Clinical Characteristics of Celiac Disease Seropositivity and Coexisting Inflammatory Bowel Disease in Pediatrics

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Background

- Celiac disease (CeD) and inflammatory bowel disease (IBD) are both immune-mediated conditions triggered by a complex interface of environmental and genetic factors.
- Distinguishing the two entities is challenging due to:
  - Bidirectional association of CeD and IBD.
  - Limited literature on the coexistence of pediatric CeD and IBD.
  - Overlapping symptoms and history.
  - Predilection for false positive celiac serology in IBD patients.
- Inaccurate diagnoses can lead to harm:
  - Starting IBD therapy or a gluten-free diet inappropriately.
- Our aims are to:
  - Describe the unique phenotype of IBD patients with positive CeD autoantibodies.
  - Identify the prevalence of CeD seropositivity and CeD in patients before and after their diagnosis with IBD.

Methods

- Single center retrospective cohort study at Children’s Hospital Colorado.
- With the following inclusion criteria:
  - Age ≤ 18 years old.
  - Positive celiac serology (as defined in Figure 1).
  - Confirmed diagnosis of IBD between 2006-2020 in EHR.
- Patients were classified in the IBD-CeD cohort if they met diagnosis of CeD at the time of endoscopy:
  - Duodenal histology per NASPGHAN criteria (Hill, et al., 2005), or
  - Providers suspected CeD as determined by a survey.
- Patients were classified in the IBD-only cohort if they did not meet criteria for CeD diagnosis.
- IBD-CeD and IBD-only cohorts were compared statistically by unpaired t-test using GraphPad Prism version 8.4.3.

Figure 1: Study Flow Chart

- Retrospective Chart Review (n=475):
  - Positive CeD Autoantibodies with IBD (n=75)
  - Negative CeD Autoantibodies with IBD (n=75)
  - IBD Only + No villous atrophy (n=175)
  - IBD Only + villous atrophy (n=175)

Results

- Prevalence of Positive Celiac Autoantibodies and Celiac Disease.
  - The prevalence of anti-tTG IgA, tTG IgA, and IBD-Only in our study was comparable to pediatric case reports, but limited literature on IBD only patients.
  - Seropositivity and IBD was found in all 3/3 IBD-only patients with tTG IgA > 10x ULN and no villous atrophy compared to 2/17 (12%) with normal tTG IgA and no villous atrophy.
  - These 19 patients all had Crohn’s Disease subtype of IBD. (Iversen et al., 2011) indicates statistical significance (p = 0.005) between IBD-CeD and IBD-only cohorts.

Figure 2: Tissue Transglutaminase (TTG) Serology

- Comparing percentages of patients in IBD-CeD and IBD-only cohorts with normal tTG IgA, > 10x ULN, and < 10x ULN.
  - Of the 17 (6%) with normal tTG IgA, 2/17 (12%) had villous atrophy.
  - Of the 9/17 (53%) with normal IgA, 2/17 (12%) had villous atrophy.

Figure 4: Histologic and Endoscopic Findings

- Comparing percentages of patients in IBD-CeD and IBD-only cohorts with histological findings (esophageal eosinophilia, duodenal cryptitis, and duodenal ulceration).
  - These findings were determined from chart review per pathology reports and provider notes.

Table 1: Prevalence* of Positive Celiac Autoantibodies and Celiac Disease

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<thead>
<tr>
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<th>Before Diagnosis of IBD</th>
<th>After Diagnosis of IBD</th>
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<tbody>
<tr>
<td>Prevalence of Positive Celiac Autoantibodies</td>
<td>22/475 (4.6% ± 1.9%)</td>
<td>3/475 (0.6% ± 0.7%)</td>
</tr>
<tr>
<td>Prevalence of Abnormal tTG IgA</td>
<td>15/475 (3.2% ± 1.6%)</td>
<td>1/475 (0.2% ± 0.4%)</td>
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<tr>
<td>Prevalence of Celiac Disease</td>
<td>8/475 (1.7% ± 1.2%)</td>
<td>0/475 (0%)</td>
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Conclusion

- Preliminary results support the hypothesis that patients with CeD seropositivity and coexisting IBD are characterized by a unique phenotype:
  - tTG IgA as a better predictor for villous atrophy in IBD-CeD when > 10x ULN.
  - Absence of esophageal eosinophilia, duodenal cryptitis, and duodenal ulceration in IBD-CeD.
  - Prominent thrombocytosis and elevated fecal calprotectin in IBD-only.
- Ileal ulceration in IBD-only patients lead to:
  - Mucosal injury and inflammation that may be a mechanism for elevated tTG IgA not specific to CeD.
- Prevalence of IBD-CeD in our study was comparable to pediatric case reports, but limited by incomplete serological data available for review.

Future Direction

- Given the challenge of distinguishing CeD and IBD, our next goals are to:
  - Collect responses on a provider survey to classify CeD diagnosis in seropositive patients with IBD.
  - Characterize provider confidence and factors used to delineate co-occurrence of CeD and IBD.

Acknowledgements

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