

Features and Outcomes of Inflammatory Bowel Disease among Filipino Children in a Tertiary Hospital: An Eleven-year Review

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ABSTRACT

Background. Inflammatory bowel disease (IBD), comprising Crohn's disease, ulcerative colitis, and IBD-unclassified, is a chronic relapsing inflammatory disorder of the gastrointestinal tract, with up to 25% of cases presenting in childhood or adolescence. Although historically uncommon in Asia, the incidence of pediatric IBD in the region has been increasing, and disease phenotype appears to differ from Western populations. In the Philippines, data on pediatric IBD remain limited, with no comprehensive local studies describing its clinical features, subtypes, and outcomes.

Objectives. To describe the clinico-demographic factors that are associated with remission and relapse rates in Filipino pediatric patients with IBD.

Methods. Retrospective review of records of patients <19 years old with IBD from January 2013 to December 2023 in a tertiary government hospital. The clinical, biochemical, imaging, endoscopic, and histologic features, treatment, and outcomes were obtained. Chi-square and T-tests were done to compare the variables and odds ratios to check for associations; significance level set at $p < 0.05$.

Results. Forty-seven (47) children (mean age 11 ± 5.46 years; 64% males) had IBD. Median age at diagnosis was 13 (IQR 8 years). Twelve (25%) were very early onset IBD (VEO-IBD). Median duration of symptoms was 9 (IQR 4-20) months. Bloody stools were more common in UC and IBDU than in CD. Active perianal disease was seen in 30% of CD patients. For induction, UC and IBDU patients used mostly steroids and 5-ASA, while CD patients used mostly exclusive enteral nutrition and steroids. Only 30 patients had at least a 1-year follow-up. Twenty-seven (57%) went into remission within one year. Five CD patients underwent surgery. There was no difference in the 1-year steroid-free remission among the subtypes. One-year relapse rate was significantly higher in UC than in CD. VEO-IBD was associated with not achieving 1-year steroid-free remission (OR 20.8; p value 0.045). One-year relapse rate was associated with diagnostic delay (OR 13.6; p value 0.034), presence of wasting (OR 12.6; p value 0.029), and pancolitis in UC (OR 75; p value 0.043).

Conclusion. The majority of pediatric IBD has CD, with 25% VEO-IBD. 30% of CD had active perianal disease. All subtypes responded similarly to steroids. A higher relapse rate was associated with diagnostic delay, wasting, and pancolitis in UC patients.

Keywords: IBD, Crohn's disease, ulcerative colitis, IBDU



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INTRODUCTION

Inflammatory bowel diseases (IBD) are chronic, relapsing inflammatory diseases of the gastrointestinal tract and include ulcerative colitis (UC), Crohn’s disease (CD), and IBD-unclassified. It can affect both adults and children, and it is estimated that about 25% of patients initially present during childhood or adolescence.¹

The diagnosis of IBD in children requires the presence of chronic intestinal inflammation as well as the exclusion of other causes of inflammation, such as infectious or allergic causes or primary immunodeficiency states. The differentiation of IBD from other causes of chronic intestinal inflammation is based on the constellation of signs and symptoms after a thorough history and physical examination, laboratory findings, endoscopic and histological evaluation of the mucosa, and small bowel imaging, if any.²

The pathogenesis of IBD, though extensively studied, is yet to be fully understood, with the interplay of three emerging themes in recent studies: genetic predisposition, environmental insults, and microbial influences.³⁻⁵

In the past, the incidence and prevalence of pediatric IBD in Asia have been known to be low compared to that in the US and Europe but growing evidence shows that there has been a steady increase in the incidence and prevalence of pediatric IBD in the Asian region from mean annual incidence rates of CD and UC of 0.05 and 0.34 per 100,000 persons, respectively, in 1986–1990 to 1.34 and 3.08 per 100,000, respectively, in 2001–2005.⁶ As compared to adult populations, it has been reported that the IBD disease phenotype and behavior is different among the pediatric population in Asia.⁴ Furthermore, studies have shown that geography plays a role in the differences in the characteristics of IBD patients in terms of epidemiology, disease phenotype, and genetic susceptibility.⁷

There is limited information on inflammatory bowel diseases among Filipino children. The Philippine Pediatric Society (PPS), Inc. Registry listed 1122 (0.02%) cases of IBD (Crohn’s disease and ulcerative colitis) from January 2006 up to March 2024.⁸ As part of the multi-center study from 1995 to 2019, there were a total of 29 IBD patients reported from the Philippines, 24 (83%) were CD, one with UC, and 4 with IBD-U.⁹ There are currently no local studies on the prevalence, clinical, biochemical, endoscopic, and histopathologic features, and the outcomes of pediatric patients with IBD.

This study described the features, treatment, and outcomes, and determined the differences in the IBD subtypes of pediatric patients with inflammatory bowel disease admitted to the Philippine General Hospital, as well as determined the clinico-demographic factors that are associated with remission and relapse rates in pediatric patients with IBD.

METHODS

Patients and Study Design

The study was conducted following the approval of the University of the Philippines Manila – Research Ethics Board and with adherence to the National Ethical Guidelines for Health and Health-Related Research of 2017 and the Data Privacy Act of 2012.

This was a single-center, retrospective cohort study that involved the review of medical and electronic records of children (aged <19 years) who were diagnosed with inflammatory bowel disease and admitted at the University of the Philippines Manila– Philippine General Hospital from January 2013 to December 2023.

The manual database (division census, endoscopy reports, histopathology reports) of the Division of Pediatric Gastroenterology, Hepatology, and Nutrition was reviewed, and a list of patients with confirmed and suspected inflammatory bowel disease was made. The search resulted in 110 patients in the census list: 102 endoscopy records and 112 histopathology reports of patients. A total of 132 unique names were eventually listed for screening, and the medical records of these patients were retrieved and reviewed. All patients who fulfilled the diagnosis of IBD were included in the study, and the diagnoses of either CD, UC, or IBD-unclassified (IBD-U) were established in accordance with the criteria set by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition.¹⁰ This diagnostic process involved a comprehensive assessment, including an evaluation of clinical history, physical and biochemical examinations, endoscopy with histopathological assessment, and small bowel imaging. For Paris classification, identifying the disease location and extent was based on the upper and lower GI endoscopy, histopathologic findings, and small bowel imaging, if any. Figure 1 shows the flow diagram of the patient screening and review.

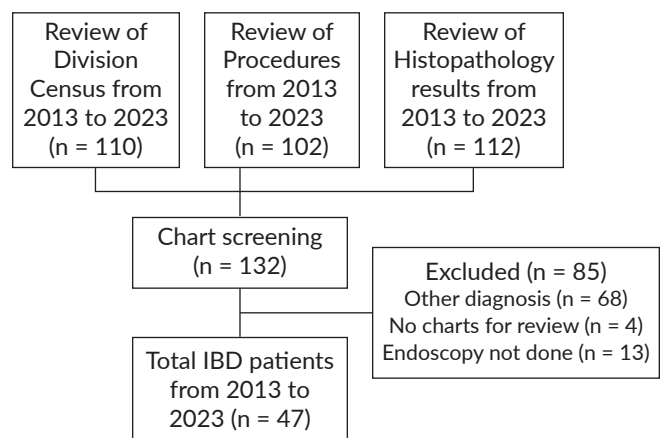


Figure 1. Flow diagram illustrating the selection of charts for review.

Clinical and Biochemical Data

The clinical data collected included demographics, clinical features, presence of co-morbidities, and previous history of tuberculosis, and family history of IBD and autoimmune diseases. The clinical manifestations included abdominal pain, bloody rectal bleeding, chronic diarrhea, abdominal distension, vomiting, oral aphthous ulcers, perianal disease, constipation, weight loss, pallor, fever, anorexia, joint pains, uveitis, and growth failure, defined as stature (length or height) for age z-scores at less than -2.

The biochemical parameters that were recorded were complete blood counts, ESR, CRP, and serum albumin; and based on the age of the patient, patients were identified as to the presence or absence of anemia, leukocytosis, thrombocytosis, elevated ESR, elevated CRP, and hypoalbuminemia.

Pathogenic microorganisms such as bacteria, viruses, and parasites detected via stool studies (direct fecal smear, stool antigen tests, stool cultures) were also noted, and concurrent tuberculosis infection was also documented.

Imaging studies, upper and lower gastrointestinal endoscopic results, and histopathologic reports were noted, and the constellation of these findings was utilized to describe the IBD behavior and phenotype based on the Paris Classification.¹¹

Management and Disease Outcomes

Therapeutic interventions for the induction of remission and for maintenance were recorded, including oral and parenteral steroids, anti-TNF agent, 5-ASA, exclusive enteral nutrition, methotrexate, and azathioprine. Any disease-related surgical intervention done within one year of diagnosis was also documented. Any adverse effects related to therapy were also noted.

For the disease outcomes, the following data were documented: level of disease activity (mild, moderate, or severe) at diagnosis and on one-year follow-up; duration from time of diagnosis to last follow-up, duration from time of diagnosis to remission, and the medications that led to remission. Within a one-year follow-up period, the number of times the following were noted: number of times that the patient (1) had episodes of relapse after going into remission; (2) required hospitalization; and (3) acquired infections. Any IBD-related surgical intervention the patient underwent was verified. The maintenance medications and the adverse effects of treatment were also documented.

Definitions

Ulcerative colitis is characterized by continuous mucosal inflammation of the colon, from the rectum, without small bowel involvement, and without granulomas on biopsy. On the other hand, Crohn's disease is defined by the presence of skipped, non-contiguous chronic inflammation of the gastrointestinal tract with or without granulomas. Other features unique to Crohn's disease include the serpentine ulcers and cobblestoning, stenosis, or strictures. IBD-

unclassified is an inflammatory colitis having uncertain endoscopic and histologic findings, making differentiation between UC and CD difficult even after a complete workup with endoscopic, histologic, and imaging studies.²

The age of onset of symptoms was the age when the clinical manifestations were first reported, and the duration of symptoms was from the date of initial onset to the date of diagnosis. The date of diagnosis was after the endoscopic and histologic findings were noted and correlated with the clinical and biochemical findings. The duration of symptoms was based on the date of onset of symptoms to the date of diagnosis, and duration to remission was from the date of diagnosis to the date of first clinical remission as defined by the clinical scoring systems.

The standard clinical scoring system used was the Pediatric Ulcerative Colitis Activity Index (PUCAI) score for ulcerative colitis and the Pediatric Crohn's Disease Activity Index (PCDAI) score for those with Crohn's Disease.^{12,13} For Ulcerative Colitis, those with a PUCAI score of 10-34 points were classified as having mild disease, 35-64 points as having moderate disease, and >65 points as having severe disease. Those with PUCAI <10 points were classified as having inactive disease (in remission). For Crohn's disease, PCDAI scores of 10-30 points and >30 points were classified as having mild and moderate to severe disease, respectively. A PCDAI score of <10 points was classified as having inactive disease (in remission). For those with IBDU, PUCAI scoring system was used to categorize disease severity.

Data Analysis

The patient demographics, characteristics, and diagnostics were summarized and reported as frequencies and proportions. Univariate analysis of clinical and laboratory data using chi-square and t-tests was conducted. Chi-squared test was done to compare the frequencies of variables such as age, sex, presence of co-morbidities, disease severity at disease onset, family history of inflammatory bowel disease, one-year remission rate, one-year surgery-free rate, and disease severity at one-year follow-up among the three IBD subtypes. T-tests were done to compare the means of variables such as age at disease onset, biochemical parameters, number of relapses, admissions, and infections acquired among the three IBD subtypes and the median of variables such as duration of symptoms and the duration of follow-ups. The significance level was set as a *p*-value of <0.05. The results were analyzed using SPSS version 28.

RESULTS

Clinical and Demographic Characteristics

From January 2013 to December 2023, a total of 132 patients were reviewed and screened. Of these, 85 were excluded (81 patients with other diagnoses such as infectious colitis (2), non-specific colitis (38), rectal polyp (15), hemorrhoids (5), arterio-venous malformation (1), eosinophilic

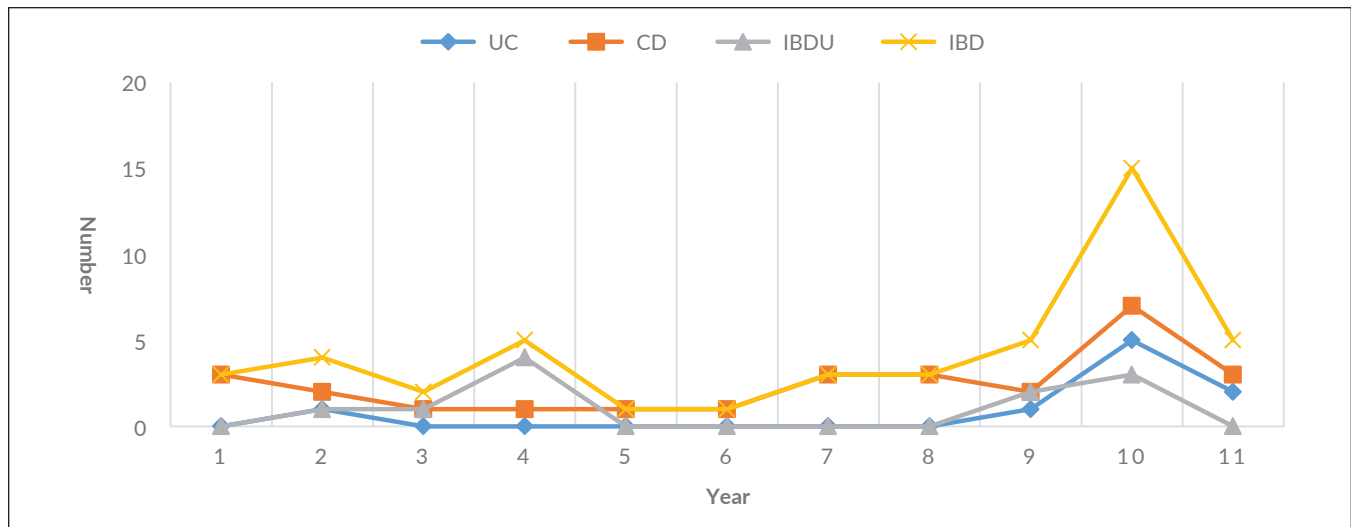


Figure 2. Pediatric patients with inflammatory bowel disease in 11 years (2013 to 2023).

Table 1. Demographic and Clinical Features at Diagnosis of 47 Patients with Pediatric Inflammatory Bowel Disease

	All, N (%)	UC (n=9), n (%)	CD (n=27), n (%)	IBDU (n=11), n (%)	p-value
Male	30 (64%)	7 (78%)	16 (59%)	7 (64%)	0.606
Age (years) at disease onset					0.225
<2	4 (8%)	2 (22%)	1 (4%)	1 (9%)	
2-<6	8 (17%)	3 (34%)	2 (7%)	3 (27%)	
6-<10	7 (15%)	2 (22%)	3 (11%)	2 (18%)	
10-<18	28 (60%)	2 (22%)	21 (78%)	5 (46%)	
Symptoms duration, in months (median, interquartile range)	9 (4-20)	9 (3-18)	9 (4-20)	8 (3-14)	0.672
Severity at onset					0.978
Mild	15 (32%)	1 (11%)	11 (41%)	3 (27%)	
Moderate	14 (30%)	5 (56%)	6 (22%)	3 (27%)	
Severe	8 (17%)	3 (33%)	5 (19%)	0	
Remission	1 (2%)	0	1 (4%)	0	
Missing info	9 (19%)	0	4 (15%)	5 (45%)	
Co-morbidity	16 (34%)	3 (33%)	10 (37%)	3 (27%)	0.804
Past TB infection	12 (25%)	2 (22%)	9 (33%)	1 (9%)	0.008
Family history of IBD	2 (4%)	0	2 (7%)	0	0.340
With stunting	14 (30%)	2 (18%)	9 (33%)	3 (27%)	0.404
With wasting	20 (42%)	4 (44%)	16 (59%)	0	0.002

UC - ulcerative colitis; CD - Crohn's disease; IBDU - inflammatory bowel disease unclassified; TB - tuberculosis infection

colitis (4), food protein-induced enterocolitis syndrome (1), vasculitis (1), Meckel's diverticulum (1), and no endoscopy done (13). There were also 4 patients with a diagnosis of IBD, but with the charts no longer available for review. Ultimately, 47 patients were included in the study. Among them, nine (19%) patients had ulcerative colitis, 27 (58%) patients had Crohn's disease, and 11 (23%) patients had IBD-unclassified. Figure 2 shows the trend in the number of cases of pediatric inflammatory bowel disease in the 11-year study period.

Table 1 shows a summary of the demographic and clinical profile of the patients. The majority (64%) were males. The mean age at diagnosis was 11 ± 5.46 years old. The majority (60%) had their onset at the age of 10 years and older, but

25% (12 out of 47) presented before 6 years old. The median duration of symptoms was 9 months (range 1-84 months).

Of the 47 patients, 15 (32%) had mild disease at presentation. Sixteen (34%) patients had co-morbidities, including bronchial asthma (8), epilepsy (1), chronic liver disease from sclerosing cholangitis (1), G6PD deficiency (1), cerebral palsy (1), vasculitis (1), thalassemia trait (1), and neurodevelopmental disorders (autism spectrum disorder, attention deficit hyperactivity disorder) (2). The patient with sclerosing cholangitis was a seven-year-old female who presented first in the institution with hematemesis from Grade 3 esophageal varices and hepato-splenomegaly. In further history, there was a note of chronic diarrhea since

she was three years old. She was eventually diagnosed with ulcerative colitis after a complete work-up.

Twelve patients (23%) had previous treatment for tuberculosis: five of these were for gastrointestinal tuberculosis (with positive stool AFB and positive terminal ileum TB-PCR), while seven were treated for pulmonary tuberculosis (with positive sputum AFB, sputum GeneXpert, and TB Quantiferon). UC and CD patients had a higher percentage of history of TB infection (22% and 33%, respectively) compared to IBDU patients (9%), with a *p*-value of 0.008.

The clinical manifestations of patients are detailed in Table 2. For all IBD patients, abdominal pain was the most common (72%) symptom, followed equally by bloody stools (68%) and chronic diarrhea (68%). Bloody stools and pallor were significantly more common in UC than in CD, whilst perianal disease and extraintestinal manifestations were more common in CD. UC and IBDU patients presented similarly with bloody stools and chronic diarrhea; however, weight loss and pallor were more common in UC than in IBDU. An 18-year-old with CD presented with an enterocutaneous fistula (Figure 3A). Another 12-year-old CD patient initially presented with erythema nodosum and, on further history, had a 5-year duration of chronic diarrhea and abdominal pain (Figure 3B).

Biochemical Features

The baseline biochemical features of patients are presented in Table 3. UC and CD patients had significantly more ESR elevation than IBDU patients (*p* value 0.034), but there were no significant differences among the three subtypes in terms of anemia, leukocytosis, thrombocytosis, elevated CRP, hypoalbuminemia, and presence of stool pathogens. Of the 39 children with stool studies, 11 (28%) had positive stool pathogens identified, and these included *Entamoeba* (6), *Giardia* (1), *Clostridium* (1), *Salmonella* (1), *Candida* (1), and *Ascaris*. (1) None of our patients had fecal calprotectin determination.

Disease Location And Extent

For the 27 patients with CD, the lesions were mostly in the ileocolonic area (75%), with 16 (59%) having non-structuring or non-penetrating disease. All but one of the nine patients with UC had pancolitis (89%) (Appendix A.).

Endoscopic findings. Endoscopically, all patients had erosions, edema, erythema, ulcers, friable mucosa, loss of vascular pattern, pseudopolyps, and cobblestoning. For UC patients, these findings were confined to the colon, while in the 24 CD patients who underwent upper GI endoscopy, similar endoscopic findings were also found in the stomach

Table 2. Clinical Manifestations at Diagnosis of 47 Patients with Pediatric Inflammatory Bowel Disease

	All (N=47) N (%)	UC (N=9) N (%)	CD (N=27) N (%)	IBDU (N=11) N (%)	<i>p</i> -value
Abdominal pain	34 (72%)	7 (78%)	20 (74%)	7 (64%)	0.435
Bloody stools	32 (68%)	9 (100%)	12 (44%)	11 (100%)	<0.001
Chronic diarrhea	32 (68%)	8 (89%)	16 (59%)	8 (73%)	0.238
Perianal disease	8 (17%)	0	8 (30%)	0	0.005
Fever	9 (19%)	2 (22%)	5 (19%)	2 (18%)	0.970
Weight loss/failure to gain weight	27 (57%)	7 (78%)	18 (67%)	2 (18%)	0.009
Pallor	17 (36%)	7 (78%)	8 (30%)	2 (18%)	0.016
Anorexia	16 (34%)	4 (44%)	8 (30%)	4 (36%)	0.720
Extra-intestinal manifestations					
Erythema nodosum	8 (17%)	1 (11%)	7 (26%)	0	0.012
Joint pains	7 (15%)	2 (22%)	5 (19%)	0	

UC - ulcerative colitis; CD - Crohn's disease; IBDU - inflammatory bowel disease unclassified

Table 3. Biochemical Features at Diagnosis of 47 Patients with Pediatric Inflammatory Bowel

	All IBD, N (%)	UC, N (%)	CD, N (%)	IBDU, N (%)	<i>p</i> -value
Anemia	14/46 (30%)	5 (56%)	5 (19%)	4/10 (40%)	0.085
Leukocytosis	6/46 (13%)	3 (33%)	3 (11%)	0	0.088
Thrombocytosis	31/46 (67%)	6 (67%)	20 (74%)	5/10 (50%)	0.382
Elevated ESR	26/32 (81%)	5/6 (83%)	19/23 (83%)	2/3 (67%)	0.034
Elevated CRP	17/28 (61%)	3/7 (43%)	11/15 (73%)	3/6 (50%)	0.297
Hypoalbuminemia	19/41 (46%)	3/7 (43%)	13 (48%)	3/7 (43%)	0.086
Positive stool pathogen identified	11/39 (28%)	4 (44%)	5/23 (22%)	2/7 (29%)	0.214

IBD - inflammatory bowel disease, UC - ulcerative colitis, CD - Crohn's disease, IBDU - inflammatory bowel disease unclassified, ESR - erythrocyte sedimentation rate, CRP - C-reactive protein

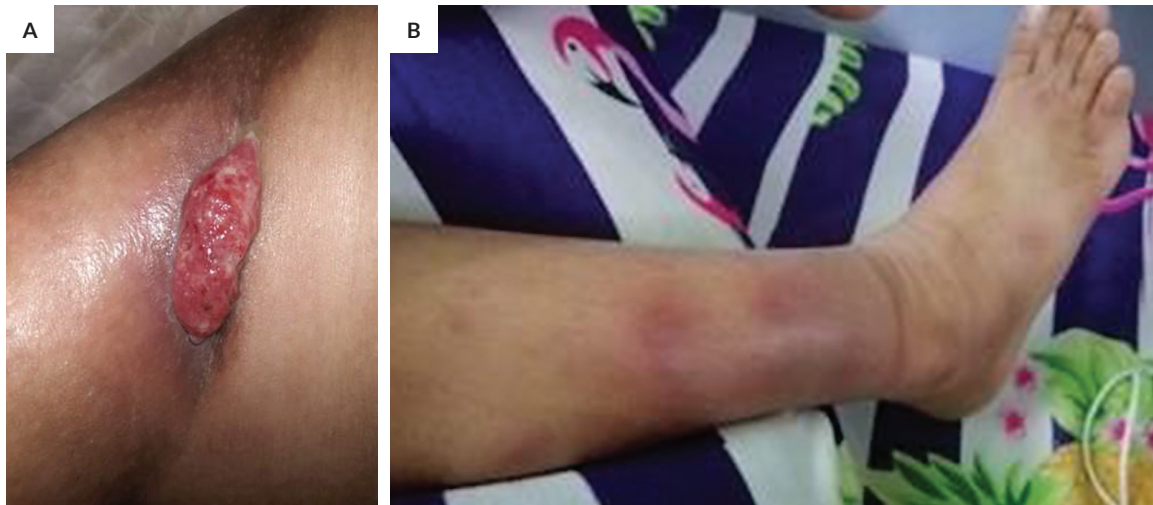


Figure 3. Physical examination findings of pediatric patients with inflammatory bowel disease. (A) Enterocutaneous fistula in the right lower quadrant in an 18-year-old male patient with Crohn's disease presenting with a 9-month history of abdominal pain, diarrhea, and weight loss, and later with a carbuncle at the right lower quadrant with draining pus. **(B)** Erythematous nodosum in a 12-year-old male patient who presented with a 5-year history of diarrhea and abdominal pain and was initially diagnosed as ulcerative colitis but later re-classified as Crohn's disease.

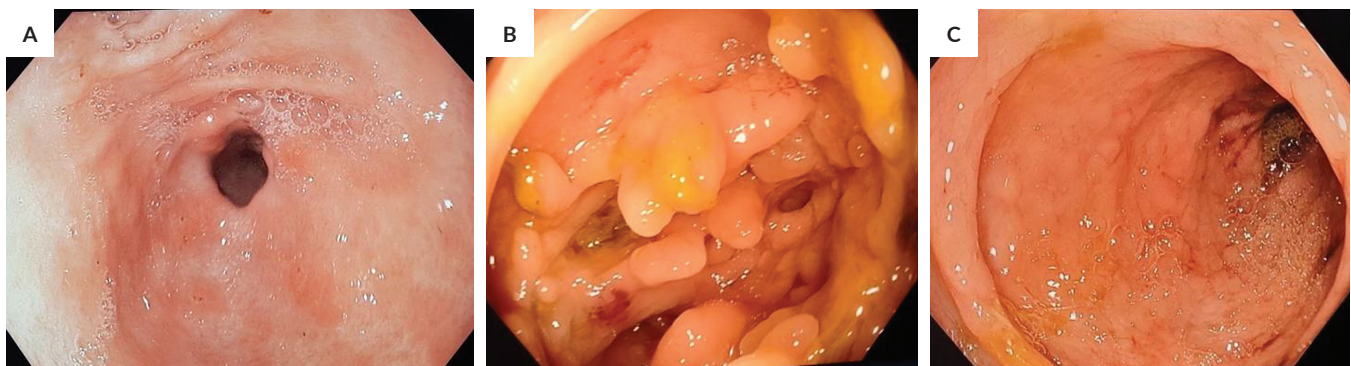


Figure 4. Endoscopic findings of pediatric patients with inflammatory bowel disease. (A) Multiple aphthous ulcers in the pyloro-antral area in a 12-year-old male with a 19-month history of peri-anal fistula with no associated abdominal pain, diarrhea, or weight loss. Histopathology findings showed granuloma in the duodenum and terminal ileum. **(B)** Multiple pseudopolyps with friable mucosa in the distal transverse colon in the 18-year-old male patient with enterocutaneous fistula described in Figure 3A. **(C)** Erythematous, edematous, friable mucosa, and with loss of vascular pattern in a 7-year-old female diagnosed with a case of primary sclerosing cholangitis, and also presented with a 4-year history of chronic, bloody diarrhea, and was later diagnosed to have ulcerative colitis.

and duodenum, and the lesions were not continuous with intervening areas of normal mucosa (Figure 4).

Imaging studies. (Figure 5) Of the 29 patients with small bowel imaging, 25 (86%) were done through abdominal CT scan with contrast, 1 (4%) by upper gastrointestinal series with small bowel follow-through, and 3 (10%) by abdominal ultrasound. All patients who had small bowel imaging had findings including intra-abdominal lymphadenopathy (18), bowel wall thickening (17), mucosal enhancement (6), perforation (1), abscess formation (3), and fistula (5). No patient had magnetic resonance enterography.

Histopathologic findings. (Figure 6) All nine UC patients had one or more of the following: focally active colitis (9), cryptitis (7), architectural distortion (3), and crypt abscesses (4) confined to the colon while the 27 CD patients had granuloma formation (7), chronic inflammation (18) and crypt architectural changes (10) similar to UC patients but these findings were also seen in the esophagus (4), stomach (16), and duodenum (15). Histopathologic findings in IBDU patients were similar to those seen in UC patients.

Disease location. Of the 27 patients with CD, 26 had an upper and lower endoscopy. Twenty (75%) had ileocolonic

disease only, and six (22%) had concomitant d upper GI disease involvement. One patient (18-year-old male), who presented with bowel perforation, underwent hemicolectomy and ileo-colostomy for bowel perforation. Post-operative histopathology findings consistent with Crohn's disease. The majority of the CD patients (59%) had non-stricturing and non-penetrating disease behavior, and 30% had perianal disease such as perianal fistula and/or perianal abscess. For the 9 patients with ulcerative colitis, 8 (89%) had pancolitis,

and 6 (77%) had severe disease. For the 11 IBDU patients, 4 patients had pancolonic disease involvement, 6 had ileo-colonic disease, and 1 had disease confined only to the rectum.

Management

A summary of medical management of the patients can be found in Table 4, where pair-wise comparisons were done with UC and CD patients only. Only 36 (76%) patients had data on management: 9 UC, 22 CD, and 5 IBDU. Twenty

Table 4. Medical Management of Patients with Pediatric Inflammatory Bowel Disease

	All IBD, N (%)	UC, N (%)	CD, N (%)	IBDU, N (%)	p-value*
Had >1 induction treatment	20/36 (56%)	5/9 (56%)	13/22 (59%)	2/5 (40%)	<0.001*
Initial induction treatment					0.062*
Oral steroids	11/36 (31%)	4/9 (44%)	6/22 (27%)	1/5 (20%)	
Parenteral steroids	4/36 (15%)	3/9 (33%)	0	1/5 (20%)	
5-ASA	7/36 (19%)	2/9 (22%)	4/22 (18%)	1/5 (20%)	
EEN	12/36 (33%)	0	10/22 (45%)	2/5 (40%)	
Anti-TNF	2/36 (6%)	0	2/22 (9%)	0	
Treatment leading to remission					<0.001*
Oral steroids	13/27 (48%)	3/6 (50%)	9/19 (47%)	1/2 (50%)	
Parenteral steroids	1/27 (4%)	1/6 (17%)	0	0	
5-ASA	4/27 (15%)	1/6 (17%)	2/19 (10%)	1/2 (50%)	
EEN	3/27 (11%)	0	3/19 (16%)	0	
Anti-TNF	5/27 (19%)	1/6 (17%)	4/19 (21%)	0	
Methotrexate	1/27 (4%)	0	1/19 (5%)	0	
Maintenance treatment					<0.001*
5-ASA	9/27 (33%)	4/6 (67%)	3/19 (16%)	2/2 (100%)	
Anti-TNF	4/27 (15%)	0	4/19 (21%)	0	
Methotrexate	4/27 (15%)	0	4/19 (21%)	0	
Azathioprine	10/27 (37%)	2/6 (33%)	8/19 (42%)	0	
Had adverse events related to treatment	11/32 (34%)	4/8 (50%)	5/21 (24%)	2/3 (67%)	0.006*

UC – ulcerative colitis, CD – Crohn's disease, IBDU – inflammatory bowel disease unclassified, EE – exclusive enteral nutrition, 5-ASA – 5-amino-salicylates, anti-TNF – anti-tumor necrosis factor

*comparing only UC and CD

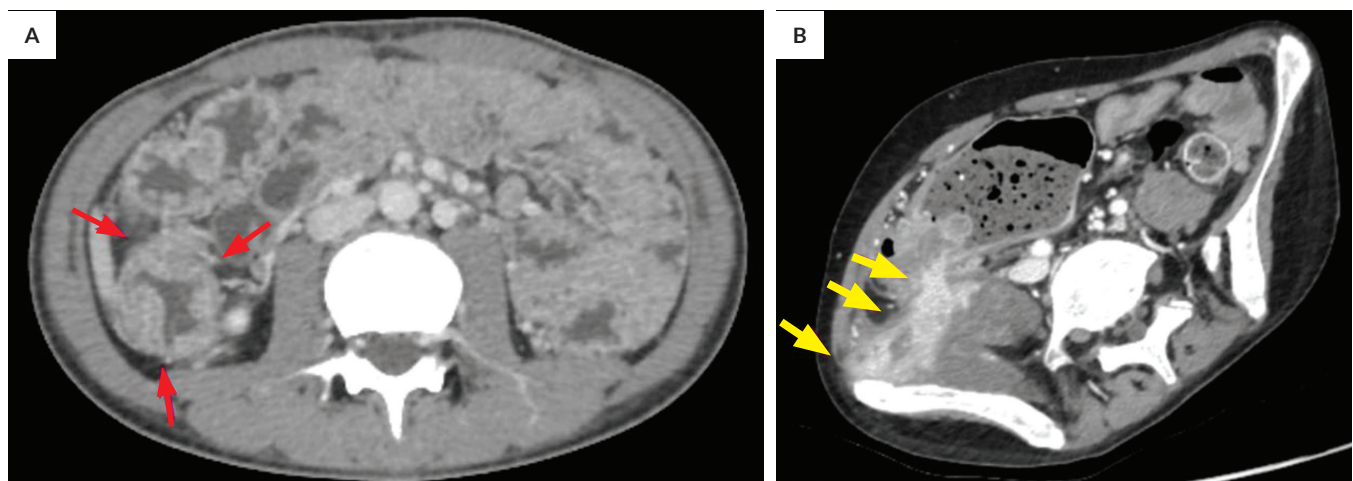


Figure 5. Abdominal CT scan findings of pediatric patients with inflammatory bowel disease. (A) Irregular thickening and hyper-enhancement of the mucosa of the sigmoid colon (red arrows) in a 15-year-old male patient with ulcerative colitis presenting with 1-year history of bloody diarrhea, abdominal pain and weight loss. **(B)** Irregular enhancing tracts from the ileo-cecal wall thickening with communications through the right iliopsoas and through the cutaneous layer (yellow arrows) at the right lower quadrant in the 18-year-old male patient described in Figures 3A and 4B.

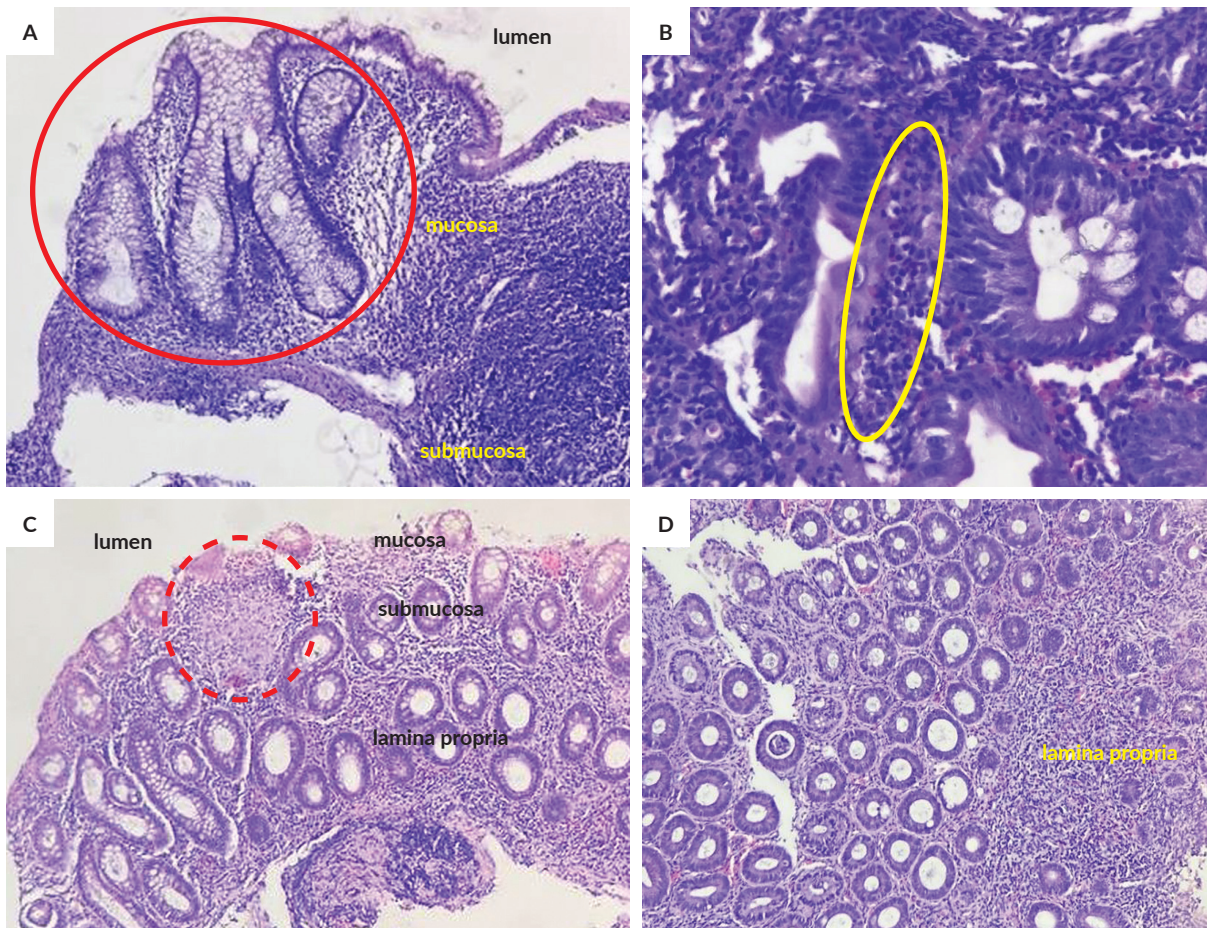


Figure 6. Histopathologic findings of pediatric patients with inflammatory bowel disease. (A) Benign colonic mucosa with crypt architectural distortion (red circle) and **(B)** crypt abscess (yellow oval) in the ascending colon of a 7-year-old female with primary sclerosing cholangitis and ulcerative colitis, as described in Figure 4C (H/E stain; 100x magnification). **(C)** Granuloma formation (within broken circle) without associated crypt rupture or lymphoid aggregates in the 18-year-old male patient with Crohn's disease described in Figure 3A (H/E stain; 40x magnification). **(D)** Mild expansion of the lamina propria by lymphoplasmacytic infiltrates, with the incorporation of lymphoid aggregates in the same patient described in Figure 6C.

(56%) of our patients required more than one treatment for induction of remission. For the initial treatment for induction, UC and IBDU patients used mostly oral and parenteral steroids and ASA, while the majority (45%) of CD patients were on exclusive enteral nutrition and oral steroids. Only two of the CD patients used biologics. Within the one-year follow-up period, only 27 patients reached remission: 6 UC patients, 19 CD, and 2 IBDU. Oral steroids were used by most patients who went into remission. Of the 19 with CD, responded with EEN and four with anti-TNF. For those who reached remission, the maintenance therapy was mostly 5-ASA and Azathioprine for UC, while biologic therapy and Methotrexate were also used for CD ($p = <0.001$). The treatment strategy of PIBD in the institution follows the management guidelines of the Asian Pan-Pacific Society for Pediatric Gastroenterology, Hepatology, and Nutrition (APPSPGHAN) PIBD Working Group, wherein a “step-

up” approach (escalating treatment to biologics for severe or steroid-refractory UC cases), and a “top-down” approach (use of anti-TNF as initial therapy for high-risk CD patients) is done. Deterrents to the strategy are the cost and availability of the treatment. Thirty-two percent of the patients had adverse events related to treatment, and these included cushingoid facies (6), pancreatitis (2), seizures (1), and anaphylaxis (2). We noted a significant difference (p value = 0.006) between CD and UC in terms of the rate of adverse events.

Disease Outcomes

For those on follow-up for at least one year, we looked at the number of patients who were: (1) steroid-free; (2) in remission; (3) surgery-free; (4) admitted to hospital; (5) on relapse after remission; and (8) treated for at least 1 infection.

The outcome of patients with at least one year of follow-up is shown in Table 5, where pair-wise comparisons were

Table 5. Outcomes of the Patients with Pediatric Inflammatory Bowel Disease

	All IBD, N (%)	UC, N (%)	CD, N (%)	IBDU, N (%)	p-value*
1-year steroid-free remission rate	11/30 (37%)	1/8 (12%)	9/19 (47%)	1/3 (33%)	0.639*
1-year relapse rate	18/27 (67%)	6/7 (86%)	11/18 (61%)	1/2 (50%)	0.004*
1-year admission rate	17/30 (57%)	6/8 (75%)	8/19 (42%)	3/3 (100%)	<0.001*
1-year infection rate	20/30 (67%)	6/8 (75%)	11/19 (58%)	3/3 (100%)	0.114*

UC - ulcerative colitis, CD - Crohn's disease, IBDU - inflammatory bowel disease unclassified

*comparing only UC and CD

done with UC and CD patients only. Out of the 47 PIBD patients, only 30 patients had at least 1-year follow-up: 8 UC patients, 19 CD, and 3 IBDU. No difference was noted on the 1 year steroid free remission rate and the one year infection rate among the three IBD subtypes. The one year relapse rate was significantly more in the UC than in the CD patients. The one year hospital admission rate was higher among UC and IBDU than in the CD patients. Indications for admission included: disease flare (18), infection (17), and surgery (1). The median duration of follow-up of 30 patients was 20 (12-26) months, and the median duration from diagnosis to remission was 6 (2-12) months. Overall, 37% (11 of 30) were in steroid-free remission at 1-year follow-up. The steroid-free remission rate between CD and UC was not significantly different. Among those who had initial remission, 18 (67%) had relapses. All UC and IBDU patients remained surgery-free within 1 year of diagnosis; however, five of the 19 (26%) patients with CD had surgery within a year of diagnosis, which included fistulotomy (1 patient), seton placement (2 patients), and hemicolectomy with stoma placement (2 patients). One patient with VEO-IBD (ulcerative colitis) died within 1 year of diagnosis of nosocomial infection after developing a hemorrhagic stroke (right posterior cerebral artery).

Associations of Features with Outcomes

In the 30 patients with at least one year of follow-up, the association of the features with the one-year steroid-free remission and one-year relapse rate was determined.

Age of onset less than six years old was the only feature associated with not achieving steroid-free remission at one-year follow-up (OR 20.8; *p* value 0.045). There were no statistically significant associations with sex, duration of symptoms, severity of disease, degree of wasting and stunting, presence at diagnosis of bloody stools, abdominal pain, diarrhea, anemia, thrombocytosis, elevated ESR or CRP, hypoalbuminemia, and more than one induction therapy. (Appendix B).

Higher relapse rate after one year was associated with the presence of symptoms of more than 6 months (OR 13.6; *p* value 0.034), wasting at onset (OR 12.6; *p* value 0.029), and pancolitis among the UC patients (OR 75; *p* value 0.043).

After the data was obtained, we noted that 25% of our patients have VEO IBD. Thus, we also looked at the association of age with the disease outcome and noted the

association of VEO IBD with need for more than one induction therapy (OR 5.7; *p* value 0.047) and more adverse events related to treatment (OR 10.5; *p* value 0.008).

There were no statistically significant associations with sex, age at onset, disease severity, bloody stools, diarrhea, weight loss, perianal disease, and presence of anemia, thrombocytosis, elevated ESR, and hypoalbuminemia. There were no differences seen in the outcome in those with stunting, abdominal pain, elevated CRP, and more than one treatment for induction. (Appendix C).

DISCUSSION

Demographic Characteristics

This is the first study to discuss pediatric IBD among Filipino children, and our results have shown the distinct features of inflammatory bowel disease in our country.

A total of 47 cases were seen in the 11-year study period, which was higher than the number of Filipino children reported in the Asia multi-centre study, with 29 cases over a period of 25 years (1995 to 2019).⁹ The patients, however, reported in the Asian registry were only from two private institutions in Metro Manila, and thus the true numbers could be underestimated.

The majority of the pediatric IBD cases in this study had Crohn's disease (58%), and this is consistent with the Asia registry.⁹ This finding also supports the general trend in the findings in the majority of countries reporting higher CD prevalence compared to UC, and these included Canada and New Zealand.¹⁴ This contrasts with the findings in Colombia, Japan, Puerto Rico, and Sweden, where there is a higher prevalence of UC than CD.¹⁴ These differences in epidemiological patterns suggest underlying environmental, genetic, or population-specific factors and mechanisms that influence the prevalence of CD and UC in different regions. We noted that five of our patients had a disease re-classification, four patients who were initially classified as ulcerative colitis were later diagnosed to have Crohn's disease, and one patient was initially diagnosed as IBDU and later diagnosed to have ulcerative colitis.

We report a higher male predominance with a male:female ratio of 1.8:1 for all PIBD cases, and this is higher than that of the ASIA registry, which reported a 1.4:1 ratio for all PIBD cases.⁹ This finding is similar to the ratio reported in Korea.¹⁵ Across three PIBD subtypes, there were

no noted differences in the male: female ratio, similar to the Croatia study.¹⁶

Looking at the age of disease onset, our percentage of very early onset inflammatory bowel disease (VEO-IBD) is high at 25%, and this is similar to the Asian data at 29.3%. This is in contrast with data in other countries, including the EPIMAD registry in France at 3%, in Canada at 4%, in Italy at 7.2%, in the UK at 4.4%, and in Japan at 13.9%.^{9,17-20} Comparing the three PIBD subtypes, we noted that there are no differences in age at disease onset. It is noted, however, that 78% of CD patients had their onset at 10 years old or older. The high proportion of VEO-IBD in our study is still unclear, but this subgroup deserves special attention due to its distinct phenotype and variable course and response to therapy.

In terms of the duration from onset of symptoms to diagnosis, we report a median duration of 9 months (interquartile range 4-20 months). This is longer than what was reported in of 2 to 5 months in Croatia, Finland, Canada, and Spain.^{16,21-23} This reveals the diagnostic delay in our country, especially the referral to a specialist for appropriate diagnostics. It should, however, be pointed out that this study was done in a tertiary government hospital where patients are mostly of low-income status, and financial constraints might be a reason for seeking immediate consultation. Furthermore, there is no difference in the duration of symptoms from onset to diagnosis across the three PIBD subtypes. This is contrary to the PIBD study of 107 patients in Croatia and Finland where UC patients have a shorter duration of symptoms compared to CD patients.^{16,21}

Previous studies have reported that PIBD cases tend to show more aggressive inflammation and a greater extent of lesion.¹⁵ In our study, the majority presented with mild (32%) and moderate (30%) disease severity. Comparing among the three PIBD subtypes, we noted that there were no differences as to disease severity at presentation: UC patients presented most with moderate disease, CD patients with mild disease, and PIBD patients with mild and moderate disease activity. This is contrary to the Korean data reporting more UC patients with moderate to severe disease (60%) and more CD patients with moderate disease (61.9) at presentation.²⁴ However, our data is limited to missing information on the disease activity at presentation of 19% of our patients.

Pediatric IBD patients are at high risk of growth failure, and the causes are multifactorial, such as inadequate intake, increased demands, malabsorption, inflammatory factors, genetic contribution, and medications affecting growth factors.²⁵ Previous studies have shown that CD patients present with more growth problems compared to UC patients, and in our study, we report that more CD patients had stunting (33%) compared to UC (18%) and IBDU (27%), but the differences were not statistically significant. This finding is similar to the findings in the Asia registry, which also reported no significant differences in the height z-scores across three PIBD subtypes.⁹ In terms of wasting, we noted that at disease presentation, more UC and CD patients

had wasting compared to IBDU patients (p -value 0.002), and this can be due to the shorter duration of symptoms to diagnosis among IBDU compared to the two other subtypes. This finding is in contrast to the Asia multi-center registry who reported that wasting is significantly more common in CD than in UC (14.4% CD vs 5.9% UC, $p = 0.022$).⁹

Clinical and Biochemical Features

In our study, the most common clinical feature of both UC and IBDU was bloody stools, and abdominal pain in patients with CD, and this is consistent with the existing literature.¹⁶ Similar to UC patients, the other clinical manifestation of IBDU was abdominal pain. Interestingly, patients with IBDU tend to have a significantly lower rate of reported weight loss or failure to gain weight compared to UC and CD patients. The classic triad of CD symptoms of abdominal pain, diarrhea, and weight loss was noted in only 37% of our CD patients, but 45% had extraintestinal manifestations (erythema nodosum, joint pains) and active perianal involvement. Perianal manifestations were present in 30% of CD patients, while none of the UC and IBDU patients had such manifestations, $p = 0.005$, similar to the study in Croatia.¹⁶

Our CD patients had 30% active perianal disease in the form of perianal fistula and perianal abscess; and perianal involvement in these patients was even higher at 48% if asymptomatic perianal skin tags were included. The finding of a non-penetrating perianal lesion, such as a skin tag, may suggest a potentially developing symptomatic perianal disease, as shown by a higher rate of fistulizing Crohn's disease in those who initially presented with non-penetrating perianal lesions.²⁶ The high percentage of perianal involvement in our study is consistent with studies in New Zealand and Korea, which reported 39% and 64.5%, respectively.^{24,27} In contrast, lower percentages of perianal disease were reported in China at 11%, 7% in the UK.^{28,29} In the Asia registry, 13% had symptomatic perianal disease.⁹ The differences in the rates of perianal involvement may suggest potential population-specific factors and environmental exposures that deserve further prospective studies to establish causality. Some postulated explanations are related to inherent genetic predisposition resulting in a distinct disease phenotype in the setting of specific environmental exposures; dietary changes to highly processed food intake; increased exposure to urban pollutants, and decreased exposure to potentially protective factors like Vitamin D, *H. pylori*, and helminths.⁹

Biochemical markers, despite their general lack of specificity, provide valuable information with regard to disease progression and treatment response. In terms of biochemical studies, our study revealed that the majority of PIBD patients had elevated ESR (83%), and there was a significantly higher ESR in UC and CD patients compared to IBDU patients. Across the three PIBD subtypes, there were no significant differences in the percentages of anemia, leukocytosis, thrombocytosis, elevated CRP, and hypoalbuminemia. This

contrasts with previous studies, which showed that patients with CD had higher ESR and CRP levels and lower albumin levels compared to UC patients.²⁰ However, our data is limited to missing information on some laboratory tests for some of our patients. Additionally, fecal calprotectin, which is a direct biomarker of intestinal inflammation and has relatively high sensitivity and specificity, was not measured in any of our patients in this study.

Disease Location, Extent, Behavior, and Severity

Our study reports that the ileocolonic location (75%) was the most common location among our CD patients, followed by the colonic (18%) location. This finding is consistent with the data from the Asia registry and the Finland study.^{9,21} Isolated upper gastrointestinal disease was not found in our patients, but upper GI involvement was found to be present in 41% of our CD patients. For the disease behavior, we noted that the purely inflammatory disease (non-stricturing/non-penetrating) was the most common disease behavior found in 59%, followed by penetrating disease (7%) and both stricturing/penetrating disease behavior (4%). These findings of disease location and disease behavior are consistent with the data from the Asia registry, which reported that the most common location is the ileocolonic location and 90.7% inflammatory disease behavior.⁹ This contrasts with the higher incidence of stricturing disease reported in 14 to 34% reported in the EUROKIDS registry, Taiwan, and Shanghai.³⁰

For UC patients, our study showed that pan-colonic (89%) involvement was the most common extent of disease among our UC patients, and that 77% had severe disease, which is higher than the Asia registry study, which reported 72.6% ileocolonic extent and at least 49% with moderate severity.⁹

These findings are consistent with the previous studies showing that PIBD patients have a more severe course and are more likely to have upper gastrointestinal involvement compared to adults with IBD.¹⁵

Management

The ideal management of PIBD follows a treat-to-target strategy and that is aiming for other therapeutic targets (intermediate and long-term goals) apart from attaining symptomatic response as measured by the PUCAI and PCDAI scoring systems).³⁰ Failure to achieve these targets should make us consider changing or escalating treatment and this reflects what is reported in our study, having more than half of our patients requiring more than one treatment for induction of remission.

The high use of corticosteroids in the study for UC (67%) is consistent with the study in Greece which reported 57.9% use of steroids as initial therapy to induce remission.³¹ In contrast, this study also reported high use of steroids as induction therapy for their CD patients, while the most common initial induction therapy for our CD patients was

exclusive enteral nutrition (45%). The high use of EEN in our case may be due to its relative affordability and provision of a window of opportunity for live vaccines to be given prior to any immunosuppressive therapy.

In terms of the treatment leading to remission, the majority of our UC patients (67%) and CD patients (47%) required steroids to attain remission. For the IBDU patients, both steroids and 5-ASA were able to induce remission. The use of EEN induced remission in three of our CD patients who tolerated EEN for at least 2 weeks, with noted improvements in PCDAI scores and ESR and CRP. The effectiveness of EEN to induce remission was consistent with the SEA study, which reported 91% of children with CD achieving remission.³² Our study reported only a total of 19% use of anti-TNF to induce remission; one in a UC patient that presented with mild disease at presentation, and four in CD patients (3 perianal CD and 1 inflammatory CD refractory to steroids).

For the maintenance of remission among UC and IBDU patients, 5-ASA was the most used medication, and for CD patients, Azathioprine was the most used for maintenance of remission. The use of biologics to maintain remission was only for CD patients at a relatively low rate of 21%. Our use of biologics to maintain remission is low compared to other studies, where 52.9% in CD and 50% in UC, and this is mainly due to the high cost of biologic therapy. Interestingly, we report the use of oral Methotrexate (MTX) with a similar rate to biologics (21%) to maintain remission of our CD patients. In the studies, MTX is an effective maintenance agent in CD, but the route used is subcutaneously at a dose of 15 mg/m² with concurrent use of weekly Folate.³¹ In our case, the route of MTX is oral due to its ease and convenience of administration, following the same dose and frequency as the subcutaneous route.

Alongside the goal of reaching these targets, we also want to avoid the complications not just of the disease but also of the medications. We reported common adverse effects related to medications, and these included cushingoid facies from prolonged steroid use, pancreatitis from Azathioprine use, urticaria related to Azathioprine, and seizures and anaphylaxis from Infliximab therapy. These prompted tapering of the steroids or switching to another therapeutic option. The commonly reported bone marrow toxicity from Azathioprine or elevation of liver enzymes from Methotrexate and/or Azathioprine use were not reported in our study.³¹ Furthermore, there was also no reported development of hematopoietic malignancy secondary to thiopurine use, but our study may be limited to the short duration of follow-up of our patients (20 months, IQR 12-26 months).

Disease Outcomes

Our study noted that more CD patients were in steroid-free remission at one-year follow-up period compared to UC and IBDU patients. Across the three PIBD subtypes, there were no significant differences in the duration of diagnosis

to remission. This finding may be due to the development of relapses or unsustained remission among UC and IBDU patients, as shown by a significantly higher number of UC patients who had relapses at one-year follow-up. Interestingly, the 1-year admission rates of the three PIBD subtypes parallel the 1-year infection rates; with IBDU patients most likely to be admitted and develop infections, followed by UC patients, then CD patients.

Consistent with published studies, CD patients required the most surgical interventions compared to UC and IBDU, but our study is limited to one year of follow-up only. We report a 26% surgery rate among our CD patients within one year of diagnosis. Published study of 57 pediatric patients with perianal CD, 67% underwent abscess drainage, 33% underwent seton placement, 23% underwent defunctioning ileostomy, and 9% underwent subtotal colectomy.³³

Associations of Features with Outcomes

The present study investigated whether there were any clinical features associated with patients' outcomes, especially the features distinct in our study, such as a high rate of VEO-IBD (age of onset <6 years old), longer duration of symptoms (≥6 months), and a high rate of perianal CD disease.

We noted VEO-IBD was associated with more than 1 induction therapy and more adverse events related to treatment. In other series, VEO-IBD was associated with more severe activity, diagnostic delays, refractory course, and poorer outcomes.^{34,35} Consistent with previous studies, we also showed that perianal lesions among CD patients were associated with increased risk of surgery. It has also been reported to be an indicator of disease activity, poor outcome, and impaired quality of life. Diagnostic delay has also been linked to complications, poor growth, poor treatment response, and surgery risk, and in our study was associated with the presence of wasting and relapse within 1 year.²¹

In terms of steroid-free remission rate, we have noted that very early onset IBD, referring to those <6 years of age, is the only feature that was significantly associated with not achieving steroid-free remission rate at 1-year follow-up. This contrasts with the study in Italy which reported a relatively high rate (57.4%) of VEO-IBD patients achieving steroid-free remission at 1-year follow-up.³⁶ There were no significant differences associated with the steroid-free remission rate with other features, but this may be due to the limited sample size in the study. Previous studies observed that steroid-free remission at 3 months after diagnosis was the strongest predictor of 1-year sustained steroid-free remission. There was no clinical, endoscopic, or laboratory parameter that could predict one-year steroid-free remission or need for colectomy.³⁷

On the other hand, the relapse rate at 1-year follow-up in our study was significantly associated with the presence of wasting at disease onset, duration of symptoms of more than six months, and the extent of pancolitis among UC patients. In a study that analyzed the clinical variables as

predictors of relapse among CD patients (32% relapse rate at 1 year follow-up), low BMI percentile at diagnosis was a predictor of relapse.³⁸ There is a paucity of studies regarding predictors of relapse rates among UC and IBDU patients. Other studies on prognostic factors in IBD in general studied associations with need for biologic therapy, and these factors included perianal disease, complicated disease behavior, high PDAI and PUCAI scores, fatigue, hypoalbuminemia, hypoproteinemia, and elevated CRP.³⁹

Limitations

The retrospective nature of the study limits the available data that we could obtain; there was a challenge in retrieving old clinical charts and in getting the complete data from the available charts. Some patients were also lost during follow-up. Further, the fact that only PIBD patients who were admitted to the hospital, which is an end-referral tertiary center, can impair the generalizability of the results. Additionally, the follow-up of the outcomes for this study was limited to one year of diagnosis, and other parameters, other than disease activity, such as growth monitoring, fecal calprotectin, nutritional deficiencies, cancer, and surgery risks, and effects on quality of life were not included. Nevertheless, our data represent the first record of pediatric inflammatory disease in the country because the data were collected in a tertiary government hospital over a decade.

CONCLUSION

The majority of pediatric IBD in our setting has CD, with a fourth of patients presenting before 6 years of age. Bloody stools were a more common sign in UC and IBDU, and CD had a high rate of active perianal disease. All subtypes responded similarly to steroids. The one-year relapse rate was more common in UC. VEO-IBD was associated with more than 1 induction therapy, not achieving steroid-free remission at one year follow-up, and more adverse events related to treatment. A higher relapse rate was observed in patients with diagnostic delay, wasting at onset, and in UC patients with pancolitis, which is associated with the presence of wasting and relapse within 1 year.

Recommendations

We recommend future studies that are prospective in nature for more accurate data collection and more defined endpoints. We also recommend the inclusion of detailed history-taking to include possible genetic and environmental risk factors associated with PIBD. We also recommend that future studies follow Porto's recommendations in doing complete endoscopies (both upper and lower gastrointestinal endoscopies) and small bowel imaging, if indicated. Additionally, we recommend that future studies make use of standardized endoscopic scoring systems and have the histopathological findings read by pathologists with special training and experience in gastrointestinal pathology.

Further, for prospective studies, we recommend a longer duration of follow-up for long-term disease course and the inclusion of other parameters such as growth, nutritional deficiencies, cancer risk, surgery risk, disease re-classification, and effects on quality of life.

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Author Disclosure

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APPENDICES

Appendix A. Disease characteristics based on Paris classification of patients with ulcerative colitis and Crohn's disease

Disease characteristics	UC (n=9), n (%)	CD (n=27), n (%)	Disease characteristics	UC (n=9), n (%)	CD (n=27), n (%)
Location of Disease			Extent		
L1 (T1 +/- cecal)	-	2 (7%)	E1 (ulcerating proctitis)	0	-
L2 (colonic)	-	5 (18%)	E2 (left-sided UC)	1 (11%)	-
L3 (ileocolonic)	-	20 (75%)	E3 (extensive UC)	0	-
L4 (isolated upper GI)	-	0	E4 (pancolitis)	8 (89%)	-
With upper GI involvement*	-	6 (23%)	Severity		
Disease Behavior			S0 (never severe)	3 (33%)	-
B1 (non-stricturing/non-penetrating)	-	16 (59%)	S1 (ever severe)	6 (77%)	-
B2 (stricturing)	-	0	UC=ulcerative colitis; CD=Crohn's disease		
B3 (penetrating)	-	2 (7%)	*Seen in 26 CD patients with both upper and lower endoscopy and/or small bowel imaging		
B2B3 (stricturing/penetrating)	-	1 (4%)			
Perianal disease	-	8 (30%)			

Appendix B. Associations of features with steroid-free remission rate at 1-year follow-up of patients with pediatric IBD

Clinical feature	No. of cases	Steroid-free remission* (%)	Not steroid-free remission* (%)	OR (95% CI)	p-value
Male	18	7 (39%)	11 (61%)	0.8 (0.2-3.6)	0.757
<6 years old age of onset	9	0	9 (100%)	20.8 (1.1-403.3)	0.045
>6 months duration of symptoms to diagnosis	23	8 (35%)	15 (65%)	1.4 (0.3-7.9)	0.699
Severe activity at onset	5	0	5 (100%)	7.2 (0.4-146)	0.198
With stunting	10	5 (50%)	5 (50%)	0.4 (0.1-2.0)	0.288
With wasting	13	4 (31%)	9 (69%)	1.6 (0.3-7.2)	0.558
Previous TB infection	4	1 (25%)	3 (75%)	1.1 (0.1-13.0)	0.929
Abdominal pain	22	9 (41%)	13 (59%)	0.5 (0.1-3.0)	0.429
Bloody stools	19	5 (26%)	14 (74%)	3.4 (0.7-16.1)	0.128
Diarrhea	22	9 (41%)	13 (59%)	0.5 (0.1-3.0)	0.428
Weight loss	17	4 (24%)	13 (76%)	3.8 (0.8-18.0)	0.094
Perianal disease	6	1 (17%)	5 (83%)	3.6 (0.4-35.4)	0.277
Anemia	12	4 (33%)	8 (66%)	1.3 (0.3-5.9)	0.756
Thrombocytosis	21	8 (39%)	13 (61%)	0.8 (0.2-4.2)	0.804
Elevated ESR	20	8 (40%)	12 (60%)	1.5 (0.2-13.0)	0.712
Elevated CRP	12	4 (33%)	8 (67%)	1.0 (0.2-6.2)	1.000
Hypoalbuminemia	11	3 (28%)	8 (72%)	2.4 (0.5-12.1)	0.300
Positive stool pathogens	8	1 (12%)	7 (88%)	6.3 (0.6-61.6)	0.114
Pancolonic extent	9	1 (11%)	8 (89%)	8 (0.3-255.1)	0.239
>1 Treatment for induction	19	5 (26%)	14 (75%)	3.4 (0.7-16.1)	0.129

*On 1-year follow-up

n/m wherein n = number of subjects fulfilling the parameter and m = total number of subjects tested

Appendix C. Association of features with relapse rate at 1-year follow-up of patients with pediatric IBD

Clinical feature	No. of cases	Relapse-free*, N (%)	With relapse*, N (%)	OR (95% CI)	p-value
Male	16	5 (31%)	11 (69%)	1.3 (0.3-6.4)	0.782
<6 years old age of onset	6	1 (17%)	5 (83%)	3.6 (0.3-37.5)	0.278
>6 months duration of symptoms to diagnosis	20	5 (25%)	15 (75%)	25.4 (1.2-551.6)	0.040
Severe activity at onset	4	1 (25%)	3 (75%)	1.5 (0.1-17.2)	0.744
With stunting	9	3 (33%)	6 (67%)	0.9 (0.2-5.0)	0.926
With wasting	12	1 (8%)	11 (92%)	12.6 (1.3-123.5)	0.029
Previous TB infection	4	0	4 (100%)	5.4 (0.3-115.0)	0.280
Abdominal pain	19	7 (37%)	12 (61%)	0.6 (0.1-3.6)	0.554
Bloody stools	16	3 (19%)	13 (81%)	5.2 (0.9-29.3)	0.061
Diarrhea	19	5 (26%)	14 (74%)	2.8 (0.5-15.7)	0.241
Weight loss	15	3 (20%)	12 (80%)	4.0 (0.7-21.8)	0.100
Perianal disease	6	1 (17%)	5 (83%)	3.1 (0.3-31.3)	0.342
Anemia	10	2 (20%)	8 (80%)	2.8 (0.4-17.4)	0.269
Thrombocytosis	19	6 (31%)	13 (69%)	1.3 (0.2-7.3)	0.776
Elevated ESR	17	5 (29%)	12 (71%)	2.4 (0.3-22.1)	0.439
Elevated CRP	11	4 (36%)	7 (64%)	0.6 (0.1-4.4)	0.600
Hypoalbuminemia	10	3 (30%)	7 (70%)	1.2 (0.2-6.6)	0.861
Positive stool pathogens	6	1 (17%)	5 (83%)	3.2 (0.3-33.3)	0.337
Pancolonic extent	7	0	7 (100%)	75 (1.1-4869.0)	0.043
>1 Treatment for induction	16	6 (38%)	10 (62%)	0.6 (0.1-3.3)	0.581

*On 1-year follow-up

n/m wherein n = number of subjects fulfilling the parameter and m = total number of subjects tested