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OTHER REVIEWS

Children With Celiac Disease

Effect of Gluten-Free Diet on Growth and Body Composition

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Celiac disease is an autoimmune disorder characterized by immunologically mediated intolerance to gluten, the only medical intervention is lifelong gluten withdrawal or avoidance. Celiac disease is a common disorder among children. Early diagnosis and diet therapy are crucial, as children experience high growth velocity in this phase of their life. This article reviews recent literature on the impact of celiac disease on growth and body composition on children and describes the outcome following a gluten-free diet. **Key words:** *body composition*, *celiac disease*, *children*, *gluten-free diet*, *growth*

CELIAC DISEASE is an autoimmune disorder characterized by chronic inflammation of the small intestinal mucosa. Individuals with celiac disease have an immunologic reaction to gluten-containing foods, which contain specific sequences of amino acids found in wheat, rye, and barley. Resulting inflammation and villous atrophy may lead to malabsorption of nutrients.[1,2]

In the past, celiac disease was thought to be a rare childhood disease, but it is now recognized as a fairly common genetically based disorder. The overall prevalence of celiac disease is similar in Europe and North America, affecting up to 1% of the population.[3,4] In a large multicenter study in the United States, the prevalence of celiac disease with no evident risk factors was 1:133, making it one of the most common autoimmune disorders.[5] In children, reported prevalence ranges from as few as 1:300 to as many as 1:80.[6] Celiac disease is most common in whites and people of European ancestry.[7] It is rare in people of Japanese, Chinese, and purely African-Caribbean descent.[8] Women are affected more often than men.[7] Table 1 shows population groups with a high prevalence of celiac disease.[2]

The diagnosis of celiac disease is established by positive results of serological testing and evidence of characteristic histopathology on intestinal biopsy.[6] Traditionally, celiac disease was thought to present primarily with gastrointestinal symptoms in children, with malabsorption as a common cause of growth delay. However, as serological testing and the understanding of celiac disease have improved, "atypical" presentations of celiac disease are being increasingly recognized and, in fact, obesity is more common in children with celiac disease than previously identified.[9] Therefore, being overweight or without evidence of malnutrition does not exclude the diagnosis of celiac disease.[10] Celiac disease can be diagnosed at any age and in general, children younger than 3 years present

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Table 1. Individuals With a High Prevalence of Celiac Disease

First- and second-degree relatives of individuals with a history of celiac disease
Insulin-dependent diabetes mellitus
Autoimmune thyroiditis
Down syndrome
Turner syndrome
Williams syndrome
IgA deficiency
Dental enamel defects
Osteoporosis
Iron-deficiency anemia resistant to iron therapy
Short stature
Delayed puberty

with symptoms of classical celiac disease whereas children older than 3 years usually present with symptoms of atypical celiac disease.[2]Tables 2 and 3 list the different symptoms in classical and atypical celiac diseases.[2]

The treatment of celiac disease is lifelong adherence to a gluten-free diet. The recent literature examines the impact of celiac disease on growth and body composition in children and the clinical outcomes of adhering to a gluten-free diet.

EFFECT OF A GLUTEN-FREE DIET ON GROWTH OF CHILDREN WITH CELIAC DISEASE

Because of gastrointestinal malnutrition, failure to thrive, decreased weight or height

Table 2. Classical Symptoms of Celiac Disease

Weight Loss	Distention
Vomiting	Abdominal pain
Diarrhea and/or constipation	Failure to thrive
Gas	Chronic fatigue/pain
Bloating	

Table 3. Atypical Symptoms of Celiac Disease

Iron-deficiency anemia	Angular chelitis
Macrocytic anemia	Recurrent aphtous ulcers
Migraines	Delayed motor development
Neurological changes	Concentration alterations
Seizures	Hypothyroidism/hyperthyroidism
Delayed puberty	Dental enamel hypoplasia
Short stature	Hyposplenism
Kidney stones	Primary biliary cirrhosis
Bone disease	Isolated hypertransaminasemia
Bone fractures	Myasthenia gravis
Recurrent miscarriages	Psoriasis
Infertility	Alopecia universalis
Hepatic steatosis	

for age, protuberant abdomen, and buttock wasting are seen frequently in children with untreated celiac disease.[2,11] Short stature is a common presenting sign of celiac disease, especially in the pediatric population[2] and, therefore, celiac disease should be considered if children are short in stature.[12]

Typically, classical celiac disease is diagnosed during the first 3 years of life. Infants may experience normal growth in the first few months of life until the introduction of weaning foods containing gluten. If a child is gluten-sensitive, a progressive decrease in weight gain occurs with a decline in the percentile for weight for age and weight for height (parabolic curve of weight growth).[13] This poor growth is attributed to reduced food intake and nutrient malabsorption.[13] Bosio et al[14] indicated that with the initiation of a gluten-free diet, children with celiac disease would undergo significant growth acceleration ($P < .05$), and this catch-up growth appears to be most evident during the first year on a gluten-free diet (n = 24, age >4 years).

However, the catch-up growth may not always be achieved and those with celiac disease may remain slightly below average in height for age and skeletal age into adolescence, probably due to the marked acceleration in bone maturation that parallels the rapid increase in growth velocity.[13] In contrast, when there is a delay in the diagnosis and treatment resulting in a gluten-free diet being initiated after the onset of puberty, there may be unsatisfactory final height attained in adulthood.[14] When catch-up growth on a gluten-free diet is not observed, further evaluation and possible growth hormone replacement may need to be considered.[2]

Severe growth delay is less common today, especially in developed countries due to an increased awareness of celiac disease among pediatricians.[13] This awareness can result in a shorter delay from the onset of symptoms to diagnosis and eventually may decrease the number of children with celiac disease who experience suboptimal growth.[13] Other environmental factors delaying the onset of celiac disease include longer periods of breast-feeding and continuation of breast-feeding after gluten introduction.[13,15]

Although celiac disease has been regarded as a malabsorption disorder with diarrhea and weight loss, these presentations are now seen less frequently, with many patients presenting with atypical symptoms of celiac disease. Adults with celiac disease may be overweight or obese, and there is concern that these patients gain more weight after adopting a gluten-free diet.[10,16] Reilly et al[17] conducted a retrospective review (from years 2000 to 2008), using the Center for Disease Control and Prevention growth charts. Among 318 patients (57% females, aged 13 months to 19 years), 19% of the patients had a high body mass index at diagnosis (12.6% overweight, 6% obese) and only 6.5% of the patients were underweight at the time of diagnosis. After treatment with a gluten-free diet, the body mass index of overweight children with diet compliance was significantly decreased in the study ($P = .01$). However, conflicting results were shown in the study conducted by Valletta et al,[18] who studied 149 children (57 males, 92 females, aged 0.7-17 years) with celiac disease between 1997 and 2007. In this study, 11% were overweight and 3% were obese, whereas only 5% were severely malnourished at diagnosis.[18] These observations were similar to the observations of Reilly et al, where starting on a gluten-free diet indicated a significant ($P = .008$) increase in the body mass index z score and the percentage of overweight subjects almost doubled ($P = 0.03$). The percentage of obese patients remained similar (3% vs 4%).

A gluten-free diet is the only treatment of celiac disease, and it also seems to increase the risk of becoming overweight or obese. It is noted that for patients adopting a gluten-free diet, they tend to decrease fiber intake and increase the consumption of fats and proteins to replace the intake of gluten-containing carbohydrates. Poor dietary choices could be induced by unpalatability and the expense of commercial gluten-free products or by the availability of commercial high-fat gluten-free snacks. As a result, adolescents are likely to be at a higher risk of poor eating habits and nutrient deficiencies.[18] Therefore, besides help with adapting a gluten-free diet, nutritional monitoring and follow-up by registered dietitians are important to maximize compliance to diet as well as nutritional adequacy of the diet with an effort to improve growth patterns in children. Nutritional advice is important for those who are already overweight or obese at the diagnosis of celiac disease. More studies are warranted on the effects of gluten-free diets upon growth patterns.

EFFECT OF A GLUTEN-FREE DIET ON BODY COMPOSITION OF CHILDREN WITH CELIAC DISEASE

In addition to growth, body composition is significantly affected by celiac disease in children. In a study conducted by Barera et al,[11] children and adolescents (14 boys and 15 girls, mean age of 9.54 $\pm$ 3.42 years) with newly diagnosed celiac disease had

significantly decreased weight ($P = .04$), fat mass ($P < .01$), and muscle mass ($P < .01$) compared with control subjects. The study concluded that after being on a gluten-free diet for a year, affected children were found to have complete restoration of body composition with no significant differences in weight, fat mass, or lean mass of the limbs compared with healthy controls. The restoration of body composition appears to occur more rapidly and more completely when the gluten-free diet is initiated during childhood or adolescence than during adulthood. The effect also appears to be long lasting because body composition in young adults who initiated a gluten-free diet during childhood or adolescence was within normal limits.[11]

Similar results were attained in a longitudinal prospective study conducted by Rea et al[19] (n = 23, aged 1-12 years), who concluded that no significant difference was found between patients and controls for triceps skinfolds, subscapular skinfolds, fat area index, and bone mineral content after following a gluten-free diet for 1 year. For patients with atypical celiac disease, decreased fat mass has also been described in children (n = 8) in a study by Mazure et al.[20] In a study by Carbone et al[21] (n = 78), the researchers concluded that body composition would be improved if adolescent patients were on a long-term gluten-free diet; the results showed positive improvement even when compliance was not strict. On the contrary, Blazina et al[22] (n = 107) indicated that children and adolescents with celiac disease should adhere strictly to a gluten-free diet to allow normal bone mineralization. Bone mineral density in patients on a strict gluten-free diet was significantly higher than in patients who were noncompliant (lumbar: $P = .01$; total body: $P = .005$).[22] Since the pediatric literature has been limited on prospective controlled studies of the effects of a gluten-free diet upon the body composition changes in children with celiac disease, more study is recommended.

Children with celiac disease are at risk for reduced bone mineral density including osteoporosis, rickets, and osteomalacia.[23] Various studies have shown that in children and adolescents with celiac disease, bone mineral density is decreased (prevalence rate between 3% and 39%) at the time of diagnosis.[24] The specific mechanism of reduced bone mineral density is unclear but may be related to malabsorption of calcium and vitamin D and the effect of increased interleukins (ILs) and other inflammatory mediators.[24]

Reduced calcium intake and impaired calcium absorption in the proximal small intestine due to celiac disease may trigger a sequence of events that leads to reduced bone mass. These events include hypersecretion of parathyroid hormone (PTH), enhanced $1,25(OH)_2$-vitamin D, and diminished 25-OH-vitamin D. The level of 1-α-hydroxylase enzyme is enhanced because the defective enterocytes cannot respond to $1,25(OH)_2$-vitamin D and eventually result in increased levels of PTH. Calcium malabsorption and impaired activity of $1,25(OH)_2$-vitamin D may result due to the relative resistance of the vitamin D receptor to vitamin D. The vitamin D–dependent transporter protein (calbindin-D9K) may be undetectable in patients with celiac disease, which may further reduce the level and biological activity of vitamin D.[24] Fortunately, studies have reported that after being on a gluten-free diet for 1 year, the bone mineral density of children and adolescents with celiac disease appears to be restored to the level of healthy controls,[23,25,26] thus calcium and vitamin D absorption is restored after initiation of a gluten-free diet. Although strict diet adherence is important in children with celiac disease, early diagnosis and implementation of a gluten-free diet also play vital roles by ensuring increased activity of bone metabolism and obtaining peak bone mass.[26]

Currently, the association between systemic inflammation in celiac disease and bone mineral density has been explored minimally. In a conducted study by Fornari et al,[27] high levels of IL-1β, IL-6, and IL-1 receptor antagonists were found in untreated patients with celiac disease (n = 16, aged 18-75 years). After a mean period of 37 months on a gluten-free diet, serum levels of IL-6 were

significantly decreased ($P < .05$) and serum levels of IL-1 receptor antagonist were significantly increased ($P < .05$). IL-6 recruits osteoclast precursors in blood and induces their differentiation and functioning, whereas IL-1 is an activator of bone resorption and inhibits the effect of IL-1; this may explain why untreated patients with celiac disease have low bone mineral density. However, because of the small number of participants in this study,[27] more research is recommended to determine the clinical significance of cytokine production in the pathogenesis of bone disease in celiac disease, particularly in the pediatric population.

The recent discovery of the receptor activator of nuclear factor-κB ligand (RANKL)/RANK/osteoprotegerin (OPG) cytokine network has provided a better understanding of the regulation of osteoclast biology and bone turnover.[28] This discovery may explain why patients with celiac disease have low bone mass density. RANKL, a member of the tumor necrosis factor superfamily, expressed by osteoblasts and their immature precursors, is necessary for osteoclastogenesis. RANKL activates its receptor, RANK, in the presence of macrophage colony-stimulating factor and therefore promotes osteoclastogenesis and induces the activation of osteoclasts. The activation of RANK also prolongs the survival rate of osteoclasts by suppressing apoptosis. Osteoprotegerin acts as a soluble decoy receptor for RANKL and blocks the effects of RANKL It is produced by different tissues and cell types including osteoblasts. Imbalance in the RANKL/OPG ratio is related to altered bone turnover; this was confirmed by recent studies in which the RANKL/OPG ratio was altered in adult patients with celiac disease.[28]

Insulin-like growth factor-1 (IGF-1) exerts an anabolic effect on bone, whereas PTH increases bone resorption. An increase in serum IGF-1 is correlated with increased bone mineral density, but this was found only in subjects with normal baseline serum PTH levels. The levels of PTH are usually higher in patients with celiac disease than in healthy persons.[24]

Nutritional status also is positively correlated with IGF-1 levels. The enterocyte defect in celiac disease impairs the zinc absorption in the body, resulting in zinc deficiency. Zinc deficiency impairs IGF-1 production and further decreases bone density. In addition, diets high in calcium may reduce zinc absorption. As a result, administering calcium supplementation without correcting the mucosal lesions of celiac disease may exacerbate zinc depletion and indirectly lead to impaired bone metabolism.[24]

SUMMARY

Celiac disease is an autoimmune disorder, and individuals with celiac disease have an immunologic reaction to gluten-containing foods. It is a common disorder in children with the prevalence ranging from 1:300 to 1:80. Traditionally considered a malabsorption disease, its diagnosis has been altered with patients having higher rates of "overweight" and "obesity" than being underweight. Thus celiac disease affects children's growth and body composition. In pediatric age groups, early diagnosis and implementation of a gluten-free diet are crucial in preventing nutritional deficiencies and maintaining normal health and growth. Nutrition education and monitoring by registered dietitians are important, especially to those who are overweight or obese at the presentation of the disease.

REFERENCES

1. Celiac Disease Evidence Analysis Project. American Dietetic Association Evidence Analysis Library Web site. http://www.adaevidencelibrary.com/topic.cfm?cat=2826. Updated: January 14, 2009. Accessed September 17, 2011.
2. Pediatric nutrition care manual.Academy of Nutrition and Dietetics Web site. http://www.nutritioncaremanual.org/content.cfm?ncm_content_id=90998. Updated May 2011. Accessed September 17, 2011.

3. Mustalahti K, Catassi C, Reunanen A, et al.; Cluster, Project Epidemiology. The prevalence of celiac disease in Europe: results of a centralized, international mass screening project. *Ann Med*. 2010;42(8):589-595.
4. Carlsson AK, Axelsson IE, Borulf SK, Bredberg AC, Ivarsson SA. Serological screening for celiac disease in health 2-5 year-old children in Sweden. *Pediatrics*. 2001;107:42-45.
5. Fasano A, Berti I, Gerarduzzi T, et al. Prevalence of celiac disease in at-risk and non-at-risk groups in the United States: a large multicenter study. *Arch Intern Med*. 2003;163:286-292.
6. Hill ID, Dirks MH, Liptak GS, et al. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2005;40(1):1-19.
7. Celiac disease—sprue. Medline Plus Web site. http://www.nlm.nih.gov/medlineplus/ency/article/000233.htm. Updated August 29, 2011. Accessed September 17, 2011.
8. Farrell RJ, Kelly CP. Celiac sprue. *N Engl J Med*. 2002;346:180-188.
9. Narayannan V, Grzegorz T, Steven LW. Obesity in pediatric celiac disease. *J Pediatr Gastroenterol Nutr*. 2010;51(3):295-297.
10. Dickey W, Kearney N. Overweight in celiac disease: prevalence, clinical characteristics, and effect of a gluten-free diet. *Am J Gastroenterol*. 2006;101:2356-2359.
11. Barera G, Mora S, Brambilla P, et al. Body composition in children with celiac disease and the effects of a gluten-free diet: a prospective case-control study. *Am J Clin Nutr*. 2000;72:71-75.
12. Troncone R, Kosova R. Short stature and catch-up growth in celiac disease. *J Pediatr Gastroenterol Nutr*. 2010;51(suppl 3):S137-S138.
13. Catassi C, Fasano A. Celiac disease as a cause of growth retardation in childhood. *Curr Opin Pediatr*. 2004;16:446-449.
14. Bosio L, Barera G, Mistura L, Sassi G, Bianchi C. Growth acceleration and final height after treatment for delayed diagnosis of celiac disease. *J Pediatr Gastroenterol Nutr*. 1990;11:324-329.
15. Radlovic NP, Mladenovic MM, Lekovic ZM, Stojsic ZM, Radlovic VN. Influence of early feeding practices on celiac disease in infants. Croat Med J. 2010;51(5):417-422.
16. Cheng J, Brar PS, Lee AR, Green PH. Body mass index in celiac disease—beneficial effect of a gluten-free diet. *J Clin Gastroenterol*. 2010;44:267-271.
17. Reilly NR, Aguilar K, Hassid BG, et al. Celiac disease in children with normal weight and overweight: clinical features and growth outcomes following a gluten-free diet. *J Pediatr Gastroenterol Nutr*. 2011;53(5):528-531.
18. Valletta E, Fornaro M, Cipolli M, Conte S, Bissolo F, Danchielli C. Celiac disease and obesity: need for nutritional follow-up after diagnosis. *Eur J Clin Nutr*. 2010;64:1371-1372.
19. Rea F, Polito C, Marotta A, et al. Restoration of body composition in celiac children after one year of gluten-free diet. *J Pediatr Gastroenterol Nutr*. 1996;23(4):408-412.
20. Mazure RM, Vazquez H, Gonzalez D, et al. Early changes of body composition in asymptomatic celiac disease patients. *Am J Gastroenterol*. 1996;91:726-730.
21. Carbone MC, Pitzalis G, Ferri M, et al. Body composition in coeliac disease adolescents on a gluten-free diet: a longitudinal study. *Acta Diabetol*. 2003;40:S171-S173.
22. Blazina S, Bratanic N, Campa AS, Blagus R, Orel R. Bone mineral density and importance of strict gluten-free diet in children and adolescents with celiac disease. *Bone*. 2010;47(3):598-603.
23. Tau C, Mautalen C, De Rosa S, Roca A, Valenzuela X. Bone mineral density in children with celiac disease. Effect of a gluten-free diet. *Eur J Clin Nutr*. 2006;60:358-363.
24. Bernstein CN, Leslie Wd, Leboff MS. AGA technical review on osteoporosis in gastrointestinal diseases. *Gastroenterology*. 2003;124:795-841.
25. Mora S, Barera G, Beccio S, et al. A prospective, longitudinal study of the long-term effect of treatment on bone density in children with celiac disease. *J Pediatr*. 2001;139(4):526-521.
26. Scotta MS, Salvatore S, Salvatoni A, et al. Bone mineralization and body composition in young patients with celiac disease. *Am J Gastroenterol*. 1997;92(8):1331-1334.
27. Fornari MC, Pedreira S, Niveloni S, et al. Pre- and post-treatment serum levels of cytokines IL-1β, IL-6, and IL-1 receptor antagonist in celiac disease. Are they related to the associated osteopenia? *Am J Gastroenterol*. 1998;93(3):413-418.
28. Mora S. Celiac disease in children: impact on bone health. *Rev Endocr Metab Disord*. 2008;9:123-130.