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Coeliac disease screening is suboptimal in a tertiary gastroenterology setting

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Abstract

Background and aims—Coeliac disease (CD) is widely prevalent in North America, but case-finding techniques currently used may not be adequate for patient identification. We aimed to determine the adequacy of CD screening in an academic gastroenterology (GI) practice.

Methods—Consecutive initial visits to a tertiary academic GI practice were surveyed over a 3-month period as a fellow-initiated quality improvement project. All electronic records were reviewed to look for indications for CD screening according to published guidelines. The timing of screening was noted (before or after referral), as well as the screening method (serology or biopsy). Data were analysed to compare CD screening practices across subspecialty clinics.

Results—616 consecutive patients (49±0.6 years, range 16–87 years, 58.5% females, 94% Caucasian) fulfilled inclusion criteria. CD testing was indicated in 336 (54.5%), but performed in only 145 (43.2%). The need for CD screening was highest in luminal GI and inflammatory bowel disease clinics, followed by biliary and hepatology clinics ($p<0.0001$); CD screening rate was highest in the luminal GI clinic ($p=0.002$). Of 145 patients screened, 4 patients (2.4%) had serology consistent with CD, of which 2 were proven by duodenal biopsy. Using this proportion, an additional 5 patients might have been diagnosed in 191 untested patients with indications for CD screening.

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Conclusions—More than 50% of patients in a tertiary GI clinic have indications for CD screening, but <50% of indicated cases are screened. Case-finding techniques therefore are suboptimal, constituting a gap in patient care and an important target for future quality improvement initiatives.

BACKGROUND AND AIMS

Celiac disease (CD) is common in North America, with an estimated prevalence of 1% in non-Hispanic whites.¹ CD may be underdiagnosed in US clinical practice, particularly since CD prevalence was underestimated in older literature. Recent data suggest a true incidence close to 17.4/100 000 person-years.²³ CD diagnosis relies on case-finding techniques rather than population-based screening programmes.⁴⁵ This is because CD prevalence is higher in specific populations, such as those with a family history of CD (prevalence 5%–20%), type I diabetes mellitus (prevalence 3%–10%) and irritable bowel syndrome (IBS) (prevalence 3%).⁶

In addition to the high-risk groups, screening is also indicated in those with classic symptoms (diarrhoea, weight loss), unexplained iron deficiency anaemia, elevated liver enzymes and comorbidities such as osteoporosis, autoimmune liver disease, autoimmune thyroid disease, primary biliary cholangitis, inflammatory bowel disease (IBD), microscopic colitis and infertility.⁷⁸ However, it is now well recognised that classic symptoms may not be present in adult patients with CD.⁹ Despite that, diagnosis remains important as there is evidence suggesting that CD diagnosis can improve quality of life, or highlight previously unrecognised symptoms that resolve following initiation of a gluten free diet.¹⁰¹¹

Gastroenterology (GI) clinics evaluating various GI symptoms within the realm of both bowel and liver disorders are optimal for initial case-finding. It is essential that practitioners in these settings understand CD-testing options, and recognise clinical scenarios where CD testing is warranted. With this background, the aim of this study was to determine the adequacy of case-finding and screening for CD in a tertiary academic GI practice with multiple GI subspecialty clinics within the practice. Our hypothesis was that screening would be underused, even in this setting of specialised GI providers.

METHODS

All initial patient visits to the Division of Gastroenterology academic faculty practice in our institution over a 3-month period were eligible for inclusion in this retrospective study. Only initial visits were used, not return visits, to avoid any duplication; therefore, all encounters represented unique patients. Electronic medical records were scrutinised using data collection criteria established a priori for indications for CD testing, extracted from clinical guidelines published by the American Gastroenterological Association and American College of Gastroenterology.⁷¹² African-American patients were excluded due to the low rates of CD in this group.¹¹³ This was a fellow-initiated quality improvement project, and all GI fellows enrolled in the programme participated in data review. The study protocol, review of medical records and data collection were approved by the Human Research Protection Office (institutional review board) at Washington University in St. Louis.

Indications for CD testing were assigned a priori based on published guidelines.¹¹³ Specific indications evaluated were: (1) chronic gastrointestinal symptoms including evidence of malabsorption, chronic diarrhoea and weight loss, postprandial abdominal pain and bloating, (2) laboratory abnormalities seen in CD, including iron deficiency anaemia and unexplained elevated liver enzymes, (3) comorbidities commonly associated with CD, including osteopenia, osteoporosis, type 1 diabetes, autoimmune thyroid disease, primary biliary cirrhosis, autoimmune hepatitis, IBD, microscopic colitis and IBS, (4) other less common associations of CD, including Down syndrome, Turner syndrome, infertility and recurrent foetal loss and (e) family history of first-degree relative (s) with CD.

Initial patient visits were identified on review of electronic medical records by the lead investigator (HI), who assigned patients to individual fellows proportionately. Each fellow reviewed office notes, referring physician notes, test results (both in referral documents, and those ordered following the office visit) and final diagnoses. The method and timing of CD testing were recorded.

Statistical analysis

Our assumption was that all patients with indications for CD screening should be screened, either previously by the referring physician or the physician who was treating in our GI clinics at or contemporaneous to the time of the encounter. For the purpose of this study, if adequate CD testing had been performed prior to the office visit, CD screening was considered done; if a patient carried a diagnosis of CD, testing was considered not indicated. Adequate testing by a referring provider was defined as coeliac serology using tissue transglutaminase (TTG) IgA and total IgA.

Data are reported as mean and SE of mean unless otherwise indicated. The number of initial patient visits over the study period was determined collectively and for individual subspecialty clinics, and the proportion where CD testing was indicated was calculated. The proportion of potentially undiagnosed CD was determined by projecting the CD diagnosis rate across all initial patient visits. Categorical values were compared using the χ^2 test. A p value of <0.05 was required for statistical significance. All statistical analysis was performed using SPSS Statistics V.20.0 (SPSS, Chicago, Illinois, USA).

RESULTS

Over the 3-month study period (October to December 2012), 704 consecutive initial patient visits were identified across all the GI subspecialty clinics at our institution. Exclusions consisted of 85 visits that involved African-American patients, and 3 visits with missing notations or data. Therefore, 616 unique initial patient visits (mean age 49 ± 0.6 years, range 16–87 years, 58.5% females, 94% Caucasian, 2% Asian, 0.6% Native American and 3.4% self-identified as other) were eligible and formed the study cohort (figure 1). According to predesignated criteria, CD testing was indicated in 336/616 patients (54.5% of the study cohort). Indications for CD testing were predominantly chronic luminal GI symptoms in nearly one-half (165/336, 49.4%) of the cohort; other testing indications are listed in figure 2. However, CD testing was only performed in 145/336 patients (43.2% of patients where

testing was indicated), and 56.6% (191/336) where CD testing was clinically indicated remained uninvestigated for CD following the initial office visit (figure 1).

When testing was performed, a variety of serologic tests and/or duodenal biopsy were used, with 91/145 (62.7%) patients undergoing more than one testing modality. IgA anti-TTG was performed in 106/145 (73.1%), but quantitative IgA level was concurrently evaluated in only 77/145 (53.1%) (table 1). Antigliadin antibody was used in one-third of cases. Other tests employed included antiendomysial antibody, and IgG antideamidated gliadin peptide (table 1). Finally, upper endoscopy and duodenal biopsy was performed in 102/145 patients (70.3%). Approximately half of the duodenal biopsies (47/102, 46.2%) were performed by the referring doctor. Of the remainder, 12.7% (13/102) were performed as part of diagnostic testing concurrent with serologic testing and 11.7% (12/102) were performed after serologic testing. Seventeen patients had coeliac testing done without a clear indication.

Results were further analysed by subspecialty clinic. According to our predetermined criteria, CD testing was highest in the luminal GI and IBD clinics, followed by biliary clinic and lowest in hepatology clinic (table 2, $p<0.0001$). Proportions actually tested ranged from 27.0% to 53.5% of indicated cases (table 2), highest in the luminal GI clinic compared with other subspecialty clinics ($p=0.002$).

Of 145 patients screened, 4 patients (2.8%) had positive CD serology and 2 cases were confirmed by duodenal biopsy (table 3). The indication for screening was iron deficiency anaemia in three patients and unexplained elevated liver enzymes in the fourth. All four patients had elevated anti-TTG antibodies. IgA was checked in three of these patients, and was normal when checked. Antiendomysial antibody was also checked in two patients.

Assuming similar prevalence of CD, if the remainder 191 patients had been screened, we estimate that five additional patients with CD may have been identified.

DISCUSSION

In this retrospective cohort study at a tertiary care GI clinic, we report that CD screening practices are suboptimal at tertiary care specialty clinics and their referring physician practices. Over half of patients with indications for CD screening remained uninvestigated, despite the fact that greater than 50% of initial patient visits had clinical presentations requiring screening for CD as per societal guidelines. Our study thus suggests suboptimal case-finding to be a possible reason that a substantial portion of CD cases remain undiagnosed in the USA, and highlights the importance of screening high-risk populations.¹ Suboptimal case-finding constitutes a gap in patient care and an important target for future quality improvement initiatives.

The value of testing may be enhanced in populations with higher prevalence of CD, such as those with iron deficiency anaemia. Nevertheless, more than half of patients do not have classic CD symptoms, increasing the importance of heightened awareness and provider education.⁹¹⁴ Given the prevalence rate of around 1 in 100 individuals, universal screening is not deemed cost effective, rendering targeted testing as the main strategy for CD screening.

For this strategy to succeed, our results suggest that the proportion of patients screened needs to increase far above those observed at our institution.

When symptoms are overt, and with the implementation of targeted testing, most coeliac patients likely would be diagnosed in the office of primary-care physicians or managed by the community gastroenterologist, leaving few cases to reach tertiary care practices. When active screening was implemented in a multicenter primary-care setting, this yielded a positive serologic diagnosis (abnormal anti-TTG) in approximately 3% individuals, which is higher than the prevalence in our setting.⁴ This suggests that a case-finding strategy can be successful if all providers participate in actively seeking out settings where CD testing is indicated. While our study did not include survey of providers to identify barriers to CD testing, we speculate that the busy clinic environment, patients with non-classic symptoms for CD and suboptimal recognition of settings requiring CD screening are potential causes for the low screening rate. Most of these barriers should be successfully overcome by increasing educational opportunities and reminders, a strategy that we currently are piloting in a follow-up quality improvement study. Knowledge deficits have previously been implicated in low coeliac screening rates by primary-care physicians.¹⁵ 16 At present, delays in diagnosis among adult patients with CD remain long; one Scandinavian study reported that over 30% of patients diagnosed with CD had a diagnostic delay of more than 10 years.¹⁷

Our findings demonstrate a difference in screening rates across different GI subspecialty clinics, suggesting that case-finding guidelines may need enhancement within GI subspecialty societies. In liver and IBD clinics, perhaps the lower rate of testing was partly due to alternate diagnoses (eg, active colitis, chronic liver disease) that could explain clinical presentations. This may not necessarily be the case in luminal GI clinics, where patients present with more general complaints, and where superimposed IBS may be more common, prompting CD to rise on the differential diagnosis.

Some limitations are inherent to our retrospective design. We were unable to fully evaluate the overall clinical impression of the physicians who were treating, which may have influenced test-ordering practices. Furthermore, it is conceivable that patients could have known that they had previously been screened for CD, but without documentation of screening in referring documents of the physicians or in their medical record. On the other hand, patients may fail to recall if they were previously tested for CD. Errors in clinical documentation are also possible. In terms of the tests used, there is considerable variability in what CD test was ordered. Due to the retrospective nature of the study, testing was not uniform across all patients. Two of the cases identified did not have a confirmatory duodenal biopsy by the time of analysis, while false positive rates for anti-TTG IgA exist, we included these two patients as cases due to the high specificity of this test.¹⁸ We did not consider patients who only had positive antigliadin antibody as new CD cases due to the low specificity of this test. Finally, a limitation exists due to the relatively small number of patients studied; however, we used the traditional 3-month interval (quarterly data) used in healthcare quality studies evaluating gaps in care.

Future studies should target the problem of underused CD screening in a 'plan-do-study-act' quality improvement cycle. Other areas of study include identifying patient and provider

factors that influence lack of CD testing to target our efforts further. Such an intervention would anticipate the difficulties in recalling all the coeliac screening indications, and could eventually decrease waste by minimising repeated visits for undiagnosed CD.

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Main messages

- ▶ Less than 50% of patients where coeliac testing was indicated were screened for coeliac disease.
- ▶ This gap in care was present in a tertiary gastroenterology (GI) clinic setting, higher in hepatology and biliary clinics than in luminal GI and inflammatory bowel disease clinics.
- ▶ This represents an area for future quality improvement efforts.

Current research questions

- ▶ What is the optimal method to increase rates of appropriate coeliac testing among gastroenterology providers?
- ▶ What are the patient factors that are most associated with missed opportunities for coeliac testing?
- ▶ What are the provider factors most associated with missed opportunities for coeliac testing?

Figure 1.
Flow chart for study. CD, coeliac disease.

IBD: inflammatory bowel disease, IBS: irritable bowel syndrome, IDA: iron deficiency anemia,
* :osteopenia, type I diabetes, 1st degree relative with CD, autoimmune diseases

Figure 2.

Coeliac disease (CD) testing indications. *Osteopenia, type 1 diabetes, first degree relative with CD, autoimmune diseases. IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IDA, iron deficiency anaemia; GI, gastroenterology.

Table 1

CD tests used

CD test	Test usefulness* n=145	Proportion abnormal n=5
Anti-TTG IgA	106 (73.1%)	4 (0.04%)
Quantitative IgA	77 (53.1%)	4 (0.05%)
Antigliadin antibody [†]	49 (33.8%)	1 (0.02%)
Antiendomysial antibody	68 (46.9%)	3 (0.04%)
Antideamidated gliadin peptide	20 (13.8%)	0
Duodenal biopsy [‡]	102 (70.3%)	5 (0.05%)

* Some patients had more than one test performed, % of tests used are within those tested.

[†] Patients who had antigliadin antibody also had other forms of testing.

[‡] Performed by referring MD in 46.2%, before serology in 12.4% and after serology in 11.7%, the number of biopsy samples could not be determined from the retrospective review.

CD, coeliac disease; TTG, tissue transglutaminase.

Table 2

CD testing by subspecialty clinic

Type of clinic	n	% testing indicated [*]	% tested ^{†‡}
Luminal GI	252	159 (63.1%)	85 (53.5%)
IBD	88	79 (89.8%)	31 (39.2%)
Liver	202	63 (31.2%)	17 (27.0%)
Biliary	74	35 (47.3%)	12 (34.3%)
Total	616	336 (54.5%)	145 (43.2%)

^{*}
p<0.0001 across groups.

[†]
p=0.002 across groups.

[‡]
% tested calculated from patients where testing was indicated.

CD, coeliac disease; GI, gastroenterology; IBD, inflammatory bowel disease.

Table 3

CD cases identified

	Patient 1	Patient 2	Patient 3	Patient 4
Anti-TTG IgA	High	High	High	High
Quantitative IgA	Normal	Normal	–	Normal
Antigliadin antibody	Normal	–	Normal	–
Antiendomysial antibody	High	High	–	–
Antideamidated gliadin peptide	–	–	–	–
Duodenal biopsy	Total villous atrophy	Total villous atrophy	–	–
Indication for testing	IDA	IDA	IDA	Unexplained elevated liver enzymes

–, not done; CD, coeliac disease; IDA, iron deficiency anaemia; TTG, tissue transglutaminase.