

An epidemiologic survey of celiac disease in the Terni area (Umbria, Italy) in 2002-2010

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Key words

Celiac disease • Epidemiology

summary

The present work is an epidemiology survey of celiac disease in the province of Terni (Umbria, Italy) in 2002–2010. Data were collected from the Local Health Unit (LHU) 4 (ASL 4), Terni database and were extrapolated from the overall population of 232,540 (as of 2010) by identifying residents with prescription charge exemptions for celiac disease-oriented drugs. Prevalence and incidence analysis over the timeframe being examined showed that prevalence (330 cases in 2010) has consistently been increasing from 2002 to 2010, whereas incidence has remained essentially the same with minor, yearly fluctuations. Both prevalence and incidence were higher in females than in males. Most patients were diagnosed as

young adults, with the highest rates in the 10-14, 35-40 and 55-60 age groups. Thus, in the area of investigation, there is evidence for consistent delayed diagnosis, raising the possibility that the atypical form the disease, more difficult to recognize and more likely to escape early diagnosis, may have become increasingly commoner over time. Because the current prevalence of the disease in the Terni area is estimated to approximate 1%, the anticipated number of cases should amount to 2,325, which value contrasts with the currently reported 330 diagnoses. It is suggested that the current illness-defining criteria should be revised so to implement early diagnosis and improve the patients' quality of life and access to treatment.

Introduction

Celiac disease, a gluten-dependent enteropathy, is a chronic, systemic autoimmune disorder. Onset, at any age in genetically prone subjects, is triggered by gluten-containing foods, such as wheat, barley, rye and oatmeal [1, 2].

Research into the genetics of celiac disease started in the 1980s, and in 1984-89, the HLA-DQW2 and HLA-DQ8 haplotypes were identified as playing a role in predisposing to disease onset. Specific types of autoantibodies were found in patients with celiac disease between 1983 and 1984, and the discovery of the anti-gliadin antibody (AGA) and anti-endomysium antibody (EMA) confirmed that celiac disease was, mechanistically, an autoimmune condition [3]. Celiac disease was proposed as a model for elucidating autoimmune diseases when recent studies hypothesized that, as in most autoimmune disorders, three factors acted synergistically [4, 5], namely, genetic predisposition, dietary gluten consumption (the environmental trigger), and an abnormally increased intestinal permeability.

Celiac disease presents *classically* as a malabsorption syndrome, *atypically* with a late onset (which is associated with nonspecific and even extra-intestinal signs and/or symptoms that cannot otherwise be accounted for), *silently* in symptom-free patients who escape being diagnosed, and *potentially* in individuals with serum positivity but no intestinal lesions [5].

Serum screening programmes, greater awareness, and improved knowledge of pathogenesis have now led to

the detection of celiac disease in subjects with only few, or only extra-intestinal, symptoms. Prevalence is similar in Europe and in countries such as the USA, the Middle East, North Africa and Central and South America, where, until the 1990s, it was considered rare [6, 7]. In the 1950s-60s, the prevalence of celiac disease was estimated at 1:4000–8000 worldwide; in the 1970s prevalence estimates stabilized around 1:450-500, rising to 1:150-200 in the 1990s.

In Italy, the prevalence of celiac disease is estimated to be 1/100 in adults and children [8]. According to the 2009 annual report to the regional government, Umbria has 1,494 inhabitants with celiac disease (420 males and 1,074 females). The present report used some epidemiological parameters to profile celiac disease in the province of Terni.

Materials and methods

In accordance with current Italian legislation protecting personal information, data on patients with celiac disease from 2002 to 2010 are provided under anonymous format by the Terni Province Health Board No 4, in Umbria, Italy. Health Board No 4 covers the province of Terni except for the San Venanzo area. Data were extrapolated from the list of individuals with prescription charge exemptions for specific medical treatment.

The data included only gender, date of birth and year of diagnosis for each patient. Age at onset could thus be calculated on a case-by-case basis.

Tab. I. Number of celiac disease cases in Umbria (referral area, ASL4) in 2002–2010 according to gender (5-yr intervals of diagnosis).

| 5-yr intervals of diagnosis | Diagnosis Year | | | | | | | | | |
|-----------------------------|----------------|------|------|------|------|------|------|------|------|---|
| | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | |
| Females | 00-04 | 1 | 1 | 3 | 2 | | 2 | | 5 | 2 |
| | 05-09 | 3 | 1 | 1 | 1 | 4 | 2 | 1 | 5 | 3 |
| | 10-14 | 10 | 2 | 1 | 2 | 1 | | 4 | 3 | 1 |
| | 15-19 | 3 | | 2 | 1 | 1 | | 1 | | 4 |
| | 20-24 | 2 | 1 | 1 | 5 | 2 | 1 | 1 | 1 | 1 |
| | 25-29 | 4 | 2 | 3 | 3 | 5 | 2 | | 3 | 2 |
| | 30-34 | 3 | 3 | 1 | 5 | 2 | 4 | 4 | 2 | |
| | 35-39 | 6 | 1 | 5 | 4 | 4 | 5 | 4 | 2 | 8 |
| | 40-44 | 3 | 2 | | 6 | 6 | 4 | 6 | 2 | 7 |
| | 45-49 | 1 | 2 | 1 | 3 | 3 | 3 | 2 | 1 | 2 |
| | 50-54 | 1 | | 1 | | | 1 | 1 | | 3 |
| | 55-59 | 2 | 1 | 1 | | 1 | | 1 | 1 | |
| | 60-64 | 1 | | 1 | | | | 1 | 3 | |
| | 65-69 | 1 | | | 1 | | | 1 | | |
| | 70-74 | | | | | | 1 | 1 | | |
| | 75-79 | | | 1 | | | | | | |
| Total | 41 | 16 | 22 | 33 | 29 | 25 | 28 | 28 | 33 | |
| Males | 00-04 | 2 | | | 1 | 1 | | 3 | 3 | 3 |
| | 05-09 | 1 | | 2 | 2 | 3 | 2 | 3 | | |
| | 10-14 | 2 | 1 | 2 | 2 | | | 1 | | |
| | 15-19 | 2 | 3 | 1 | | | | | 1 | |
| | 20-24 | | | | 1 | | 1 | | 1 | |
| | 25-29 | | 2 | | | 1 | | | | |
| | 30-34 | | | 1 | 1 | | | 1 | 1 | |
| | 35-39 | | 1 | 1 | | | | 2 | | |
| | 40-44 | 1 | 1 | 1 | 2 | 2 | | 1 | 1 | 1 |
| | 45-49 | | | | | 1 | | | | |
| | 50-54 | | | 1 | | | | | 1 | |
| | 55-59 | | | | | | | | | |
| | 60-64 | | | | | 2 | | 2 | | |
| | 65-69 | | | | 1 | | | | | |
| | 70-74 | | | | | | | | | 1 |
| | 75-79 | | | | | | 1 | | | |
| Total | 8 | 8 | 9 | 10 | 10 | 4 | 13 | 8 | 5 | |

Istat tables provided demographic data about the entire resident population in the Terni Province (<http://demo.istat.it/>). Using these data the prevalence and incidence of celiac disease in the province could be calculated for the years 2002 through 2010. Prevalence and incidence are expressed, as the respective numbers of total cases and news cases within a specified time period divided by the size of the population at risk per 100,000.

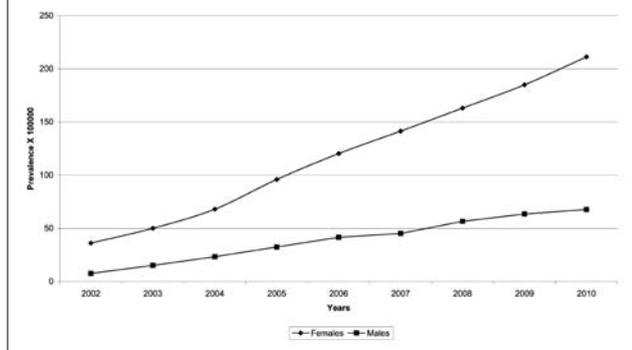
Results

In 2010, the Terni Province of Umbria had 330 patients (75 males, 255 females) with celiac disease. Table I reports the number of cases, gender and 5-year stratification for age at diagnosis.

Consistent with data from international reports, the prevalence of celiac disease was higher in females than in males, and it increased constantly over the 2002–2010 study timeframe (Tab. II, Fig. 1). Prevalence increased more markedly in the male population (+18.85) than in

Tab. II. Prevalence in celiac disease according to gender groups in Umbria (referral area, ASL4) years 2002-2010.

| Years | Females | Males |
|-------|---------|-------|
| 2002 | 36.25 | 7.66 |
| 2003 | 50.10 | 15.22 |
| 2004 | 68.09 | 23.37 |
| 2005 | 96.01 | 32.55 |
| 2006 | 120.34 | 41.64 |
| 2007 | 141.44 | 45.26 |
| 2008 | 163.14 | 56.68 |
| 2009 | 185.05 | 63.52 |
| 2010 | 211.30 | 67.77 |

Fig. 1. Prevalence in celiac disease in Umbria (referral area, ASL4) years 2002-2010.

the female (+5.83). Consequently prevalence of celiac disease was 4.7-fold higher in females in 2002 and 3.11-fold higher in 2010.

Annual *incidence* oscillated in both males and females, tending to stabilize in both sexes in later years. The number of new cases was increasingly higher in females on a per-year basis (Tab. III, Fig. 2)

Analysing the incidence in 5-year age groups over the 2002-2010 period showed that the highest number of new cases in males occurred in the first 10 years of life. Rates gradually dropped until 35 years of age and then rose again in the 40-44 age group. Incidence was lowest in the 60-64 age group (Tab. IV, Fig. 3). In females, the incidence was always greater than in males in each 5-year age group, reaching maximum peaks in the 10-14, 25-29, and 35-45 stratification groups.

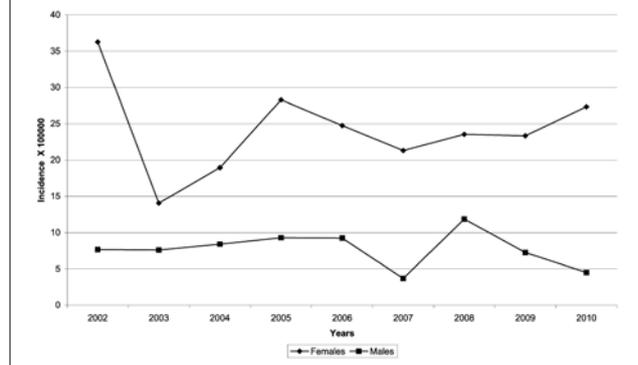
Gender-specific differences in incidence were least in the 00-04, 05-09 and 15-19 age groups.

Discussion

Knowing what impact a disease has on the general population enables physicians and healthcare professionals to plan and organise effective therapeutic interventions and manage their human and material resources to best advantage. Patients receive the treatment they need and their right to health is safeguarded.

Tab. III. Incidence in celiac disease according to gender groups in Umbria (referral area, ASL4).

| Years | Females | Males |
|-------|---------|-------|
| 2002 | 36.25 | 7.66 |
| 2003 | 14.06 | 7.61 |
| 2004 | 18.96 | 8.41 |
| 2005 | 28.29 | 9.30 |
| 2006 | 24.75 | 9.25 |
| 2007 | 21.30 | 3.69 |
| 2008 | 23.55 | 11.88 |
| 2009 | 23.34 | 7.26 |
| 2010 | 27.35 | 4.52 |

Fig. 2. Incidence of celiac disease (referral area, ASL4).

Since celiac disease can no longer be considered as a rare pathology of the children, the present study was designed to profile its epidemiology as recorded by Health Board No 4 in order to determine whether prevalence and incidence had changed over the years in the province of Terni, as in the rest of Italy.

We found that prevalence increased constantly between 2002 and 2010. In contrast, though incidence oscillated slightly, it tended to remain constant over time. These data confirm that early diagnosis together with life style changes by the patient involving a gluten-free diet ensure that celiac-related complications, such as gastrointestinal cancer and intestinal lymphoma, are avoided and life expectancy equals that of the general population.

That prevalence and incidence are greater in women is consistent with the general pattern of celiac disease distribution. In fact, the M:F ratio is reported to be as high as 1:2. The 5-year age at diagnosis stratification shows that the majority of patients were young adults when celiac disease was diagnosed, as only 63 were less than 10 years of age at the time of diagnosis. The number of diagnoses peaked in the 10-14, 35-40, and 55-60 age groups, confirming that the disease was distributed uniformly across the entire general population and highlighting the need to rectify the assumption that celiac disease is a rare disease.

The present results are in line with regional and national trends of celiac disease [9]. Indeed, in the past 10 years,

Tab. IV. Incidence of celiac disease according to age groups in Umbria (referral area, ASL4).

| Years 2002-2010 | | |
|-----------------|---------|--------|
| Diagnosis age | Females | Males |
| 00-04 | 376.84 | 287.20 |
| 05-09 | 502.62 | 289.54 |
| 10-14 | 559.43 | 177.02 |
| 15-19 | 266.25 | 147.06 |
| 20-24 | 288.77 | 54.73 |
| 25-29 | 363.35 | 44.47 |
| 30-34 | 299.63 | 50.10 |
| 35-39 | 453.83 | 46.81 |
| 40-44 | 429.73 | 120.91 |
| 45-49 | 230.74 | 13.39 |
| 50-54 | 90.60 | 27.69 |
| 55-59 | 89.30 | 0.00 |
| 60-64 | 78.58 | 56.12 |
| 65-69 | 40.08 | 14.76 |
| 70-74 | 27.43 | 16.69 |
| 75-79 | 14.39 | 19.93 |

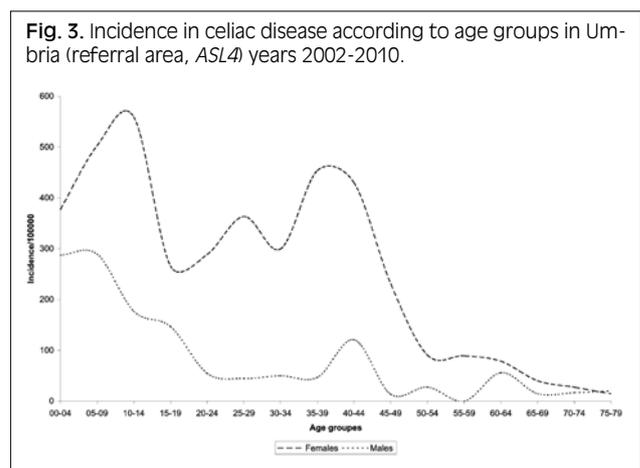
age at diagnosis has risen in Terni and in the Region of Umbria as a whole. The prevalence of celiac disease is at present estimated to be around 1% in adults and children according to the Italian Ministry of Health Report for the year 2009. Patients with celiac disease should amount to 2,325 in the Terni population, as this population was 232,540 in 2010 [9]. However, only 330 were actually diagnosed as of 2010. (Those patients were identified as meeting the stringent biochemical and histologic criteria needed to obtain nearly free medications.) This figure is considerably less than the expected 1%. Missing or delayed diagnoses might be due to the multiplicity of clinical manifestations of the disease at onset, considering that early symptoms may be limited to sites other than

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the gastrointestinal tract, and they may involve the skin, or may be gynecologic or autoimmune in nature. The use of the public registries of patients with celiac disease is an efficient and direct way to estimate incidence/prevalence of the disease. However, it is well known that this approach may generate an underestimation of real cases, e.g., because of the loss of subjects that may not benefit of the exemption (because they are not aware or refuse this possibility) or for delays in registration, or because of changes of residence. This possible bias might contribute to the severe loss of diagnoses in Terni. Nevertheless, we feel that diagnostic criteria need to be revised. Only by establishing universally accepted, clearly valid criteria can we increase the number of early diagnoses, which are essential if we are to offer patients best care, quality of life, and survival. Finally, finding so many cases of celiac disease in the Province of Terni and the rest of Italy suggests that health services for patients need to be optimized. Today, for example, more than in the past, many patients are adults and have the right to employment safeguards. One step in the right direction would be to establish a network of specifically oriented canteens offering appropriate foods.

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