac disease is a permanent intolerance to gluten, and that a strict gluten-free diet should be followed for life.

Long delays in diagnosis were reported in this survey confirming findings by others (35,45). Many respondents reported frustration and concern about inaccuracy and delays in their diagnosis. Complaints of a lifetime of tiredness and anemia were common. The numbers of family physicians and the variety of specialists who were consulted about the symptoms of the respondents attest to problems experienced by many physicians in diagnosing this disease. In this survey, delays in diagnosis had not improved in the past ten years, despite the increased amount of information in the literature about the diverse clinical presentations of this disease.

Of note was the increase from 3.8% to 31.5% in positive serological results among patients screened before 1998, and those screened after 1998. Since then, further improvements have been made in serological screening tests. The most specific tests are IgA-based endomysial antibody (EMA) and the more recent tissue transglutaminase (tTG) antibody test, with the human recombinant tTG now becoming the test of choice (46).

Increased screening of at-risk individuals has been recommended for first degree relatives of individuals with celiac disease (11), patients with persistent iron deficiency, especially when it does not respond to iron supplements (8), chronic diarrhea, unexplained weight loss, and chronic fatigue (5,9), type 1 diabetes with gastrointestinal disorders (21) and lactose intolerance (44). It should be noted that both serological screening tests and the intestinal biopsy must be done while the individual is consuming gluten, since antibody levels drop rapidly once a gluten-free diet is initiated, often resulting in inconclusive or negative results (47). In an attempt to improve diagnosis of celiac disease in a large population of adults in Italy, a program of celiac awareness, targeted to primary care physicians, has been launched (10). This program has proven very successful in speeding up diagnosis of this disease. Similar programs in North America could help to improve diagnosis and quality of life and reduce the risk of many of the complications of this common disease.

Currently the only treatment for celiac disease is a gluten-free diet, and it is often assumed that the symptoms will resolve when the diet is followed. However, one report suggested that gastrointestinal symptoms in patients with celiac disease on a gluten-free diet are significantly higher than controls, especially among women, (48). In our survey, 90% of the respondents reported being on a strict gluten-free diet, but low recoveries from both gastrointestinal and more atypical symptoms were reported (Table 1, Column 2). The low recoveries from gastrointestinal symptoms may be due, at least in part, to continued consumption of gluten. Inadvertent

consumption of gluten has been identified as a major reason for incomplete recovery from symptoms in more than 50% of individuals (49). Although individuals with celiac disease may think they are following a gluten-free diet, many may not be aware of a number of hidden sources of gluten in their diet. To ensure that the diet is well understood, newly diagnosed patients should be referred to a dietitian with expertise in celiac disease for education and follow up (5,50). Continuing gastrointestinal symptoms can also be caused by co-existing irritable bowel syndrome (38) and/or lactose intolerance (44). In this survey, 18% of the respondents had been diagnosed with lactose intolerance, and only 36% reported full recovery on a gluten-free diet.

Anemia in celiac disease is common. Serum ferritin levels are known to be associated with the extent of villous atrophy (51). In the present survey recovery from anemia was reported by only 72% of the respondents which is much lower than the 95% recovery reported among a study on newly diagnosed adults with celiac disease who were treated by a gluten-free diet alone (52). The negative impact of continued consumption of gluten on villous recovery is a possible explanation for these results. Individuals following a strict gluten-free who do not recover from their symptoms should consult with their physician for further investigation.

The association between celiac disease and osteoporosis has been highlighted in a number of studies (13,26,53), and routine screening for osteoporosis among patients with celiac disease is recommended (13,54). In this survey, of the total respondents 35% had been diagnosed with osteoporosis or osteopenia and 57% reported having their bone density measured. This result could be expected to be even higher if bone density evaluations had been done on all the respondents. Of this group, less than 20% were taking an anti-osteoporosis medication. Wrist fractures are the most common fractures in celiac disease (26). In this survey 16% of respondents reported a history of a fracture of one or more wrists. This may, in part, reflect cortical bone loss that results from secondary hyperparathyroidism which is common in celiac disease (55). Many researchers have reported improvements in bone density resulting from treatment with a gluten-free diet, especially during the first year of treatment (56).

The association between celiac disease and other autoimmune conditions such as thyroiditis and type 1 diabetes is well established (23). In this survey respondents reported having hypothyroidism (12%) and type I diabetes (2%), which is similar to previous studies (21). There is some evidence that the risk of developing other autoimmune conditions increases with length of exposure to gluten (23), indicating the need for early diagnosis and treatment.

A recent study indicated that celiac disease is associated with a far greater variety of malignant lymphomas than was previously shown (19). European population-based studies have shown that continued exposure to gluten in individuals with celiac disease is associated with an increased risk of mortality from malignancies, especially T cell lymphoma (57), and adenocarcinoma of the small intestine (17,58). An increased risk of small bowel malignancies in a North American population with celiac disease has been reported (59), and our results were similar. However, because of the anonymity of the respondents, the temporal relationship between diagnosis of celiac disease and malignancy could not be confirmed from pathology reports. Studies have shown that maintaining a gluten-free diet can reduce the risk of developing malignancy (17,29).

Both women and men reported reproductive problems, which is consistent with other studies (14,60,61). In a case controlled study of untreated and treated women with celiac disease, it was reported that the relative risk of abortion (which as 8.9 times higher among untreated patients), a higher risk of low birth weight babies and short breast feeding periods could all be corrected

after a year of treatment with a gluten-free diet (27). Celiac disease in the father can also have an impact on pregnancy outcome, possibly because of genetic factors, resulting in lower birth weight and perhaps a shorter duration of pregnancy (61). It has been suggested that women having recurrent miscarriages or intrauterine growth retardation be screened for celiac disease (14). However, general screening of all pregnant women is not recommended unless they show clinical symptoms of celiac disease (16,62).

Among the first-degree relatives 15% were diagnosed with celiac disease, which is higher than the 10% often reported (11). Many first-degree relatives were reported to have a wide variety of medical conditions associated with celiac disease (Table 4), which are similar to those reported elsewhere (63). They included iron deficiency anemia, osteoporosis and a number of autoimmune diseases including hypothyroidism (13%) and type 1 diabetes (9%). The presence of one or more of these conditions, in a first-degree relative of someone with celiac disease, should raise a suspicion about the need for screening for celiac disease.

Over 80% of individuals felt that their health improved after starting a gluten-free diet. Their Health-Related Quality of Life (HRQoL) scores were found to be similar to the mean Quality of Life for Canadians. However, when the results were analyzed according to gender, the scores were significantly lower in women. In a Swedish study, 89 individuals who had been on a gluten-free diet for ten years did not rate their quality of life as high as age and sex matched members of the general population, with the women scoring lower than the men (64). A follow-up study reported that women expressed more concern about the impact of a gluten-free diet on socializing and having to abstain from important things in life (65). Also, women with celiac disease continue to report more gastrointestinal symptoms than men (48) that may, in part, explain the lower HRQoL scores.

Non-compliance with the diet; severity of illness at diagnosis; and the presence of other associated diseases are other factors that can negatively affect HRQoL (66). The lower scores reported by respondents in the first year after diagnosis were not unexpected, since the difficulties encountered in learning and following a gluten-free diet, and the lifestyle changes that it imposes, especially in the early stages, can often be overwhelming.

Celiac disease is currently treated only by diet, but a lifetime of major dietary change is a difficult challenge. Hence we were interested in looking at disease-specific quality of life issues as they relate to a gluten-free diet. Many (81%) avoided going to restaurants and some (38%) avoided traveling, all of which have an impact on their perceived quality of life. These results are similar to those of a recent survey in the U.S. (67).

We wish to acknowledge some limitations of the survey. Only members of the Canadian Celiac Association (CCA) were surveyed, which could have resulted in a selection bias since not all individuals with celiac disease become members of the CCA. As with any survey, the responses are self-reported and are subject to recall bias. However, the self-reporting was of less concern given the measures taken to ensure strict anonymity. There was no control group without celiac disease, but the large number of respondents and the similarity of the results with those of the pilot study suggest good accuracy of the results.

CONCLUSIONS:

The results of this study emphasize the need for early diagnosis, treatment and follow-up of celiac disease. Despite the availability of excellent antibody screening tests, delays in diagnosis

of celiac disease remain a key issue. This needs to be addressed given the current prevalence estimates of 1 in 133 having celiac disease in North America. Better awareness among family physicians, dietitians and other health professionals about the variety of clinical presentations, especially anemia, osteoporosis, reproductive problems and autoimmune disorders is essential. Utilization of antibody testing for screening at-risk groups, especially first-degree relatives, would be potential strategies to reduce delays in diagnosis.

Having to follow a strict gluten-free diet for life has a major impact on the quality of life of individuals with celiac disease. Given the difficulty in determining the gluten-free nature of foods, there is a need for food manufacturers to ensure complete and accurate labeling of gluten sources and for food service establishments to provide accurate information on the gluten content of food served. Comprehensive education of newly diagnosed patients, by dietitians and physicians with expertise in celiac disease, will help optimize compliance, improve quality of life and reduce the risk the numerous complications associated with this common disease.

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Competing Interests – None.

Figure 1: Age at diagnosis of celiac disease

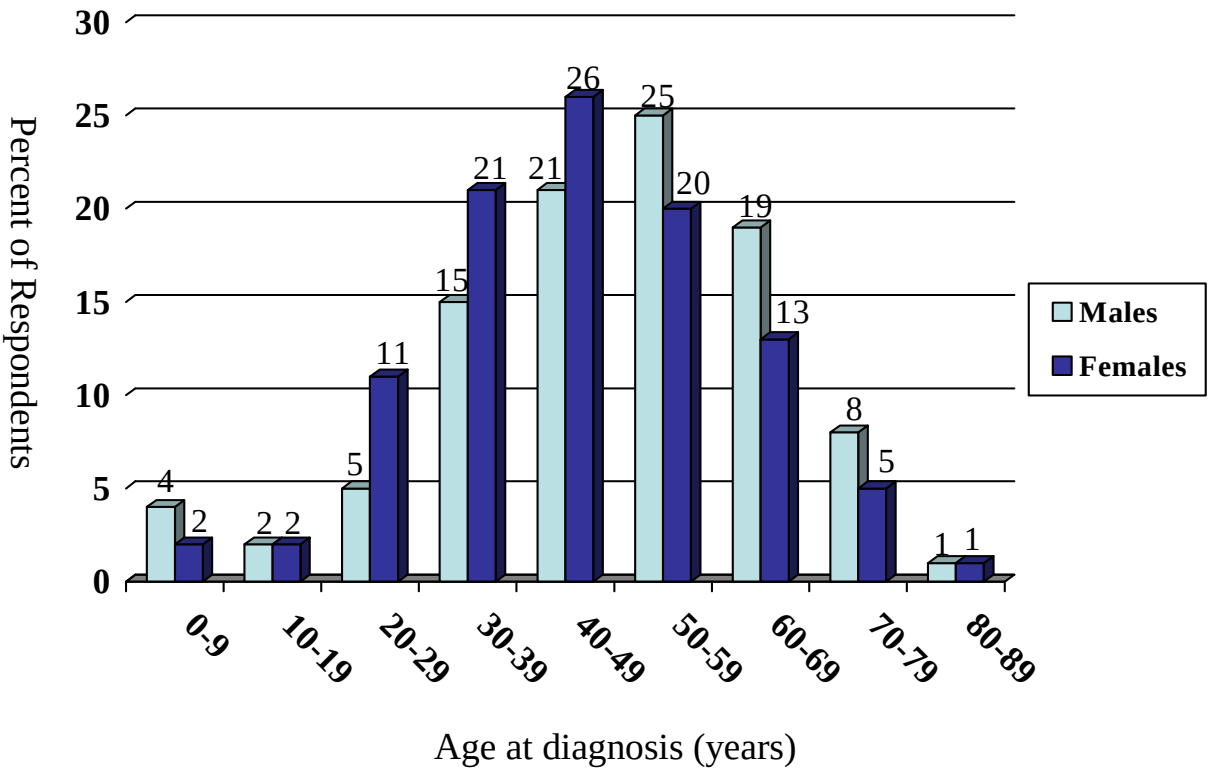

Table 1 - Clinical symptoms and conditions prior to diagnosis (n = 2,681)

Clinical Symptom/Condition	Symptom (%)	Fully Recovered % (n)
Bloating, abdominal pain	83	52 % of 83 (1146)
Diarrhea	76	66 (1347)
Weight loss	69	84 (1536)
Extreme weakness/tiredness	68	53 (960)
Anemia	66	72 (1283)
Mood swings/depression	44	41 (476)
Bone/joint pain	38	23 (234)
Easy bruising	35	27 (256)
Constipation	32	47 (403)
Nausea or vomiting	29	73 (566)
Lactose Intolerance	26	36 (247)
Aphthous ulcers	26	60 (418)
Migraine	24	40 (250)
Edema of hands and feet	20	45 (246)

Table 2. Diagnoses prior to celiac disease (n = 2,681)

Medical Condition	Respondents (%)
Anemia	40
Stress	31
Irritable bowel syndrome	29
Vitamin deficiency	16
Peptic ulcer disease	15
Food allergies	13
Chronic fatigue syndrome	9

Table 3. Medical Conditions in individuals with celiac disease (n = 2,681)

Medical Condition	Individuals with celiac disease (%)
Celiac disease	All
Iron deficiency anemia	49
Osteoporosis	26
Lactose intolerance	18
Hypothyroidism	12
Rheumatoid arthritis	5
Type I diabetes	2
Breast Cancer	2
Colon cancer	1
IgA deficiency	1
Sjogren's syndrome	1
Melanoma	0.9
Lymphoma	0.7
Small intestinal cancer	0.4

Table 4. Medical conditions among first-degree relatives of individuals with celiac disease

Medical Condition	First-degree relatives (%)
Celiac disease	15
Iron deficiency anemia	22
Lactose intolerance	16
Osteoporosis	15
Hypothyroidism	13
Rheumatoid arthritis	13
Type I diabetes	9
IgA deficiency	0.6
Sjogren's syndrome	0.7

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