Predictors of Gluten Avoidance and Implementation of a Gluten-Free Diet in Children and Adolescents without Confirmed Celiac Disease

Pornthep Tanpowpong, MD, MPH[1], Sarabeth Broder-Fingert, MD[1], Aubrey J. Katz, MD[1], and Carlos A. Camargo, Jr., MD, DrPH[2]

Objectives To determine independent predictors of gluten avoidance and of a physician's decision to initiate a gluten-free diet (GFD) in children and adolescents without confirmed celiac disease.

Study design We performed a structured medical record review of 579 patients aged 1-19 years presenting for evaluation of celiac disease between January 2000 and December 2010 at a large Boston teaching hospital. We collected data including demographic information, medical history, serology, small intestinal biopsy, history of gluten avoidance, and the postworkup recommendation of implementation of a GFD. Predictors of gluten-related issues were identified by multivariate logistic regression.

Results Among 579 children without a previous diagnosis of celiac disease (mean age, 8.7 years), 43 (7.4%) had ever avoided gluten. Independent predictors of gluten avoidance were irritability or poor temper (OR, 3.2), diarrhea (OR, 2.5), weight issues (OR, 0.4), pervasive developmental disorder (OR, 5.3), and family history of celiac disease (OR, 2.2). Among 143 children without confirmed celiac disease who underwent diagnostic evaluation, several predictive factors were associated with a physician- recommended/parent-initiated GFD: irritability (OR, 6.4), diarrhea (OR, 3.4), pervasive developmental disorder (OR, 7.9), and positive serology before the referral (OR, 4.3).

Conclusion Gluten avoidance among children and adolescents without a previous diagnosis of celiac disease is relatively common. The identified predictors suggest that gluten avoidance is associated with nonspecific behavioral and gastrointestinal complaints and perhaps with the perceived dietary responses in another family member thought to have celiac disease. *(J Pediatr 2012;161:471-5)*.

Recent population-based studies suggest that celiac disease affects approximately 1% of the general population of industrialized countries.[1,2] The prevalence has risen in children and adolescents over the past 2 decades.[3,4] The current mainstay of management of celiac disease remains a strict lifelong gluten-free diet (GFD).[5] However, dietary gluten avoidance requires remarkable effort from both the child and the family.[6] Furthermore, in some settings, gluten avoidance can have disadvantageous effects on quality of life,[7,8] self-perceived health,[9] psychosocial dynamics,[10] nutritional status,[11] and increased healthcare costs.[12] Concomitant with the increasing prevalence and awareness of celiac disease, anecdotal evidence suggests that gluten avoidance is prevalent among the general population without celiac disease. We recently found a higher rate of gluten avoidance in New Zealand children compared with the actual prevalence of celiac disease (5% vs 1%), and identified 3 independent predictors of gluten avoidance in children without a previous diagnosis of celiac disease.[13]

Nonspecific symptoms (eg, behavioral changes, bowel movement changes, subjective or vague abdominal complaints), suspected/diagnosed conditions (eg, wheat "allergy" or "intolerance," irritable bowel syndrome, pervasive developmental disorder [PDD, or autistic spectrum disorder]), or equivocal positive celiac disease serology may sometimes lead to a trial of gluten restriction before evaluation for celiac disease. Nevertheless, few studies support the beneficial effects of gluten-restricted diet in children with these nonspecific symptoms and conditions.[14,15] Furthermore, little is known about the reasons for or predictors of gluten avoidance in US children and adolescents without a diagnosis of celiac disease. The aims of the present study were (1) to identify independent predictors of gluten avoidance in children without previously diagnosed celiac disease; and (2) to identify predictors of a physician's decision to implement a GFD in children and adolescents without confirmed celiac disease (after diagnostic evaluation).

Methods

We created a database of all patients who presented for an initial evaluation of celiac disease at Massachusetts General Hospital, a large Boston teaching hospital and referral center, between January 2000 and December 2010. Patients were identified using the *International Classification of Diseases, Ninth Revision, Clinical Modification*

EMA	Endomysial antibody
GFD	Gluten-free diet
PDD	Pervasive developmental disorder
TTG	Tissue transglutaminase antibody

From the [1]Division of Pediatric Gastroenterology and Nutrition and [2]Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

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diagnostic code 579.0, which includes celiac disease, celiac crisis, gluten enteropathy, and nontropical sprue. Structured medical record reviews were performed using a data abstraction form that included demographic data (eg, age, sex, race/ethnicity) and information during the health care encounters (eg, initial presenting signs and symptoms, patient- or parent-reported comorbid conditions in the child and family members). We classified children at the time of the initial evaluation into 3 age groups: toddler-preschool (1-5 years), school age (6-11 years), and adolescence (12-19 years). We collected information regarding dietary gluten avoidance (yes/no) by parental or patient reports and data regarding physician-recommended/parent-initiated GFD (yes/no). Data on serologic markers (including tissue transglutaminase antibody [TTG], antigliadin antibody, and endomysial antibody [EMA]), and histopathological analysis of small intestinal biopsy were also obtained. All children were evaluated by a pediatric gastroenterologist.

As a referral hospital, our hospital also receives patients from other institutions who have undergone evaluation for celiac disease. Patients with a previous diagnosis of celiac disease from other institutions were excluded from our analysis. We used cutoff values of 20 U/mL for TTG and antigliadin positivity and any positive titer for EMA positivity. The medical records were reviewed by 2 physicians. The study was approved by the our hospital's Institutional Review Board.

Biostatistical Analysis

All analyses were performed using using Stata 11.1 (StataCorp, College Station, Texas). Subjects were described using descriptive statistics, including mean ± SD, median (IQR), and proportions (with 95% CI). Logistic regression was used to examine unadjusted associations between variables of interest and gluten-related issues (ie, gluten avoidance and physician-recommended/parent-initiated GFD). For each characteristic, OR with 95% CI was calculated. Multivariate models were created via stepwise selection. Multivariate logistic regression was performed to adjust for potential confounders. A 2-tailed P value <.05 was considered statistically significant.

Results

Of the 720 patients aged 1-19 years at the time of initial celiac disease evaluation, we excluded 78 patients with celiac disease diagnosed before the referral and 63 patients with no available information on history of gluten avoidance before the initial encounter. Thus, the study population comprised 579 children and adolescents. Mean age at the time of the initial celiac disease evaluation was 8.7 ± 5.3 years, with a slight predominance of patients in the younger age groups (1-5 years, 36%; 6-11 years, 35%; 12-19 years, 29%). The study population was predominately female and white.

Table I presents baseline characteristics, clinical presentation, celiac disease serology before referral, past medical history and family history, and history of gluten avoidance in the study population. Overall, most children and adolescents presented with subjective abdominal complaints or bowel movement changes. Reported "positive" celiac serology before the referral was found in 259 children (45%), but documented positive values of either TTG or EMA were noted in only approximately two-thirds (174 of 259) of these patients. Current generally accepted serologic markers with high sensitivity and specificity include TTG and EMA[5,16]; antigliadin antibody is no longer recommended for evaluating pediatric celiac disease.[16] However, among 85 patients without positive TTG or EMA (ie, less conventional serology), 80% were positive for antigliadin IgA, and others had other various positive tests (eg, antigliadin IgG).

Forty-three children (7.4%; 95% CI, 5.4%-9.9%) had a history of dietary gluten avoidance without previous diagnosis of celiac disease. Table II presents unadjusted predictors of gluten avoidance in children without previously diagnosed celiac disease. Significant predictors included complaints of irritability or poor temper, overall bowel movement changes, diarrhea, weight issues, history of food allergy, diagnosed PDD, and positive family history of celiac disease (all $P < .05$). There were no significant differences in gluten avoidance by age group, sex, race/ethnicity, subjective abdominal complaints, atypical manifestations, or positive serology before the referral.

In the multivariate model, 5 factors remained as independent predictors of gluten avoidance: irritability or poor

Table I. Baseline characteristics, clinical presentation, serology, medical history, and gluten avoidance in the 579 children without previously diagnosed celiac disease

Characteristic	
Age at initial encounter, years, median (IQR)	8 (4-13)
Female sex, %	61
Non-Hispanic white, %	95
Clinical presentation and previous positive serology	
Subjective abdominal complaints (pain, discomfort, bloating), %	58
Abdominal pain, %	46
Flatulence, %	9
Poor appetite, %	12
Tiredness or fatigue, %	11
Irritability or poor temper, %	8
Vomiting, %	16
Bowel movement changes, total %	56
Diarrhea (with or without constipation), %	35
Constipation (without diarrhea), %	21
Weight issues, total %	45
Weight loss, %	16
Failure to gain weight, %	29
Atypical extraintestinal presentations, total %	10
Short stature or stunted height, %	5
Iron deficiency with or without anemia, %	3
Elevated liver enzymes, %	2
Reported positive serology before the referral, %	45
Documented positive values of either TTG or EMA*	30
Medical history and family history	
Type I diabetes, %	5
Food allergy, %	7
PDD, %	6
Family history of celiac disease, %	25
Family history of gastroesophageal reflux, %	11
History of dietary gluten avoidance in the child, %	7

*Cutoff values of 20 U/mL for TTG positivity and any positive titer for EMA positivity.

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