

Celiac Disease Is Diagnosed Less Frequently in Young Adult Males

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Abstract

Background The female predominance in celiac disease is difficult to explain because population-based screening studies reveal similar rates for celiac disease-specific autoantibodies in males and females.

Aim The aim of this study was to explore the role of age and gender in the presentation of celiac disease.

Methods The frequency of presentation according to age, gender and mode of presentation was determined by analysis of a prospectively maintained database of children and adults seen at a tertiary medical center.

Results Of 1,682 patients (68 % female) aged 3 months to 86 years who were diagnosed with celiac disease, age at diagnosis in females peaked at 40–45 years, whereas the age at diagnosis for males had two peaks: 10–15 and

35–40 years. A significantly lower percentage of males in early adulthood were diagnosed compared with males in all other age groups ($P < 0.0001$). The young and elderly had a more even gender distribution.

Conclusions Based on our analysis, males are diagnosed with celiac disease less frequently than females, especially in early adulthood. There should be more emphasis on the diagnosis of celiac disease among young adult males.

Keywords Celiac disease · Gender · Diagnosis · Epidemiology

Introduction

Celiac disease is considered to be a unique autoimmune disease [1] because the environmental precipitant, gluten, has been identified [2]. Serological studies reveal that the disease is common, occurring in approximately 1 % of the population worldwide [3, 4]. The clinical presentations vary greatly, from asymptomatic individuals detected due to screening high-risk groups to gravely ill patients presenting with severe malabsorption [2, 5, 6]. Among adults, females are diagnosed with celiac disease more frequently than males, in a ratio of 2–3 to 1, respectively [7–9]. However, based on the results of serological screening studies, seropositivity for the specific autoantibodies for celiac disease occur in both males and females at a similar rate [10–12]. A search of the literature on screening for celiac disease yields a number of studies looking at sera obtained from healthy blood donors and from active screening initiatives in various population settings across the world (i.e. USA, Scotland, Tunisia, Brazil, Hungary, India, Israel, Iran, Denmark, Sweden, Finland, UK). These studies are of two types—either they do not identify a

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statistically significant gender difference in the screening [4, 11–19], or they were not designed to specifically assess gender disparities [3, 8, 10, 20–25]. The strength of these studies is that they assess populations in substantive numbers, from 1,000 to several 100,000 individuals per study. The additional capacity to assess gender differences in these previously reported studies would have added to our understanding of celiac disease. In the study reported here, our aim was to add to this body of literature by demonstrating age-specific effects of gender on the presentation of celiac disease, as studied in a large tertiary-center cohort of celiac patients ranging widely in age (early childhood to the elderly).

Materials and Methods

Patient data were analyzed from a prospectively maintained database of children and adults with biopsy-proven celiac disease seen at the Celiac Disease Center at Columbia University. Patients were considered to have biopsy-proven celiac disease if they had villous atrophy (Marsh IIIa, b or c) together with a combination of clinical, serological and appropriate human leukocyte antigen (HLA) values [13]. The study was approved by the Columbia University Institutional Review Board. Patient data were entered into the database when first seen at the Center.

We analyzed the entire cohort in groupings of 10-year age increments. Patients with celiac disease can have varied presentations that may be age specific, such as growth issues in childhood. However, some main modes of presentation are seen in both adults and children. We therefore compared three main modes of presentation that occur in both children and adults (anemia, diarrhea, and screening of high-risk groups). Due to small numbers of patients in some of the different age groups, we subdivided the patients with these specific presentations into four groups: childhood (≤ 17 years), early adulthood (18–29 years), adulthood (30–64 years) and elderly (≥ 65 years). The comparisons of frequency of presentation were made using chi-square analysis. Data analysis was performed using SAS Institute software (SAS Institute, Cary, NC).

Results

Among the 1,682 patients with biopsy-proven celiac disease enrolled in our study, 68 % were female (Table 1). Age of diagnosis ranged from 3 months to 86 years; 93 % of the diagnoses were made from 1990 onwards, and 33 % were diagnosed at our institution. Females presented at a single peak at ages 40–45 years, whereas males presented in two age peaks (10–15 and 35–40 years). Among the

Table 1 Percentage of diagnoses by gender and age across the total study population

All patients and specified subgroups of patients ^a	Age group (years)	Males, <i>n</i> (%)	Females, <i>n</i> (%)	<i>P</i> value
All patients	0–18	167 (41)	240 (59)	<0.0001
	18–30	48 (18)	215 (82)	
	30–65	254 (30)	590 (70)	
	≥ 65	70 (42)	98 (58)	
	Total patients	539 (32)	1,143 (68)	
Anemia	0–18	4 (29)	10 (71)	0.1089
	18–30	4 (17)	19 (83)	
	30–65	33 (29)	80 (71)	
	≥ 65	9 (53)	8 (47)	
	Total patients	50 (30)	117 (70)	
Diarrhea	0–18	28 (46)	33 (54)	<0.0001
	18–30	13 (12)	97 (88)	
	30–65	93 (28)	238 (72)	
	≥ 65	27 (36)	48 (64)	
	Total patients	161 (28)	416 (72)	
Screening	0–18	33 (40)	50 (60)	0.9735
	18–30	13 (36)	21 (64)	
	30–65	27 (42)	37 (58)	
	≥ 65	4 (44)	5 (56)	
	Total patients	77 (41)	113 (59)	

^a The subgroups of patients with anemia, diarrhea, screening, respectively

young adults (ages 18–29 years), the proportion of newly diagnosed patients who were male was much lower than that in any other age group (Table 1). Although males comprised 32 % of all patients, they comprised only 18 % of those diagnosed in young adulthood. Only 8.9 % of all males with celiac disease were diagnosed in young adulthood compared to 19 % of the females ($P < 0.0001$). The gender difference was least marked in the youngest and oldest groups, with males representing 41 and 42 % of those diagnosed with celiac disease, respectively. Figure 1 displays the total percentage of males diagnosed with celiac disease in each 10-year age group.

Among those diagnosed through screening programs of risk groups, 41 % were males. There were no significant differences between the age categories ($P = 0.97$), although the number of patients detected in screening programs in the age group 19–29 years was low (13 men, 21 women), and we had only 8 % power to detect the observed difference between the proportion of males in that age group (36 %) and the proportion of males in all other age groups (41 %). Among those who presented with

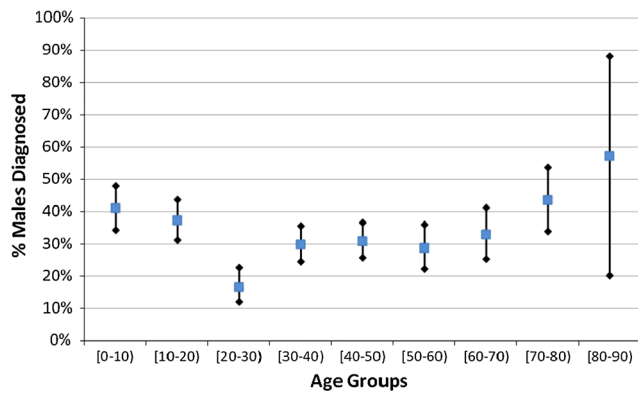


Fig. 1 Percentage of male celiac disease diagnoses by age group (95 % confidence intervals shown)

anemia, men in young adulthood were similarly under-represented (17 %), and among those presenting with diarrhea, males accounted for 28 % of all patients. However, there was a dramatic gender difference among the age groups, with only 12 % of the young adults presenting with diarrhea compared to 46 % of the children, 28 % of the adults, and 36 % of the elderly ($P < 0.0001$).

Discussion and Conclusions

In our study population, females were diagnosed with celiac disease more frequently than males. However, the gender disparity was most marked in young adults between the ages 18 and 29 years of whom only 18 % of the patients diagnosed with celiac disease were males. Among children and the elderly we found a more even gender distribution. Serological studies from the USA reveal that about 0.8–0.9 % of the general population has celiac disease [10, 11, 14]. One of these studies detected celiac disease in 0.9 % of young men [10], and the results of our study suggest a marked underdiagnosis of celiac disease in this age group that is more pronounced than the overall rate of underdiagnosis in the USA [8]. It is especially concerning that this under-represented group of young males is the same demographic group as those subjects who in a recent study had a high mortality risk associated with undiagnosed celiac disease [10].

When we examined screen-detected patients there was an even distribution across the genders for all age groups, confirming that celiac disease is present in patients of each age group and that both male and female subjects sought screening for the disease. We considered that anemia among females may be a reason that they are diagnosed with celiac disease more frequently than males; however, this gender disparity was similar among patients presenting with diarrhea as well as anemia.

What are other possible explanations for this gender disparity? Young adult women may be more symptomatic

than males, leading to a greater rate of diagnosis. The finding of a greater percentage of young women presenting with diarrhea (88 % were females within this age group) supports this concept. A previous Italian study noted that women with celiac disease were more symptomatic than men [9]. Another example of females being more symptomatic than males occurs in irritable bowel syndrome, which is also more prevalent in younger women [26]. Additionally, in what has now been well established in the literature, females are more affected by autoimmunity than males—likely a multifactorial model relating to hormonal, genetic, and environmental factors yet to be fully understood [27]. We have noted previously that adult males at the initial diagnosis of celiac disease showed evidence of greater degrees of malabsorption than women [28], suggesting that men may delay seeking health care for their symptoms or, alternatively, that men do not experience symptoms early in the disease process.

Another important factor in receiving a diagnosis is exposure to healthcare providers. Children (both males and females) are taken to the physician by their parents, and in the USA a physical examination is required prior to each school year. In addition, females start seeing a gynecologist in their late teenage years, experience pregnancies, and are followed routinely, usually annually by their gynecologists. The elderly seek health care frequently. Young men may not regularly seek routine medical care, a behavior documented in a Danish study which reported that overall male contact with general practitioners considerably drops off from the late teens through the fourth decade of life [29]. While there may be access to healthcare issues in the USA, even in countries with universal health care, men apparently do not seek it. This may be due to biological, social, or psychological factors that are associated with an under-reporting of health problems and delayed seeking of treatment by men [30].

The strengths of our observations are that the cohort is large and prospectively maintained in a database and that it includes all ages seen over an extended period of time in one tertiary referral center. A limitation is that the patients may not be representative of all celiac disease patients.

In conclusion, we found that there is a disproportionate under-representation of young male adults diagnosed with celiac disease. This may be due to a failure of men to develop symptoms of celiac disease in this age range or to factors that contribute to males not seeking health care.

Conflict of interest None.

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