

Celiac disease: experience of general practitioners in Brianza Area-Monza- Milan-Italy

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ABSTRACT

Aim: The purpose of the study was to better investigate the degree of knowledge and the diagnostic approach concerning celiac disease and its extra-intestinal manifestations by general practitioners in Italy.

Background: Celiac Disease is a common chronic disease, but often goes undiagnosed because of atypical symptoms or silent disease. Currently there are non-definitive data about the disease management approach concerning celiac disease by general practitioners.

Methods: To better investigate the degree of knowledge and the diagnostic approach concerning celiac disease and its extra-intestinal manifestations, questionnaire was used to assess the daily practice of diagnosis, treatment, and follow-up of this condition by general practitioners in two densely populated area in Italy: Monza-Brianza Area and Milan City. The questionnaire was composed of 18 questions that explored 3 precise domains: diagnosis criteria, correct management of celiac disease and availability for training. The frequencies of the domains explored were analyzed, analyzes were carried out to identify differences between the groups of general practitioners interviewed.

Results: Analysis of the questionnaires showed a degree of knowledge and preparation comparable to that of other countries, even though not sufficient to guarantee access to early diagnosis for all patients with celiac disease. The knowledge was not influenced by the years of experience or specific curriculum of health professionals. General practitioners under 40 were much more in favor of continuous training and were aware of its importance (OR=10.55; CI95%: 1.62-445.39), although this need was a high priority in the whole group interviewed (84.7%).

Conclusion: Continuous specific training aimed at primary care physicians and general practitioners is the first tool to improve early diagnosis. A second opportunity is represented by the continuous dialogue between general practitioners and tertiary level hospitals and universities.

Keywords: Celiac disease, General practitioners, Surveys, Questionnaires.

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Introduction

Celiac Disease (CD) is a common chronic autoimmune disorder first described clinically by

Samuel Gee in 1888, who was able to correlate its manifestation to the ingestion of gluten (1). A recent meta-analysis, based on serologic test results, estimated CD to affect 1.4% of the general population worldwide,

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while the pooled global prevalence of biopsy-confirmed CD was 0.7% (2). In particular, prevalence values for CD were 0.4% in South America, 0.5% in Africa and North America, 0.6% in Asia, and 0.8% in Europe and Oceania, with an increased frequency among females and children (2, 3).

In primary medicine settings, the diagnosis of CD is less frequent and still may be undiagnosed. This could be due to multiple factors, from being able to perform diagnostic tests to correctly identifying the diagnosis code (4). Data in the present scientific literature show that there could be up to 90% underdiagnosis in a population of children who underwent biopsy for CD (5).

In 2019, the Italian National Health System reported 225.418 CD cases, with an increase of over 11.000 diagnoses compared to the previous years (6). However, about one third of patients with CD are not correctly diagnosed: this fact, according to Giorgiotti et al., depends on some factors such as suspected symptoms that are difficult to recognize, such as osteoporosis, increased blood liver enzymes, infertility, recurrent miscarriage, Sjogren's syndrome and other autoimmune diseases (7).

Serology, particularly tissue transglutaminase-immunoglobulin A (TG2-IgA), IgA testing and endomysial IgA testing, plays a pivotal role in the detection and diagnosis of CD. Histological analysis of duodenal biopsies with Marsh classification is the gold-standard diagnostic method. It allows to count intra-epithelial lymphocytes per high-power field and its morphometry is important both for diagnosis and for differential diagnosis (8).

The aim of the study was to better investigate the degree of knowledge and the diagnostic approach concerning celiac disease and its extra-intestinal manifestations by general practitioners in Monza-Bianza Area and Milan City.

Methods

A cross-section survey among 183 General Practitioners (GP) was conducted between February 2019 and May 2019, in Monza-Brianza Area and Milan City, in Northern Italy. Data were collected by means of an electronic questionnaire regarding symptoms, diagnostic criteria and therapies for CD.

The questionnaire was designed to collect data from 3 domains of interest: diagnosis criteria, celiac disease management, and readiness for continuing professional education. All questions were dichotomous or multiple choice, except for the symptoms question which accepted open-ended answers (Table S1).

The questionnaire was anonymous and was shared electronically with each GP interviewed. This method made it possible to keep the collection of data anonymous, ensuring that the questionnaire was filled in only by GPs who had agreed to participate to the study.

A semi-quantitative analysis of the data obtained was conducted to evaluate the degree of readiness in the explored domains. Furthermore, for the dichotomous variables, the calculation of the odd ratio and the Fisher test were carried out to evaluate the presence of significant differences between the groups based on age.

This study obtained the local authorities simplified approval for observational studies not requiring interventions.

Results

Overall, 183 GPs responded to the questionnaire; 82 (44.5%) of them were aged more than 60 years and 101 (54.5%) had in charge more than 1500 subjects.

Symptoms leading physicians to suspect CD were divided into gastrointestinal symptoms and extra-gastrointestinal symptoms. Of the 183 GPs interviewed, 69 (37.7%) referred to consider CD only in presence of Gastrointestinal symptoms, 9 (4.9%) considered CD only in presence of extraintestinal symptoms and 43 (57.4%) reported to suspect CD in both conditions.

Regarding extraintestinal symptoms, 174 (95.1%) of the GPs replied to search for possible CD in presence of hematological disorders, especially in patients with Iron Deficiency Anemia (IDA), with the exclusion of iron deficiency and gastrointestinal bleeding. 122 (66.7%) of the GPs replied to search for possible CD in presence of Irritable Bowel Syndrome (IBS). Lower percentages for the suspect of CD, reported by GPs, were observed in case of osteoporosis (95, 51.9%), in case of unexplained infertility (73, 39.9%) or unexplained increases in transaminase levels (44, 24.0%) (Figure 1).

Few GPs suspected a CD in specific situations such as allergic syndrome and autoimmune disorders (21, 11.5%). The lowest percentages for the suspicion of CD, reported by GPs, were observed in presence of neurological disorders like epilepsy, ataxia and peripheral neuropathies (5.5% totaling 10 GPs), ocular symptoms such as uveitis (4.4% for a total di 8 GPs) and heart disease like dilatative cardiomyopathy, autoimmune myocarditis (2.7% for a total of 5 GPs) (Figure 1).

Considering familiarity and age, 158 (86.3%) of GPs answered that they look for markers of CD in 1st degree relatives, while only 68 (37.2%) of GPs declared that they would include CD in the differential diagnosis in the elderly (over 65 years).

In our study, of the 183 GPs interviewed, 182 (99.5%) reported to prescribe IgA transglutaminase antibody tests (IgA- TTG) in case of suspect of CD to

confirm the diagnosis. Also 40 (21.9%) GPs reported that they prescribed IgA anti-endomysial antibodies test (IgA-EMA) and 32 (17.4%) IgA anti-gliadin antibodies test (IgA-AGA) (Figure 2).

In case of negative serology, 118 (64.5%) of GPs reported that they did not exclude the diagnosis of CD, preferring to send the patient to a second level diagnosis, whereas 65 (35.5%) of GPs reported exploring other possible differential diagnoses compatible with the patient's symptoms.

In case of positive serology, 178 (97.3%) of GPs reported sending the patient for a visit to a gastroenterology specialist as a first action. Regarding the gluten-free diet, 58 (31.7%) of GPs reported that they prescribe it immediately after finding positive serology, while 125 (68.3%) stated that they wait for a specialist consultation before prescribing a gluten-free diet.

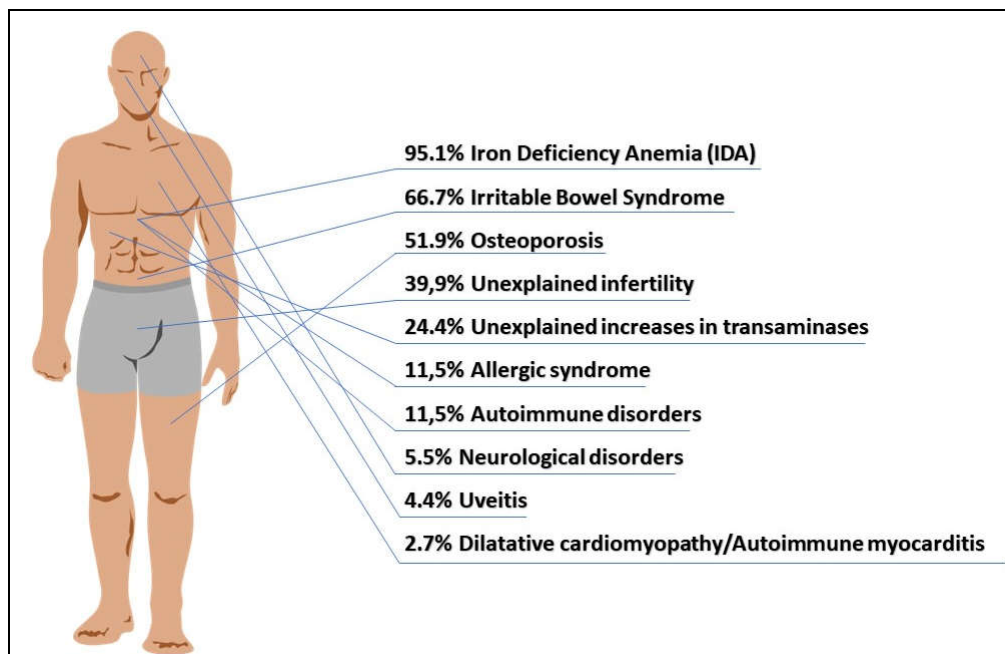


Figure 1. Symptoms identified by GPs interviewed as suspects for diagnosis of CD (extra-intestinal symptoms).

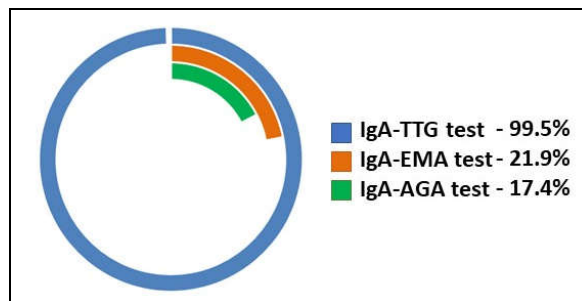


Figure 2. Frequencies in the use of serological tests for the diagnosis of reported CD by the GPs interviewed.

Regarding the management of patients with CD, 142 (77.6%) GPs said they would agree to manage patients in their own clinic if online consultancy with a dedicated gastroenterology specialist was available, while 41 (22.4%) GPs reported that they preferred to refer the patient with CD directly to a specialist center for disease management.

Stratifying the results obtained by age of the doctors interviewed, no significant difference was observed in the answers regarding the correct diagnosis and management of CD.

Concerning the need for continuous training and discussion of difficult-to-manage cases, 155 (84.7%) GPs reported that they were available to hold meetings with gastroenterologist specialists for CD, while 28 (15.3%) GPs reported that they were not interested in specific training meetings for CD. Regarding training, doctors under 40 expressed the need for continuous training 10 times greater than their older colleagues (OR=10.55; CI95%: 1.62-445.39) (Table 1).

Discussion

CD is a common chronic autoimmune disease, often undiagnosed because of atypical symptoms or silent disease. Although this condition is not diagnosed in about two thirds of cases in Italy, the sample interviewed had excellent knowledge of the criteria for making the diagnosis. Training opportunities, on the other hand, were identified in the recognition of symptoms and in the fact that their onset may be unclear. Training interventions in such fields could allow for a more appropriate diagnosis rate with the estimated incidence of CD.

Only GPs were enrolled in the present study. However, the results show a good degree of preparation in comparison with the scientific literature. This is probably due to the constant collaboration between the GPs and the gastroenterology specialists of the University of Milan.

In our study we evaluated whether a greater number of years of experience could influence the management

of CD. However, we did not observe such a difference, suggesting that a high degree of awareness and preparedness about CD can be achieved by all physicians.

Regarding the previous literature, Barzegar et al (9), in their pilot study, interviewed 197 physicians such as gastroenterologist, Gastrointestinal Fellows, Specialists, Residents and GP belonging to a group of 300 physicians; results showed that 12.2% of the physicians had a scarce knowledge of the CD, 63.5% an intermediate and 24.4% a good one. Zipser et al, in a study conducted in California analyzed physician's awareness of CD and found that this condition was diagnosed in 11% by a GP and in 65% by a gastroenterologist (10); however, only 44% of the physicians interviewed were aware that endomysial antibodies can be used for the diagnosis, and only 32% of them knew that adult onset of symptoms in CD is frequent.

Several studies showed that a diagnosis of CD, in most cases, is made by a specialist. Giorgiotti et al (7) studied the electronic databases of 16 GPs and reported a poor diagnosis of CD (0.41%). Rouvroye et al (11) analyzed almost 207.200 patients of 49 GPs; they demonstrated that the prevalence of CD diagnosis was about 0.19%. Van Gils et al (12) interviewed 7 GPs with different experience with CD; the results showed that CD diagnosis was made by specific serological tests but if those were positive, the patient was not referred to a gastroenterologist.

We analyzed our data to compare them with literature's experience. Our data suggest that CD had been researched in patients with extraintestinal symptoms such as IDA (174 GPs - 95.1%), Irritable Bowel Syndrome (IBS) (122 GPs - 66.7%) and osteoporosis (95 GPs - 51.9%). IDA is quite frequent in CD patients, and it occurs in 10-50% of patients at diagnosis according to the scientific literature (13).

Moreover, the data of our study show a particular attention of GPs to the presence of osteoporosis, as an extra-intestinal manifestation of CD. In fact, osteoporosis is often associated with CD and about

Table 1. GPs who said they were in favor of continuous professional updating by age.

Interviewed GPs	In support	Not available	Odds Ratio (95% Confidence Interval)	P-value
GPs under 40	51	1	10.55 (1.62-445.39)	< 0.01
GPs over 40	104	27		

one-third of patients with CD have osteoporosis, with men being more severely affected than women (14). Zanchetta et al (15) recommend bone densitometry screening in all celiac patients, particularly in those with symptomatic CD at diagnosis and in those who present risk factors for fracture such as older age, menopausal status, previous fracture history, and familial hip fracture history.

In addition, GPs suspected the presence of CD in case of autoimmune disorders (16); our survey confirms that 21 GPs (11.5%) know this disease association and 122 (66%) of GPs interviewed prescribe serum tests for CD in patients with IBS, in accordance with the American Gastroenterology's guidelines (17).

However, results were not very encouraging concerning the research of CD in patients with infertility, since only 73 GPs (39.9%) identified it as a possible symptom of an undiagnosed CD. The other symptoms raising a suspicion of CD that are less observed during the anamnestic evaluation are: advanced age, unexplained increase in transaminases, ocular disorders and heart disease, as Dilatative Miocardopathy or Autoimmune Miocarditis (13).

Finally, our study showed that 84.7% GPs have a considerable interest in improving their skills in the management of CD, especially in doctors aged under 40. Furthermore, 31.7% of the GPs interviewed are able to prescribe a gluten-free diet in the presence of a correct diagnosis, without consulting a specialist. Therefore, the purpose is to improve the network between Gastroenterologist and GP in order to increase the percentage of CD's diagnosis (13).

Conclusion

Delays in diagnosis can lead to complications, such as anemia, osteoporosis, or reproductive disorders. The quality of life may also be negatively impacted because undiagnosed patients spend more time and money using healthcare service (18). Therefore, an early diagnosis of CD is needed. Many are the reasons for the delay in the diagnosis. First, the lack of gastrointestinal symptoms and the extensive percentage of symptoms shown by the patients (13). Moreover, GPs usually do not know when the serological test should be performed (19) and they consider CD mainly as a childhood pathology, while CD may be diagnosed at every age (20). Scientific data about

the daily practice of CD management by GPs in case of suspected CD are few (19).

At this moment, the knowledge and skills of internal health care professionals about CD are not sufficient for the diagnosis and treatment of CD and a training for healthcare professionals is needed. Continuous specific training aimed at primary care physicians and general practitioners is the first tool to improve early diagnosis. A second opportunity is represented by the continuous dialogue between GPs and tertiary level hospitals and universities.

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Conflict of interests

The authors declare no conflict of interests.

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