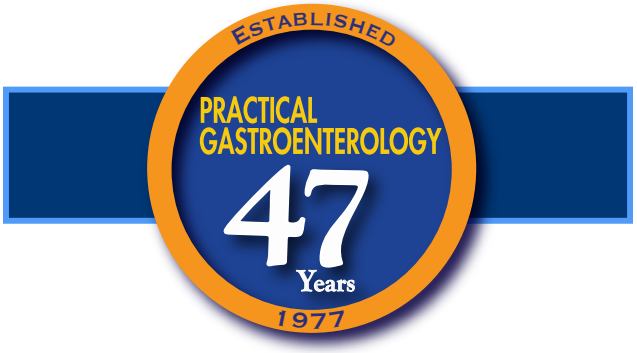
Eosinophilic Esophagitis in Children with Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a chronic inflammatory gastrointestinal condition likely caused by multiple factors, including genetic susceptibility, immune dysfunction, and microbiome abnormalities. IBD typically is divided into three types: Crohn disease, ulcerative colitis, and inflammatory bowel disease unclassified. Eosinophilic esophagitis (EoE) is a chronic inflammatory condition of the esophagus associated with eosinophilic infiltration. EoE can have an allergic component although EoE also can be associated with IBD suggesting a common inflammatory pathway for the two disorders. Minimal data is available regarding the occurrence of IBD and EoE in children, and the authors of this Italian study looked for such an association using a retrospective, case-control, multicenter study of children with IBD.

All new cases of IBD in children from 2009 to 2021 were included in the study. Included patients had standard medical information recorded, and the diagnosis of IBD was based on clinical, endoscopic, histologic, and radiographic findings defined by the Porto Criteria. All EoE cases were diagnosed using European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) criteria. Each pediatric patient under 18 years of age with IBD and EoE was compared to 3 children with IBD alone and 3 children with EoE alone. Patients with IBD and EoE had disease activity monitored by follow-up clinic visits performed 6, 12, and 24 months after IBD diagnosis. Follow up information included the need for corticosteroids use in patients with IBD, clinical relapse in patients with EoE, need for hospitalization, and need for escalation of medical therapy.



No significant difference was found regarding sex, age at diagnosis, and family history of EoE or IBD between the 3 groups. A total of 11 pediatric patients with both IBD and EoE existed in the study group of 3,090 patients with IBD (prevalence 0.35%). The majority of patients (five children) with both IBD and EoE were diagnosed with EoE after IBD with a mean time between diagnoses of 22 ± 10.1 months. Patients with both IBD and EoE were statistically more likely to have IgE-mediated food allergies compared to patients who had IBD alone. No statistical difference was noted for reactive airway disease or eczema.

When patients with both IBD and EoE were compared to patients with IBD alone, no difference was seen regarding IBD type, disease location, inflammatory marker testing results, and treatment. Patients with IBD alone were statistically more likely to have abdominal pain as a presenting symptom compared to patients with both IBD and EoE (P=0.04). Epigastric pain was statistically more common as a presenting symptom in patients with EoE alone compared to patients with both IBD and EoE (P=0.001). Approximately 64% of patients with both IBD and EoE had dysphagia as a presenting symptom with the rest of this patient group having no symptoms to suggest EoE. There were no other clinical differences between patients with EoE alone and patients with both IBD and EoE. There was no statistical difference between patients regarding esophageal eosinophilic infiltration (i.e., number of eosinophils per high-power field) between patients with EoE alone and patients with both IBD and EoE.

The number of patients who needed therapy escalation was significantly higher in patients with IBD alone compared to patients with both IBD and EoE during follow up at 12 months (P=0.04) and 24 months (P=0.04). Patients with IBD alone also were significantly more likely to require systemic steroids and require hospitalization compared to patients with EoE alone and patients with both IBD and EoE. Patients with both IBD and EoE had significantly higher erythrocyte sedimentation rates at follow up compared to patients with EoE alone.

This study appears to show that patients with a combination of IBD and EoE may present with less severe IBD as evidenced by a decreased use

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of systemic steroids and less hospitalizations. However, the number of patients with both IBD and EoE was small in this study, and further research is needed to confirm these findings.

Aloi M, D'Arcangelo G, Rossetti D, Bucherini S, Felici E, Romano C, Martinelli M, Dipasquale V, Lionetti P, Oliva S. Occurrence and Clinical Impact of Eosinophilic Esophagitis in a Large Cohort of Children with Inflammatory Bowel Disease. Inflamm Bowel Dis 2023; 29: 1057-1064.

A Cause of Infant Colic?

Infant colic is commonly seen in general pediatric clinics, and patients with such symptoms often are referred to pediatric gastroenterologists due to concerns of gastroesophageal reflux disease causing colic. However, the etiology of colic is unclear. The authors of this study from Turkey evaluated infant circadian rhythm disruption to see if this aspect was a potential cause of colic.

All included study infants were born between 37-42 weeks of age. Case and control infants were evaluated at 6 weeks of age to see if they had colic using the Wessel criteria defined as crying for at least 3 hours per day for at least 3 days per week. The subsequent study consisted of two parts. In the first stage, parents of all enrolled infants were given a questionnaire for information about infant medical history, parental coping techniques, parental smoking history, parental sleep history, potential circadian rhythm disorders in the family, and parental history of headaches and migraines. The second stage consisted of parents collecting infant 24-hour urine samples via urine bags as well as cotton swab buccal mucosa RNA specimens. Urine samples were obtained twice daily for two days (11 AM and 11 PM) and were tested for cortisol, serotonin, and 6-sulphatoxymelatonin (i.e., a melatonin metabolite) levels by ELISA testing. Buccal mucosa samples underwent quantitative analysis for H3f3b mRNA levels using real-time PCR as the *H3f3b* gene is involved with sleep regulation.

A total of 215 infants qualified for the study, and 95 infants completed the study which was comprised of 46 patient cases and 49 controls. No difference between the two groups regarding demographics was present except for a significantly higher birth weight in the colic group. No infant in the study had undergone physical abuse. Infants with colic had significantly more sound and light sensitivity, defecation difficulty, and waking frequency while having significantly less total daily sleep and sleep period duration compared to controls. Mothers of infants with colic had a significantly more waking frequency while having significantly less total sleep. Mothers of infants with colic also had significantly more headaches and migraines although no such effect was seen in the fathers.

A significant difference in melatonin levels obtained between day and night was noted in the control group suggesting the control group had a normal circadian rhythm. No such finding was present in the colic group suggesting an impaired circadian rhythm. No difference in cortisol levels was present between groups. Serotonin levels were noted to be significantly higher at night in the colic group. H3f3b mRNA levels were significantly higher in control infants compared to infants with colic regardless of samples being obtained during the day or night.

These results demonstrate potential risk factors for infant colic that may work in an aggravating fashion. Such risk factors include impaired infant circadian rhythms as evidenced by urine and mRNA biomarkers, maternal history of sleep impairment, and maternal history of headaches and migraines. The authors bring up the compelling idea that infant colic could be a type of migraine. Although these study results are intriguing, they need to be evaluated in other settings including other countries with lower smoking rates.

Egeli T, Tufekci K, Ural C, Durur D, Erdogan F, Cavdar Z, Genc S, Keskinoglu P, Duman N, Ozkan H. A New Perspective on the Pathogenesis of Infantile Colic: Is Infantile Colic a Biorhythm Disorder? J Pediatr Gastroenterol Nutr 2023; 77: 171-177.

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