

Pediatric inflammatory bowel disease in the western region of Saudi Arabia. A retrospective analysis

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Inflammatory bowel disease (IBD), with its 3 subgroups: Crohn's disease (CD), ulcerative colitis (UC), and indeterminate colitis (IC), is a chronic relapsing inflammatory disorder of the gastrointestinal (GI) tract. Inflammatory bowel disease can affect children and adolescents of all ages, and as many as 25% of all IBD cases manifest before the age of 20 years.¹ The diagnosis of IBD is based on a combination of clinical, endoscopic, histopathologic, and radiologic assessments. Further sub-classification of CD and UC is based on the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Working Group report (known as "the Porto criteria").¹ The prevalence of IBD in Saudi Arabia appears to have increased over the past few decades.² El Mouzan et al³ in a retrospective study in 218 children diagnosed with IBD in the central region of Saudi Arabia showed a predominance of males in CD (56%) and females in UC (59%). Saadah et al⁴ described the clinical pattern of UC in the Western region of Saudi Arabia and found that UC in children is not uncommon, and that the clinical manifestations of disease are similar to reports from the western population. The aim of our study was to describe the clinical symptoms, laboratory profiles, histology and endoscopy features of pediatric IBD in the western region of Saudi Arabia and to compare the features of IBD with other regions of Saudi Arabia and Western countries.

Our study is a retrospective review of medical records of all children with a confirmed diagnosis of IBD whose symptoms started before 16 years of age, between January 2005 and December 2012 in King Abdul-Aziz Medical City, National Guard Hospital, Jeddah, Saudi Arabia. For each patient, the following data was recorded: diagnosis; year of diagnosis; age at diagnosis; gender; family history; symptoms at presentation; duration of symptoms before diagnosis; localization and extent of disease, severity, and clinical behavior; laboratory results; imaging findings; endoscopy findings; histopathology findings and extraintestinal manifestations. The inclusion criteria were all Saudi children with IBD ≤ 16 years of age. Exclusion criteria were patients whose diagnosis of IBD was not confirmed

by endoscopy and histological findings. The diagnosis of IBD was based on clinical grounds, endoscopic evaluation, histological assessment of mucosal biopsy specimens and radiological findings (small bowel barium follow-through) in accordance with the Porto Criteria. Fifty-three IBD patients were identified in our database over the past 8 years. Twenty-two patients were excluded as they did not fulfil the Porto criteria for IBD diagnosis. Thirty-one children with IBD were included during the study period; 18 (58%) had CD, 12 (38%) had UC, and one (3%) had IC. The median age at presentation was 6.6 years (range, 5 months-12 years). The study population comprised of 20 (64.5%) males and 11 (35.5%) females. The frequency of a positive family history in first- and second-degree relatives of children with newly diagnosed IBD was 14%, and consanguinity was found in 13/31 parents (42%). Commonly reported symptoms of IBD were bloody diarrhea in 16 of 30 patients (53%), failure to thrive in 12/30 patients (40%) and chronic abdominal pain in 8/30 patients (27%). The most common presenting clinical feature of CD was failure to thrive (56%), while bloody diarrhea was the most common clinical feature of UC (75%). There was no significant difference in the clinical and laboratory characteristics of IBD. Perianal disease was not present in any child with IBD. Other clinical features of IBD are shown in Table 1. The initial location of CD at presentation was small bowel and colon (L3) in 50%, followed by colon (L2) in 44%, and small bowel (L1) in 5%. The common location of UC is pancolitis. The most common phenotype of CD at presentation was inflammatory (78%), followed by fibrostenotic (11%), and fistulizing disease (5%). The most common laboratory abnormality in IBD was low hemoglobin (73%). Anemia was present in 83% of UC and 67% of CD patients. Other common laboratory abnormalities observed in the IBD cohort included elevated platelet counts (70%), high CRP (77%) and ESR (67%) and low albumin (53%). Additional laboratory findings of IBD are shown in Table 1. All patients underwent upper gastrointestinal endoscopy and ileocolonoscopy. A small bowel follow-through contrast study (SBFT) was performed in 3 patients who failed ileal intubation at colonoscopy. In 29/31 patients (91%), Azathioprine was administered to maintain long remission. However, 2 patients discontinued Azathioprine because of side effects (pancreatitis and hepatitis). One of the 31 patients died from sepsis (3%); however, this patient was on Azathioprine and infliximab. There was no treatment protocol in our patients due to the lack of local guidelines of IBD management. Our study describes the clinical symptoms, biochemical

Table 1 - Clinical and laboratory characteristics of inflammatory bowel disease.

Clinical & laboratory characteristics	CD		UC		Total		P-value
	n=18 (%)		n=12 (%)		n=30 (%)		
Bloody diarrhea	7 (39)		9 (75)		16 (53)		0.052
Failure to thrive	10 (56)		2 (17)		12 (40)		0.033
Chronic abdominal pain	6 (33)		2 (17)		8 (27)		0.312
Pallor	3 (17)		3 (25)		6 (20)		0.576
Lethargy	2 (11)		1 (8)		3 (10)		NA
Perianal disease	0 (0)		0 (0)		0 (0)		NA
Anorexia	1 (6)		1 (8)		2 (7)		NA
Fever	1 (6)		0 (0)		1 (3)		NA
Bloating/flatulence	1 (6)		0 (0)		1 (3)		NA
Abdominal mass	1 (6)		0 (0)		1 (3)		NA
Eye involvement	0 (0)		0 (0)		0 (0)		NA
Joint involvement	0 (0)		0 (0)		0 (0)		NA
Mouth involvement	0 (0)		0 (0)		0 (0)		NA
Skin involvement	0 (0)		1 (8)		1 (3)		NA
Low hemoglobin (Normal: 11.5-16.5g/dl)	12 (67)		10 (83)		22 (73)		0.312
High white blood cell count (Normal: 4.0-11.0 x10 ⁹ /L)	8 (44)		7 (58)		25 (50)		0.456
Increased platelet count (Normal: 150-450 x10 ⁹ /L)	12 (67)		9 (75)		21 (70)		0.626
High erythrocyte sedimentation rate (Normal: [0-20] mm/hour)	14 (78)		6 (50)		20 (67)		0.114
High C-reactive protein (Normal: <5 mg/L)	16 (89)		7 (58)		23 (77)		0.053
Low albumin(Normal: 35-54 g/L)	11 (61)		5 (42)		16 (53)		0.296
Elevated alanine transferase (Normal: 7-40 U/L)	3 (17)		1 (8)		4 (13)		0.511
Elevated gamma-glutamyltransferase (Normal: 15-60 U/L)	6 (33)		1 (8)		7 (23)		0.113
Elevated alkaline phosphatase (Normal: 38-355 U/L)	7 (39)		3 (25)		10 (33)		0.429
Elevated total bilirubin (Normal: 3.4-20.5 umol/L)	0 (0)		0 (0)		0 (0)		NA
High amylase (Normal: 25-125 IU/L)	0 (0)		1 (8)		1 (3)		NA

NA - not applicable, CD - Crohn's disease, UC - ulcerative colitis

profile, histology, and endoscopy characteristics of pediatric patients with IBD in the Western region of Saudi Arabia. We could not determine the incidence or prevalence of pediatric IBD due to the lack of an IBD registry and unavailability of data from the other pediatric Gastroenterology Centers in Jeddah. The predominance of CD in this series is similar to that reported by El Mouzan et al,³ but the pattern of gender distribution is different. In our study, both CD and UC are more common in males, while the El Mouzan study shows a predominance of males in CD and females in UC. A positive family history of IBD was observed in 14% of patients in our study population. This was similar to the (15.3%) reported study by El Mouzan et al.³ Saadah et al⁴ reported a family history of affected first-degree relatives in 3.5% of pediatric patients with UC. However, the data of Kugathasan in the United States et al⁵ reported a similar frequency of a positive family history in first- and second-degree relatives of children with IBD to that observed in our study, with a range between 10-15%. Similar to the observations by El Mouzan et al³ the main manifestations of IBD included abdominal pain, bloody diarrhea, weight loss, and failure to thrive. However in our study, bloody

diarrhea was the most common manifestation of IBD, observed in 53 %, while abdominal pain was the most common manifestation of IBD in El Mouzan study. Failure to thrive was the most common symptom in patients with CD (56%), whereas bloody diarrhea was the most frequent presenting symptom in UC (75%). These observations are similar to that reported by studies conducted in USA where the classical features of IBD included abdominal pain, weight loss, and diarrhea.⁵ The most common laboratory results detected in our patients were anemia (73%) and thrombocytosis (70%), which is similar to El Mouzan study. The data of Kugathasan et al⁵ and El Mouzan et al³ taken together with the observation in our patients suggests that the inflammatory type of CD is the most common type in childhood CD. In our CD patients, 78% were of the inflammatory type of disease, followed by 11% with stenosing, and 5% with fistulizing disease. Consistent with previous observations, the colon was the most commonly affected anatomic segment in pediatric patients with CD, alone or in combination with the small bowel.⁵ Forty-two percent of our patients with UC had pancolitis which is similar or lower than that reported in other studies.⁵ In contrast to other reports,^{3,5} we

observed that extra intestinal manifestations seemed to be rare in our Saudi IBD patients. Perianal involvement was not present in any child with CD. However, skin involvement (pyoderma gangrenosum) was observed in one child. The absence of extra intestinal manifestations in our study might be related to the study design and small the number of patients.

Study limitations. Our registry is based on patient data from a single center, which may not allow extrapolation to the entire Saudi pediatric population with IBD. However, pediatric patients with chronic disease tend to be referred to centers such as ours, and, unlike adults with IBD, children are rarely treated solely by a pediatrician. Although this study also shares some of the disadvantages of a retrospective approach, it has some strengths. It is the first report on exclusively pediatric patients from the western region of Saudi Arabia, and it includes a well-characterized IBD population evaluated at a tertiary care center. Some patients may have been misdiagnosed in late childhood or proper diagnosis was delayed until early adulthood. Therefore, a high index of suspicion is necessary for attending physicians and prompt referral to a gastro-enterological service is required to ensure early diagnosis and optimal care.

In conclusion, CD is the most prevalent form of IBD in children in the western region of Saudi Arabia and is comparable with that reported in other Saudi regions and Western countries. Extra-intestinal manifestations appear to be rare in our Saudi IBD patients, in contrast to that observed in Western countries. Further multicenter studies are required in Saudi Arabia to elucidate the epidemiological and clinical features of pediatric IBD.

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