Pediatric Inflammatory Bowel Disease — Symptoms and Treatment

Inflammatory bowel disease is an autoimmune condition of the intestine characterized by the non-regulated immune response generated to the intestinal cells. Inflammatory bowel disease can be present at any age, but more than one-fourth to half of the newly diagnosed patients are children or adolescents. The condition is characterized by chronic inflammation of the intestinal tract and has an autoimmune etiology. Diagnosis of the disease in children can be challenging as children may be asymptomatic or may present with extra-hepatic manifestations. It is imperative for pediatricians and physicians to be aware of this condition and its complications.
Epidemiology of Pediatric IBD

Inflammatory bowel disease (IBD) comprises of Crohn’s disease and Ulcerative Colitis. Although IBD cases have been reported worldwide, the incidence of the disease is higher in developed countries than in developing countries. The cool climatic urban areas show more prevalence of IBD than warmer rural areas. Approximately 10% of patients with IBD in the United States are reportedly less than 17 years of age. The incidence of Crohn’s disease in the pediatric population is higher than Ulcerative colitis. Compared to adult-onset IBD, the incidence of pediatric IBD is higher amongst boys than girls, but the incidence in girls increases with age.
Etiology of Pediatric IBD

The etiology of IBD is multifactorial with environmental, genetic and immune factors being implicated. Genetics probably plays an important role in the etiology of pediatric IBD as children are not exposed to environmental causes like cigarette smoke and non-steroidal anti-inflammatory drugs unlike adults, and immune modifiers have not had time to exert their effects.

**Risk factors:**
- Positive family history (seen in 25% cases)
- Jewish ancestry is significant
- Smoking increases risk of CD, decreases the risk of UC
- An appendectomy may be protective

**Genetic factors**

An association between Crohn’s disease and NOD2/CARD15 gene on chromosome 16 has been reported. Children may face an increased risk of IBD if they possess IBD5 and tumor necrosis factor-alpha (TNF-alpha) genes. While the NOD2/CARD15 gene has been associated with an ileal fibro-stenotic disease, IBD5 has been implicated in perianal disease. First degree relatives and twins are more susceptible to the disease.

**Environmental Factors**

Several bacteria and fungi have been implicated in the etiology of IBD as titers against them have been found to be elevated. Some studies suggest the role of interleukin-15 (IL-15) and IL-15 receptor (IL-15R) system in IBD. Smoking in adolescent age can be a triggering agent of the onset of the disease mainly Crohn’s disease. High fiber intake and high intake fruits and vegetables can be helpful in avoiding the disease.

**Immune factors**

Exact factors are not known as children are not exposed to most of the medicines that induce autoimmunity in such a young age.
Signs and Symptoms of Pediatric IBD

The clinical manifestations of IBD in children are more aggressive with a more complicated clinical course compared to adult IBD. Approximately 35% of children may have severe pancolitis at presentation.

The common presenting features in ulcerative colitis include:

- Loss of weight
- Abdominal cramps
- Per rectal bleeding
- Diarrhea
- Abdominal pain
- Fever, sweats
- Malaise, fatigue
- Arthralgia

Presenting features in Crohn’s disease include:

- Loss of weight
- Abdominal pain which starts insidiously
- Perianal diseases, such as fistula and abscess
- Bloody stool with tenesmus

A large percentage of pediatric patients have linear growth restriction several years prior to the disease diagnosis. Growth and development of secondary sexual characteristics, as well as puberty, may be delayed by cytokines and endocrine abnormalities. In addition, treatment of IBD with long-term corticosteroids can lead to osteoporosis.

The risk of malignancies and lymphomas is high in patients who are diagnosed with IBD before the age of 25 years.

Workup of Pediatric IBD

**Detailed history:** In view of the long-term complications associated with pediatric IBD, diagnosis of the condition as early as possible is important. The workup includes a detailed history of onset, duration of symptoms, history of recent travel, food intolerance, medication intake and a family history of IBD.

**Physical examination:** The specific history of height and weight retardation must be obtained. Height and weight should also be calculated according to age-related percentiles during the physical examination. A majority of children with Crohn’s disease, as well as Ulcerative Colitis will have weight loss. An abdominal examination may reveal non-specific pain or a right lower quadrant mass in Crohn’s disease. A digital rectal examination is also required to exclude bleeding, perianal disease or fistulae.

**Laboratory assessments:** Laboratory tests like a complete blood count, C-reactive protein, Erythrocyte sedimentation rate, and stool test for fecal leukocytes, lactoferrin, and occult blood are carried out. Nutritional status can be checked with albumin, pre-albumin and transfer levels.

**Endoscopy:** Upper and lower gastrointestinal endoscopy with biopsies from the mucosa for histopathology form the gold standard test for the diagnosis of IBD. Histopathology helps to differentiate between Crohn’s disease and Ulcerative colitis.
CT scans and MRI: Computed tomography and magnetic resonance enteroclysis may be alternatives to small bowel follow-through to determine the extent of the disease and its complications.

Capsule endoscopy can be performed, but as children may not be able to swallow the capsule, it has to be placed in the duodenum endoscopically.

Serological tests: Serological markers like Anti-\textit{Saccharomyces cerevisiae} antibody (ASCA) and perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA) have high specificity for IBD, while ASCA IgA and IgG are 100% specific for Crohn’s disease in the pediatric population.

Extra-intestinal manifestations include arthritis, nephrolithiasis, erythema nodosum, pyoderma granulosum, ocular complications, choledocholithiasis, primary sclerosing cholangitis, and pancreatitis.

Management of Pediatric IBD

IBD can be managed medically to control symptoms and induce remission. This will decrease the necessity of surgical intervention.

Medical

\textbf{Crohn’s disease}

Mild to moderate disease is initially treated with sulfasalazine or mesalamine or antibiotic therapy (metronidazole and ciprofloxacin). Corticosteroids are the mainstay of treatment in moderate to severe disease but are contraindicated in children with severe growth restriction or severe bone demineralization. Immunomodulators like Azathioprine (5-ASA) and 6-mercaptopurine are used as maintenance therapy for children in remission. For cases refractory to steroids and immunomodulators, infliximab, a monoclonal antibody, can be used to treat moderate to severe disease.

\textbf{Ulcerative colitis}

Mild to moderate disease is treated with enemas or oral 5-aminosalicylic acid agents, sulfasalazine and mesalamine. Corticosteroids can be used in children with moderate to severe disease, but are refractory to treatment with aminosalicylates. Immunomodulators are prescribed to maintain remission but not to induce it.

In addition, nutritional assessment and support are important in the treatment of IBD-associated malnutrition and growth restriction in children. Iron, calcium, Vitamin D/B12, and folate supplementation are essential too. High fiber intake and high intake fruits and vegetables can be helpful in avoiding the disease.

Surgical

\textbf{Indications for surgery in pediatric Crohn's disease are:}

- Intestinal/colonic perforation
- Intestinal obstruction
- Stricture
- Fistulae
- Toxic megacolon
- Malignancy
More than 50% of the patients are likely to require surgical intervention.

**Indications for surgery in Ulcerative Colitis include:**

- Bleeding
- Perforation
- Toxic megacolon
- Refractory to medical treatment
- Severe growth restriction
- Malignancy

**Prognosis**

Crohn’s disease is associated with a chronic, relapsing course and is associated with an increased risk of adenocarcinoma of the small intestine and colon. There is an increased risk of colon cancer in Ulcerative colitis too. Children may face morbidity due to continued steroid oriented therapy. Mortality in IBD is present to some extent.

**References**

- [Diagnostic Considerations in Pediatric Inflammatory Bowel Disease Management](https://www.ncbi.nlm.nih.gov) via ncbi.nlm.nih.gov
- [Inflammatory Bowel Disease](http://pedsinreview.aappublications.org) via http://pedsinreview.aappublications.org

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