

Screening for Celiac Disease in Children: Practical Guidance for Primary Care Providers

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ABSTRACT

Celiac disease is prevalent in the pediatric population. However, screening for celiac disease can be confusing given the variety of tests available and current guidelines are not always widely known in the medical community. As most children with celiac disease will initially present to their primary care providers (PCPs), PCPs play an integral role in identifying patients at risk for celiac disease. This review provides practical guidance for PCPs screening pediatric patients for celiac disease.

KEYWORDS: Celiac disease; pediatrics; gastroenterology; gluten; screening

INTRODUCTION

Celiac disease is an autoimmune systemic disorder with a genetic component in which gluten exposure/consumption can lead to an inflammatory enteropathy with gastrointestinal and/or extraintestinal signs/symptoms of varying severity.¹ Celiac disease is highly prevalent in the pediatric population, with 0.7–1.4% of children affected globally by the disease,² thus making it one of the most common autoimmune disorders in children.³ The presenting signs/symptoms of celiac disease can be variable. Commonly, children can present with abdominal pain, constipation, diarrhea, vomiting, slow weight gain/weight loss, poor linear growth, or rashes, and some children can have no signs/symptoms at all.¹ Given the variable presentation, children sometimes remain undiagnosed.⁴ Early identification of celiac disease is vital not only for symptomatic improvement, but also in order to address potential complications of the disease as soon as possible (such as weight/growth issues, micronutrient deficiencies, certain types of cancer, fertility issues, etc.).¹ According to current guidelines in North America, screening for celiac disease occurs via bloodwork, and confirmation of celiac disease is through an esophagogastroduodenoscopy, or an upper endoscopy with biopsies.^{1,5-7} As most children with celiac disease initially present to their primary care provider, pediatricians and other primary care providers caring for children play a key role in identifying patients who need to be screened for celiac disease. However, screening for celiac disease can often be confusing, as there are many different tests available and guidelines are not always

widely known in the medical community. This review provides practical guidance for primary care providers screening pediatric patients for celiac disease. This review is intended to be an overview; individual patients may need different approaches based on their specific signs/symptoms.

WHICH CHILDREN SHOULD BE SCREENED?

Symptomatic Children

Celiac disease can be highly variable in presentation and can present with signs/symptoms (gastrointestinal and/or extraintestinal) or can be asymptomatic. Common signs/symptoms at presentation for pediatric patients include but are not limited to abdominal pain, constipation, diarrhea, vomiting, slow weight gain/weight loss, poor linear growth, rash, fatigue, abdominal distention, bloating, iron deficiency anemia, dental enamel erosions, joint pain, osteopenia, short stature, delayed puberty, neurologic abnormalities (including but not limited to migraines, neuropathy, seizures, movement disorders, difficulty concentrating), and elevated liver enzymes.¹

Children at High-Risk for Celiac Disease

The following groups of children are at high-risk for celiac disease and should be screened for celiac disease, even if they are asymptomatic^{1,5,8}:

- Children who have a first-degree relative with celiac disease
- Children with selective IgA deficiency
- Children with Trisomy 21
- Children with type 1 diabetes
- Children with juvenile idiopathic arthritis
- Children with autoimmune thyroid disease
- Children with autoimmune liver disease
- Children with Williams Syndrome
- Children with Turner Syndrome

For asymptomatic children in these higher-risk populations, current guidelines in North America recommend that screening for celiac disease begin at around three years of age (on a gluten-containing diet for at least one year prior to testing),^{1,5} or when the related condition is initially diagnosed,^{1,5} and if the initial testing is negative, at intervals thereafter.^{1,5}

Of note, a gluten-containing diet of greater than or equal to 10g of gluten (two slices of whole wheat bread) per day for

greater than or equal to eight weeks¹ is generally considered adequate to allow for more reliable screening results.

INITIAL TESTING TO SCREEN FOR CELIAC DISEASE

There are a variety of tests associated with celiac disease, which can make it difficult to know which test to use and in what age group. Furthermore, hospitals/clinics often have non-specific names assigned to certain tests, such as “celiac panel,”¹ which may or may not include the testing a patient actually needs. **Table 1** includes a general guideline as to which test to use in various groups in the pediatric population.

Importantly, the child should be on an adequate gluten-containing diet at the time of performing the screening tests. Consuming a gluten-free or gluten-limited diet may lead to a false negative result.^{1,5}

Table 1. Summary of Initial Screening Tests for Celiac Disease for Pediatric Patients

Group	Initial Screening Test(s)
≥2 years old	Tissue transglutaminase IgA (TTG-IgA) and immunoglobulin A (IgA)
<2 years old	Tissue transglutaminase IgA (TTG-IgA) and deamidated gliadin peptide IgG (DGP-IgG)
Selective IgA Deficiency	Tissue transglutaminase (TTG-IgG) or deamidated gliadin peptide (DGP-IgG)

Children ≥2 Years Old

In children ≥2 years old, tissue transglutaminase IgA (TTG-IgA) and immunoglobulin A (IgA) are recommended as initial screening tests, as they are the most reliable and cost-effective.¹ The anti-endomysium antibody IgA (EMA-IgA) is more specific but less sensitive (99% specificity, 73% sensitivity) than the TTG-IgA test (97.9% specificity, 92.8% sensitivity) and is more expensive,^{1,9} and thus is not recommended as the initial screening test in this age group.

Children <2 Years Old

In children <2 years old, TTG-IgA and EMA-IgA tests are not as sensitive.¹ Thus, in this age group, tissue transglutaminase IgA (TTG-IgA) and deamidated gliadin peptide-IgG (DGP-IgG) are recommended as initial screening tests by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN),¹ though recent adult guidelines have suggested otherwise.¹⁰

In the Case of Selective IgA Deficiency

In children with selective IgA deficiency, which is seen more often in children with celiac disease,¹ the IgA-based screening tests are not reliable. As such, IgG-based tests should be used for screening, such as tissue transglutaminase IgG (TTG-IgG) or deamidated gliadin peptide-IgG (DGP-IgG).¹

The Role of Antigliadin Antibody Tests

Antigliadin antibody IgA (AGA-IgA), antigliadin antibody IgG (AGA-IgG) are not recommended for initial screening for celiac disease.¹

The Role of HLA-DQ2 and HLA-DQ8

HLA-DQ2 and HLA-DQ8 are genetic markers for celiac disease but they can also be present in up to 40% of the general population.^{1,11} A positive result for one or both of these markers is not diagnostic of celiac disease. However, a negative result for both makes celiac disease unlikely. These tests are expensive and are generally not used as an initial screening test for celiac disease.^{1,11} They can be used in equivocal or unclear cases for additional information, such as if there is a discrepancy between serological testing and endoscopic pathology, and the diagnosis of celiac disease is in question.^{1,11}

Other Situations

It is important to remember that in the setting of an acute infection, tissue transglutaminase (TTG) may be elevated, and will return to normal after the infection is resolved.¹ If the TTG is found to be elevated in this setting, it is recommended to repeat the testing once the infection has resolved.¹

Similarly, children with autoimmune conditions that are associated with celiac disease may have an elevated TTG-IgA that is unrelated to celiac disease.¹ In these cases, if the TTG-IgA is less than three times the upper limit of normal, EMA-IgA should be tested.¹ If the EMA-IgA is positive, then referral to a gastroenterologist is warranted, as endoscopy with biopsies is likely necessary to confirm the diagnosis of celiac disease.¹ If the EMA-IgA is negative and the patient does not exhibit other signs/symptoms that could suggest celiac disease, then repeating screening tests for celiac disease in 6–12 months and monitoring signs/symptoms is recommended.¹

WHAT TO DO IF SCREENING FOR CELIAC DISEASE IS POSITIVE

If a screening test for celiac disease is positive, the patient must be referred to a gastroenterologist for further evaluation and management. Typically, after discussion with the patient/family, the gastroenterologist will perform an upper endoscopy with biopsies to confirm the diagnosis of celiac disease.^{1,12} Importantly, once a screening test for celiac disease is positive, the patient should ideally stay on a gluten-containing diet until they are able to see the gastroenterologist and undergo upper endoscopy. If the child is already consuming a gluten-free diet or a gluten-limited diet when undergoing upper endoscopy with biopsies, this may lead to a false negative result.^{1,5}

PCPS' ROLE IN DIAGNOSIS AND MANAGEMENT OF CELIAC DISEASE

PCPs play an integral role in the diagnosis and management of celiac disease.¹³ As they are usually the first provider a patient will see, PCPs can facilitate the process of recognizing signs/symptoms of celiac disease, knowing who and when to screen for celiac disease, and coordinating referral to gastroenterology as appropriate. Furthermore, PCPs play an important role in long-term follow up as well, including but not limited to monitoring weight gain and linear growth, monitoring for nutritional deficiencies or other potential complications related to celiac disease, and emphasizing the importance of adherence to the gluten-free diet for management of celiac disease.

CONCLUSION

Celiac disease is an autoimmune disease that can have a highly variable presentation and which is highly prevalent in the pediatric population.¹ Early recognition and appropriate screening is important to not only treat the signs/symptoms of celiac disease, but also to address potential complications related to celiac disease. PCPs play a vital role in this process and are at the frontlines of initiating appropriate screening for patients.¹³

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