

Celiac Disease and Functional Abdominal Pain in Children

Both celiac disease and functional gastrointestinal disorders (FGIDs) can present with abdominal pain in children, and the similarity between these two disorders can be confusing since many patients with FGIDs, in actuality, have celiac disease. The authors of this study evaluated for the presence of functional abdominal pain disorders (FAPDs) and functional constipation (FC) in a group of children with celiac disease controlled on a gluten free diet.

Children were prospectively enrolled in this study between 2016 and 2018 at a tertiary children's hospital in Italy, and study subjects were enrolled if they were between 4 and 16 years of age and had follow-up visits at the celiac disease outpatient clinic. Celiac disease diagnosis was made based on standard serologic testing followed by duodenal biopsy (based on European Society for Paediatric Gastroenterology, Hepatology, and Nutrition or ESPGHAN guidelines). During follow-up clinic visits, patients were checked for dietary compliance by tissue transglutaminase IgA antibody (TTG IgA) titers as well as by dietary recall. The presence of associated FAPDs and FC was evaluated using the Rome IV Diagnostic Questionnaire for Pediatric FGIDs. Additionally, a sibling of a child with celiac disease (or a cousin if no sibling was available) with negative TTG IgA titers were used as controls.

A total of 417 children with celiac disease and 373 control patients were used in the final study analysis. Time duration for TTG IgA titers normalization did not differ between children with celiac disease with or without an FAPD, including irritable bowel syndrome (IBS). Children with celiac disease had a significantly higher risk of developing an FAPD compared to controls (11.5% vs 6.7%; $P < .05$; relative risk [RR], 1.8; 95% CI, 1.1–3). Children with celiac disease also had a significantly higher risk of having IBS (7.2% vs 3.2%; $P < .05$; RR, 2.3; 95% CI, 1.1–4.6). No such association was seen in the setting of functional dyspepsia, functional abdominal pain, and abdominal migraines, and there was no significant difference present in the time duration of FAPDs between patients with celiac disease and control patients. Logistic regression demonstrated that younger age at celiac disease diagnosis and higher TTG IgA titers at time of diagnosis predicted

the risk of FAPD as well as IBS. Finally, FC was common in both children with celiac disease and controls, but FC was significantly more common in patients with celiac disease (19.9% vs 10.5%, respectively; $P < 0.001$; relative risk, 2.1; 95% CI, 1.4–3.2).

Thus, celiac disease appears to be associated with the occurrence of both FAPDs and FC in children. The cause is unknown although nerve fiber dysfunction or microbiome changes may account for these findings. Pediatric patients with celiac disease and their families should be informed that such children may have abdominal pain and / or constipation after a celiac disease diagnosis is made, even if a child is compliant with a gluten-free diet.

Cristofori F, Tripaldi M, Lorusso G, Indrio F, Rutigliano V, Piscitelli D, Castellaneta S, Bentivoglio V, Francavilla R. Functional abdominal pain disorders and constipation in children on a gluten-free diet. *Clinical Gastroenterology and Hepatology* 2021; 19: 2551-2558.

Pediatric Patients Who Have Celiac Disease and Inflammatory Bowel Disease

Celiac disease (CD) can occur concomitantly in patients with inflammatory bowel disease (IBD); however, there is limited data regarding both of these diseases occurring in children. The authors of this study performed a multi-center, retrospective, observational study to evaluate such patients using data from the IBD Registry of the Italian Society of Pediatric Gastroenterology, Hepatology and Nutrition (SIGENP). All patients were 17 years of age or younger, and IBD was diagnosed using the Porto criteria while CD was diagnosed using standard antibody tests for CD in addition to findings of villous atrophy on duodenal biopsy per the guidelines of the European Society of Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN). Patients with IBD and CD were compared to a control group of 98 patients with the sole diagnosis of IBD.

Patients with both IBD and CD comprised 49

(continued on page 46)

(continued from page 44)

patients from an eligible pool of 2,800 patients. Crohn disease was present in 26 patients (53.1%) while ulcerative colitis was present in 23 patients (46.9%). Females made up 53.1% of the study subjects. CD was diagnosed before IBD in 75.5% of patients (median interval 4.2 years). The median age at diagnosis for CD was 7.5 years while the median age at diagnosis for IBD was 11.5 years. When compared to patients with IBD alone, patients with CD and IBD were statistically more likely to have other associated autoimmune disease mainly consisting of thyroiditis (OR, 2.81; 95% CI, 0.97–8.37; $P = 0.04$). No difference was present between patients with IBD and CD versus IBD alone regarding immune suppression treatment regimens, surgery, or hospitalizations. Ileocolonic disease was less common in patients with CD and Crohn disease compared to control patients solely with Crohn disease. The risk of colectomy was significantly higher in patients with CD and ulcerative colitis compared to patients with ulcerative colitis alone ($P=0.03$). Growth delay was present at time of diagnosis in 7 patients (14.3%) with CD and IBD compared to 16 patients just with IBD (16.3%) (OR, 0.72; 95% CI, 0.26–1.98; $P = 0.53$). There was no statistical difference in reaching pubertal age between patients with CD and IBD compared to patients with IBD alone; however, patients with CD and IBD were significantly more likely to have pubertal delay (3.2%; OR, 5.24; 95% CI, 1.13–33.0; $P = 0.02$). Univariate analysis

determined that growth delay and a younger age at IBD diagnosis were associated with pubertal delay. CD associated with IBD, intestinal surgery, and a higher number of hospitalizations also were associated with pubertal delay. Although pubertal delay was present, final heights of both male and female patients were similar between patients in the two groups.

This study describes a unique phenotype in pediatric patients with CD and IBD and understanding the risk factors for development of other autoimmune disease as well as growth delay / pubertal delay is important, especially when explaining health outcomes to such patients and their families.

Bramuzzo M, Lionetti P, Miele E, Romano C, Arrigo S, Cardile S, Di Nardo G, Illiceto M, Pastore M, Felici E, Fuoti M, Banzato C, Citrano M, Congia M, Norsa L, Pozzi E, Zuin G, Agrusti A, Bianconi M, Grieco C, Guidici F, Aloï M, Alvisi P, on the behalf of the SIGENP IBD Group. Phenotype and Natural History of Children with Coexistent Inflammatory Bowel Disease and Celiac Disease. *Inflammatory Bowel Diseases* 2021; 27: 1881-1888.

John Pohl, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*

