

Celiac Disease in Normal-weight and Overweight Children: Clinical Features and Growth Outcomes Following a Gluten-free Diet

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ABSTRACT

Objectives: There are few data on pediatric celiac disease in the United States. The aim of our study was to describe the presentation of celiac disease among children with a normal and an elevated body mass index (BMI) for age, and to study their BMI changes following a gluten-free diet (GFD).

Patients and Methods: One hundred forty-two children (age 13 months–19 years) with biopsy-proven celiac disease, contained in a registry of patients studied at our center from 2000 to 2008, had follow-up growth data available. Patients' height, weight, and BMI were converted to z scores for age and grouped by BMI as underweight, normal, and overweight. Compliance was confirmed using results of serological assays, and data of noncompliant patients were analyzed separately. Data were analyzed during the observation period and were expressed as change in height, weight, and BMI z score per month of dietary treatment.

Results: Nearly 19% of patients had an elevated BMI at diagnosis (12.6% overweight, 6% obese) and 74.5% presented with a normal BMI. The mean duration of follow-up was 35.6 months. Seventy-five percent of patients with an elevated BMI at diagnosis decreased their BMI z scores significantly after adherence to a GFD, normalizing it in 44% of cases. Of patients with a normal BMI at diagnosis, weight z scores increased significantly after treatment, and 13% became overweight.

Conclusions: Both normal weight and overweight frequently occur in North American children presenting with celiac disease. A GFD may have a beneficial effect upon the BMI of overweight and obese children with celiac disease.

Key Words: body mass index, celiac disease, children, gluten-free diet, obesity, overweight

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Celiac disease is an autoimmune disease precipitated by the ingestion of gluten-containing foods in genetically susceptible individuals. The clinical manifestations of the disease have changed. Patients present less frequently with the classic symptoms of failure to thrive and diarrhea, and atypical, often extraintestinal, presentations are commonly identified in both adults and children (1–5). In the setting of these changes in disease presentation, there is greater awareness that celiac disease must be considered in patients without evidence of malnutrition. Reports of overweight and obese adults and children diagnosed as having celiac disease are becoming more common (1,3,4,6).

The characteristics of celiac disease among overweight children are unclear, as is the effect of long-term treatment upon the anthropometrics of children with a normal or an elevated body mass index (BMI). There is some evidence that a gluten-free diet (GFD) may lead to weight loss in some overweight adults with celiac disease (6). No studies have been conducted to evaluate BMI outcomes in children who are overweight.

Our aim was to evaluate the prevalence of normal BMI and overweight at diagnosis among a cohort of North American children with celiac disease, to describe the clinical characteristics of these patients, and to study the changes that occur in growth indices following long-term treatment with a GFD.

PATIENTS AND METHODS

Patients and Data Collection

We conducted a retrospective review of patient records contained in a registry of children with celiac disease studied by our center between 2000 and 2008. Before inclusion in the registry, a diagnosis of celiac disease was confirmed according to present guidelines (7). The criterion for inclusion in our study was the availability of biopsy results for review by our pathologist. Biopsy findings of all of the patients, reported according to the modified Marsh criteria (8), were classified as mild enteropathy (Marsh II–Marsh IIIa/partial villous atrophy), or severe enteropathy (Marsh IIIb–IIIc/ subtotal–total villous atrophy). Additional information also was collected regarding mode of presentation, growth measurements at presentation, and growth measurements at the most recent follow-up after treatment with a GFD, up to 2010.

As a gauge of dietary compliance, we noted results of serological assays (tissue transglutaminase immunoglobulin A [IgA], antiendomysial IgA, and antigliadin IgA/IgG) before treatment and throughout treatment, as well as the number of consultations with a nutritionist, if any. Patients whose positive serologies had normalized within 2 years of starting the GFD and who maintained seronegativity were assumed to be compliant with

the diet, whereas those with persistently positive serologies were assumed to be noncompliant.

Patients' height, weight, and BMI were converted to age-specific percentiles and *z* scores derived from growth charts published by the Centers for Disease Control and Prevention (9). For children younger than 2 years, weight-for-height percentiles were used in lieu of BMI. Subjects were grouped into 3 categories according to presenting BMI percentile, as defined by the Centers for Disease Control and Prevention (10): underweight (*z* score < -1.65 , or < 5 th percentile for age), normal BMI (*z* score -1.65 to 1.02 , or 5th to < 85 th percentile for age), and overweight (*z* score > 1.02 , or ≥ 85 th percentile for age). Data were analyzed during the observation period and were expressed as change in height, weight, and BMI *z* score per month of treatment with a GFD. Data of compliant and noncompliant patients were analyzed separately.

Statistical Methods

Two-sample *t* tests or generalized regression models were used for continuous variables, and 1-sample *t* tests were used to compare pre- and posttreatment BMI. A *P* value of 0.05 was considered significant. Stratifying by baseline BMI *z* groups, mean change per month of treatment was estimated with a 95% confidence interval. Data analysis was performed using R and SAS software (version 9.2 for Windows, 2010, Cary, NC). The present study was approved by the institutional review board of Columbia University Medical Center.

RESULTS

Cohort Characteristics

Presentation and Histopathology

We identified 318 patients (57% girls) with biopsy-proven celiac disease. The mean age at diagnosis was 8.3 years (range 1.1–19.5 years). The majority of patients presented with nondiarrheal symptoms (91%, $n = 267$) (Fig. 1). Growth problems (failure to thrive, decelerated growth, or short stature), abdominal pain, and screening (patients screened for the disease because of a history of type 1 diabetes mellitus, autoimmune thyroid disease, or a first-degree relative with celiac disease) represented the most frequent presentations overall. The majority of biopsies were significant for severe enteropathy (62%, $P < 0.001$), regardless of age, sex, or presenting symptoms.

Frequency of Normal Weight and Overweight at Diagnosis

Nearly 19% of patients in the cohort had an abnormally high BMI at diagnosis (12.6% overweight, 6% obese), and 74.5% of patients presented with a normal BMI. The remaining 6.5% were underweight at the time of diagnosis.

Follow-up Cohort

Clinical Characteristics and Histopathology

One hundred forty-two patients had anthropometrics recorded after initiation of a GFD. This cohort demonstrated no significant differences in age; the proportion of girls; or the proportion of patients who were underweight, overweight, or had normal BMI parameters at diagnosis.

The characteristics of the follow-up cohort at diagnosis, when grouped by BMI at presentation, are found in Table 1 and Figure 2. Female patients presented with a normal BMI more frequently than male patients (85% vs 67% of male patients, $P = 0.01$), whereas male patients were more frequently overweight or obese at diagnosis (23% vs 9% female patients, $P = 0.02$).

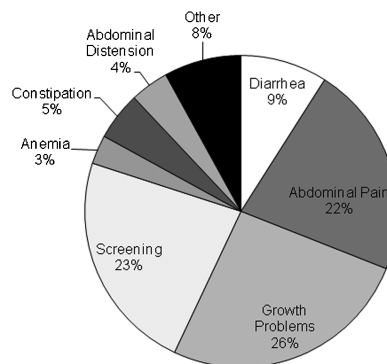


FIGURE 1. Presenting symptoms of entire cohort of children diagnosed with celiac disease. Growth problems refer to patients with failure to thrive, short stature, or decelerated growth.

The majority of patients in all 3 of the BMI groups had severe enteropathy lesions on duodenal biopsy. BMI *z* scores at diagnosis did not differ between patients with mild and severe enteropathy ($P = 0.5$).

The mean duration of follow-up was 35.6 months (95% confidence interval 31.3–39.9 months) (Table 1). Male and female patients had similar mean durations of follow-up (36.5 vs 35 months, $P = 0.8$).

Compliance With a Gluten-free Diet

Tissue transglutaminase IgA antibody was used more frequently than other serologies as a periodic gauge of dietary compliance. Seventy-six percent of patients with available serological data ($n = 126$) demonstrated sustained seronegativity following treatment. All of the patients underwent dietary review, and at least 63% of patients had 1 or more consultations with a nutritionist experienced in celiac disease and the GFD.

Compliant patients had a longer mean duration of follow-up than patients with persistently elevated serologies (41.6 ± 26.3 vs 25.9 ± 20.9 , $P = 0.003$). Differences in BMI changes were not detected between those seen by a nutritionist, those not receiving a nutrition consultation, or those with multiple visits with a nutritionist. Noncompliant patients had significantly more visits with a nutritionist (1.7 vs 0.9, $P < 0.001$).

Alterations in Growth *z* Scores Following a Gluten-free Diet

The majority of compliant patients studied increased their height (57%) and weight (67%) *z* scores for age. BMI increased in 49% of patients at follow-up. Overweight patients with confirmed dietary compliance demonstrated significant decreases in BMI *z* scores for age during the follow-up period (mean Δ BMI *z*/month = -0.01 , $P = 0.01$), whereas noncompliant overweight patients increased their BMI *z* scores significantly after follow-up (mean Δ BMI *z*/month = 0.01 , $P = 0.04$). Patients with a normal BMI at diagnosis demonstrated significant weight *z* score increases following treatment ($P < 0.01$), whereas their noncompliant counterparts showed significant decreases in weight *z* scores at follow-up ($P = 0.04$).

The proportion of overweight patients in the cohort increased after treatment (16.7% vs 19.8%) because of development of overweight in several children with previously normal BMI *z* scores

TABLE 1. Clinical characteristics at diagnosis of patients with celiac disease

| BMI | Underweight | Normal | Overweight | P |
|----------------------------------|-----------------------|---------------------|-----------------------------------|----------|
| N | 11 | 110 | 21 | NS |
| Age, y (mean) | 6.1 | 8.6 | 7.4 | NS |
| Sex (% female) | 45 | 63* | 33* | 0.01* |
| Follow-up length, mo (mean ± SD) | 40.2 ± 29.6 | 35.3 ± 26.9 | 35.1 ± 18.5 | NS |
| BMI (mean, z) | -2.1 | -0.1 | 1.7 | <0.0001† |
| Height (mean, z) | -0.3 | -0.5 | -0.5 | NS |
| Weight (mean, z) | -1.7 | -0.4 | 0.9 | <0.0001† |
| Histopathology (severe, %) | 64 | 65 | 55 | NS |
| Predominant presentation (N) | Failure to thrive (5) | Abdominal pain (27) | Abdominal pain (6)/ Screening (6) | |

BMI = body mass index; SD = standard deviation. * Reflects comparisons between 2 groups. † Reflects comparisons among all 3 of the groups.

for age, despite resolution of overweight in others (Table 2). Of the 6 obese patients studied, only 1 worsened his BMI, 1 remained stable, whereas 4 decreased their BMI z scores at follow-up. Two patients diagnosed with a normal BMI became obese after treatment. Of the 13% of patients with a normal BMI at diagnosis who became overweight after treatment, 70% were girls. Nonetheless, the degree of BMI z score changes following treatment did not vary by sex (P = 0.4).

DISCUSSION

Our cohort comprises the largest group of children with celiac disease described in the United States. Although the clinical characteristics of this disease have been studied in adult patients worldwide and in European children, the nature of celiac disease in North American children has not been characterized extensively. To our knowledge, only 3 other recent cohorts of pediatric patients diagnosed as having celiac disease in the United States have been published, although with smaller sample sizes (1,5,11). The relative size of our cohort provides further insight into the presentation of this complex disease.

An increase in the diagnosis of celiac disease in children with normal weight, overweight, and obesity may be reflective of both the shift in disease presentation and the effect of serological screening. The majority of patients in our cohort had a normal BMI at diagnosis, and recent studies have shown that children with celiac disease commonly present with a normal body weight for age (5,12,13). Furthermore, nearly twice as many patients were overweight at diagnosis as underweight and this has been noted previously (1,3,14,15), although we have additionally described the clinical presentation of these children. Among the overweight children in our study, 28% were identified because of screening and of these patients, >80% were identified because of familial screening (the remainder were screened because of an underlying autoimmune disorder). Our data and that published by Cheng et al (6) demonstrated that overweight is more common in boys with celiac disease than in girls, whether in childhood or adulthood.

Although a GFD improves the weight and body composition of children with celiac disease who are underweight at diagnosis (16–18), there are few data regarding growth outcomes of children with celiac disease with a normal or elevated BMI. Recent studies of adults in the United States with celiac disease have shown a

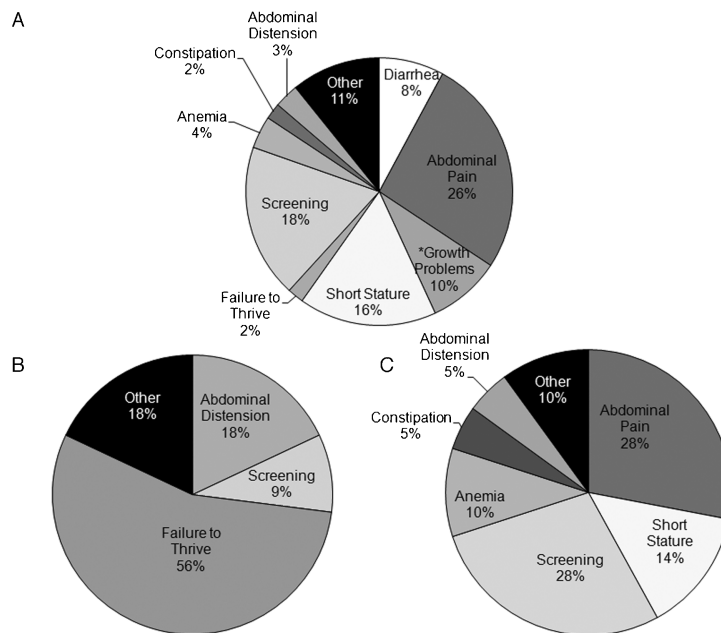


FIGURE 2. Presenting symptoms of children according to presenting BMI category. A, Normal BMI. *Growth problems refer to those with decelerated growth. B, Underweight. C, Overweight.

TABLE 2. Alterations in BMI classification following a GFD

| Initial BMI | Follow-up BMI classification after a GFD (%) | | |
|-------------|--|----------|------------|
| | Underweight | Normal | Overweight |
| Underweight | 1 (20) | 4 (80) | 0 |
| Normal | 2 (2.7) | 63 (84) | 10 (13.3) |
| Overweight | 0 | 7 (43.8) | 9 (56.3) |

BMI = body mass index; GFD = gluten-free diet.

beneficial effect of the GFD regardless of BMI at diagnosis: obese patients lost weight, whereas underweight patients gained weight (6,19). Pediatric literature on the subject has been limited up to now. Our data show that for most overweight children with celiac disease, a GFD has a beneficial effect. Two thirds of obese children receiving GFD decreased their BMI *z* scores and only 25% of overweight patients worsened their BMI *z* scores while compliant with a GFD. In contrast, all of the noncompliant overweight patients increased their BMI at follow-up. The reasons for these findings are unclear. Possible explanations are increases in daily activities resulting from an increased sense of well-being following treatment, alterations in one's diet because of dietary restrictions, and close nutritional surveillance. Prospective studies to identify the factors responsible for these BMI alterations are warranted, with particular attention paid to macronutrient intake and activity.

The development of overweight in many children diagnosed as having a normal BMI warrants attention. BMI increases, whether desired or undesired, after treatment of childhood celiac disease are probably multifactorial. Improved absorption likely plays a significant role, as suggested by substantial BMI increases among children with diarrhea in recent case reports (20,21). Lifestyle factors, particularly dietary choices, also have been shown to play a role (22), although Ohlund et al (23) recently showed that children with celiac disease on a GFD are subject to the same dietary shortcomings as healthy children consuming an unrestricted diet. Likewise, the prevalence of overweight in our cohort, whether before or after treatment, is similar to that of children and adolescents in the United States, making it unlikely that elements of the GFD alone are responsible for unwanted BMI increases (24). Nonetheless, given that 2 in 5 children with a BMI >50th percentile at age 3 years will be overweight at age 12 years (25), the opportunity for greater nutritional surveillance should be taken to avoid such outcomes in children with celiac disease.

This is a retrospective study, which has limitations. Although all of the patients underwent dietary review and most had at least 1 consultation with an experienced dietician, detailed dietary inventories were not available for review to survey macronutrient intake. Furthermore, ours is a tertiary-care referral center and, as a result, our experience may differ from the types of cases and presentations of disease encountered in the community at large.

CONCLUSIONS

Celiac disease is a prevalent disorder in children. Normal and elevated BMI are frequent presenting growth profiles among North American children with celiac disease. The GFD has a beneficial effect upon the BMI of overweight children with celiac disease. It is unclear whether the diet is responsible for unwanted BMI increases among children with a normal-presenting BMI. Expert nutritional surveillance is critical to maximize dietary compliance and nutritional balance, although even this does not guarantee optimal growth patterns. Prospective controlled studies of the effects of the GFD upon the growth patterns and dietary choices of children with celiac disease are warranted.

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