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Characteristics of pediatric ulcerative colitis in Saudi Arabia: a multicenter national study

Khalid AlSaleem,[a] Mohammad Issa El Mouzan,[a] Omar I. Saadah,[b] Bader AlSaleem,[c] Abdulrahman Al-Hussaini,[c] Mohammed Hassosa,[d] Al-Mehaidib Ali,[a] Mohammed Othman Banemai,[a] Hana Halaby,[e] Mohammed El Edreesi[f]

From the [a]Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia; [b]Department of Pediatrics, King Saud University, Riyadh Saudi Arabia; [c]Department of Pediatrics, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia; [d]Department of Pediatrics, King Abdulaziz Medical City, National Guard Hospital, Jeddah, Saudi Arabia; [e]Department of Pediatrics, Makkah Maternity and Children Hospital, Makkah, Saudi Arabia; [f]Department of Pediatrics, Aramco Medical Center, Dhahran, Saudi Arabia

Correspondence: Dr. Khalid AlSaleem · MBC 58 Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, Saudi Arabia · T: 966505445487 · ksaleem@kfshrc.edu.sa

BACKGROUND: Despite the extensive reporting of pediatric ulcerative colitis (UC) from industrialized developed countries, reports from developing countries are limited to small-case series from single centers. The objective of our large multicenter study was to determine the clinical, laboratory, endoscopic characteristics of UC in children from a developing country, Saudi Arabia.

DESIGN AND SETTINGS: A retrospective study of children diagnosed with UC under the age of 18 years during the period from 2003 to 2012.

METHODS: Patients enrolled from 15 medical centers from different regions in Saudi Arabia. A unified database collection form specifically designed for this study was completed by all participating centers.

RESULTS: A total of 188 children were diagnosed with UC during the study period (97 males [51.6%] and 91 females [48.4%]). The mean age at diagnosis was 9.1 years, and the mean duration of symptoms before diagnosis was 8.7 months. Consanguinity was present in 57 cases (32.6%), and the family history of inflammatory bowel disease (IBD) was noted in 16 cases (9%). The most common clinical presentation was blood in stool (90%), followed by diarrhea (86%) and abdominal pain (62%). Laboratory investigations revealed elevated erythrocyte sedimentation rate (82%), anemia (75%), thrombocytosis (72%), and hypoalbuminemia (33%). The extent of the disease was pan colonic in 46.1%, and confined to left side of colon and rectum in 23% and 9.6% of the cases, respectively.

CONCLUSION: This demographically pediatric IBD retrospective study revealed age-related variation in the distribution of IBD. Clinical presentation, with a high prevalence of positive consanguinity and positive family history, was noted in young patients with UC. The data from this study indicate that UC is increasingly recognized in Saudi Arabia and show many similarities to data from North America and Europe.

Inflammatory bowel disease (IBD) is a global health care problem with a sustained increasing incidence. It has been extensively reported in Caucasians of the Western world and is most prevalent in developed countries, including the USA and European countries.[1-4] Epidemiological and family studies demonstrate that genetic factors play a role in the susceptibility to IBD. There is an increased prevalence of IBD in first- and second-degree relatives and a higher relative risk among siblings.[5,6] Current etiologic theories focus not only on environmental and genetic factors, but also on immunoregulatory defects[7]

and microbial exposure.[8] Ulcerative colitis (UC) is a chronic relapsing disease of the colon that is characterized by inflammation and ulceration of the colonic mucosa. The symptoms of UC and possible complications vary depending on the extent of inflammation in the rectum and the colon.

Despite extensive reporting of pediatric UC from industrialized developed countries, reports from developing countries are limited to small case series from single centers.[9-16] Therefore, characteristics of pediatric UC have yet to be well documented in developing countries, and it remains to be determined whether

the low number of reports and small case series from developing countries reflect true low incidence of pediatric UC or just under-recognition of the disease entity in this part of the world.

This large multicenter retrospective study on pediatric UC was undertaken to clarify the demographic characteristics, clinical spectrum, and endoscopic findings. This report also discusses similarities between pediatric UC in Saudi Arabia and Western countries.

METHODS

This retrospective study of children diagnosed with UC under the age of 18 years during the period from January 1, 2003, to December 31, 2012, at 15 medical centers from different regions in Saudi Arabia. Children with UC were identified by either computerized hospital system using the International Classification of Disease codes of the hospital admissions database, endoscopy, or through personal

Table 1. Demographics of ulcerative colitis.

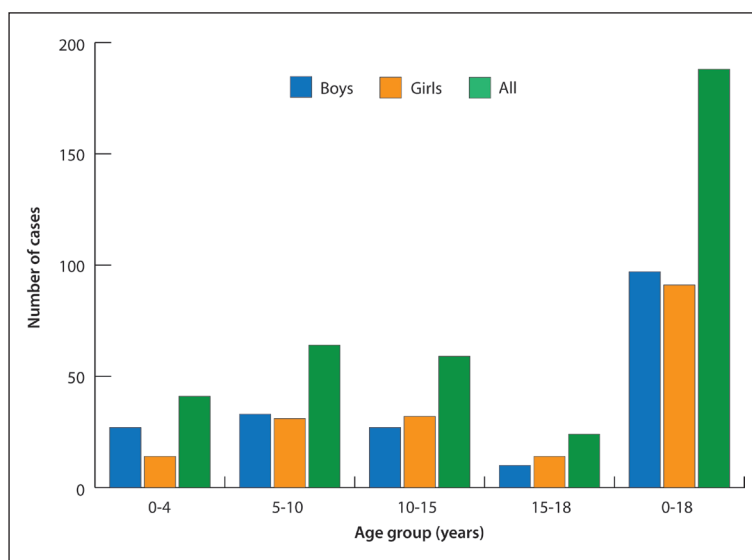| Variables	Ulcerative colitis
Gender: males (%)	97/188 (51.6%)
Age at diagnosis (mo): mean (Min, Max, SD)	109.4 (4, 215, 55.2)
Duration of symptoms (mo): mean (Min, Max, SD)	8.7 (0.0, 104, 12.3)
Positive family history	16/180 (9%)
Positive consanguinity	57/175 (32.6%)

Min: Minimum; Max: maximum; SD: standard deviation.

Figure 1. Frequency of cases by age and sex.

physician records. A unified database collection form specifically designed for this study was completed by all participating centers and reviewed by gastroenterologists. Demographic data, clinical symptoms, results of laboratory tests (including hemoglobin, erythrocyte sedimentation rate [ESR], and liver function tests), and endoscopic findings were collected from medical records and endoscopic reports at the time of diagnosis and were reviewed carefully to ensure that the final diagnosis was consistent with the published diagnostic criteria[4,9] and in accordance with ESPGHAN Porto Criteria.[17] In Saudi Arabia, pediatric patients of suspected IBD are referred to gastroenterology centers that are distributed in major cities. These centers are staffed with certified gastroenterologists and equipped with adequate facilities for the investigation and management of IBD. All suspected pediatric IBD cases presenting to any of the centers undergo extensive workup to exclude infectious causes of enteritis or colitis by stool cultures (for Salmonella, Shigella, Yersinia, and Campylobacter) and stool tests for Clostridium difficile, Giardia lamblia, and Entamoeba histolytica (parasites, cysts, and ova).

This report is part of a multicenter collaborative research project entitled "characteristics of IBD in Saudi children," which has been approved by the Institutional Review Board of the college of medicine (No: 10/2647/IRB) at King Saud University in Riyadh and the local Institutional Review Board in participating centers.

RESULTS

A total of 188 children were diagnosed with UC during the study period. The demographic characteristics of pediatric UC cases are presented in **Table 1**. Males and females were almost equally affected across all pediatric age groups. However, males were affected twice as females in children below 4 years of age (27 boys vs 14 girls). Out of 188 patients, 167 (89 %) were Saudi; the rest (11%) were from other nationalities.

Figure 1 shows the Frequency of UC by age and sex. The patients of this study presented with a combination of gastrointestinal and extra-intestinal symptoms and signs of UC (**Table 2**). Blood in stools was the most common presenting symptom (90%) followed by diarrhea (86%) and abdominal pain (62%). Only third of the patient had weight loss and anorexia (37% and 32%, respectively). Extra-intestinal manifestation, i.e., arthritis and skin rash were seen only in 2%.

The most common laboratory abnormalities (**Table 3**) were high ESR, followed by anemia, and thrombocytosis in 82%, 75%, and 72%, respectively.

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Table 2. Clinical presentation of 188 children diagnosed with ulcerative colitis.

Clinical features	Frequency (%)
Abdominal pain	117 (62)
Diarrhea	161 (86)
Blood in stools	170 (90)
Weight loss	70 (37)
Anorexia	60 (32)
Vomiting	28 (15)
Pallor	26 (14)
Fever	22 (12)
Bloating/flatulence	9 (5)
Nausea	6 (3)
Arthritis	3 (2)
Skin rash	3 (2)

- Pancolitis proximal to hepatic flexure
- Left-sided: distal to splenic flexure
- Distal to hepatic failure
- Ulcerative proctitis

Figure 2. Extent of colonic involvement in 178 patients at diagnosis.

Table 3. Laboratory presenting features of children with UC.

Test	Number/Total (%)
Hemoglobin (low)	104/139 (75)
Hematocrit (low)	52/71 (73)
White blood cells (high)	27/96 (28)
Neutrophils (high)	11/41 (27)
Platelets (high)	96/133 (72)
ESR (high)	97/118 (82)
CRP (high)	48/76 (63)
Serum albumin (low)	35/106 (33)
Alanine transferase (high)	6/101 (6)
Alkaline phosphatase (high)	7/99 (7)

UC:Ulcerative colitis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

Hypoalbuminemia was seen in 33%, and only 28% had leukocytosis. High alanine transferase was noticed in only 6% patients.

Data on colonic extent were available in 178 (95%) of 188 cases. **Figure 2** shows the extent of colonic involvement in 178 patients at diagnosis; almost half of the patients had pancolitis (46.1%) at presentation and 9.6% had ulcerative proctitis.

DISCUSSION

There are few published reports describing UC in children in the Middle East. Rising incidence of pediatric IBD (both Crohn disease and UC) were noticed in many countries worldwide[2,4,18] including Saudi Arabia.[19] This study highlights the characteristic features of pediatric UC in Saudi Arabia. The present paper probably reports the largest series describing the characteristics of UC in children from the Middle East.

The pattern of gender distribution with slight male predominance in UC is similar to the reports from other Western countries including the USA.[20] However, a significant male predominance was observed in children below 4 years of age as indicated by a 2:1 male-to-female ratio.

A considerable progress has been made in the last decade in the genetics studies of IBDs;[5] Familial association of IBD is recognized by many authors, especially in younger patients, with a great variability in the percentage of affected family members.[21] Despite the high percentage of consanguineous marriage,
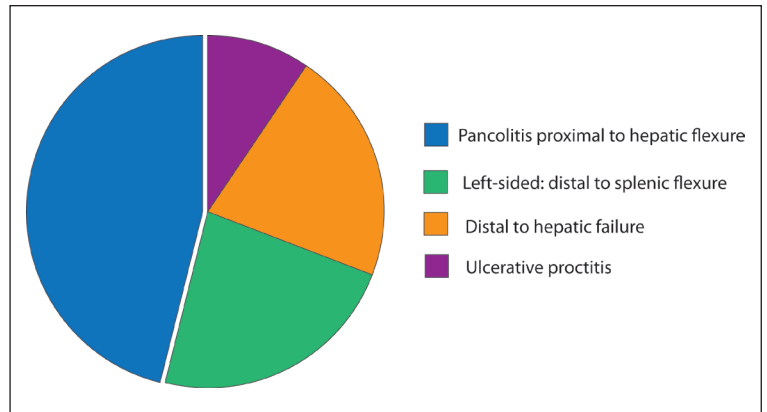
32.6% prevalence found in this study is still lower than the 56% prevalence in the general Saudi population.[22] Only 9% positive family history of IBD was reported in this study, which is higher than 6.6% reported by Roma et al[23] but lower than the 11% reported from Wisconsin, USA;[24] 15.3% reported in the central region of Saudi Arabia[15] and 31% reported in Kuwait.[11] This relatively low prevalence of positive family history in Saudi Arab children with IBD, a population with high prevalence of consanguinity,[22] is surprising and provides more support to the current etiologic theories are multifactorial and not only focus on genetic factors but also on environmental triggers,[1] immunoregulatory defects,[7] and microbial exposure.[8] However, this observation requires further investigations.

This report documents the presenting features of pediatric UC in Saudi Arabia, usually diarrhea, which

may be associated with blood. The presenting clinical and laboratory features indicate that UC in Saudi children may present at any age as early as 4 months old, and certain clinical and laboratory features are more common than others. These findings are consistent with classical descriptions of pediatric UC in other population,[25,26] which may suggest similar disease etiology and pattern. It is worth mentioning that the variation in the numbers of cases for each laboratory test is due to the fact that these patients presented were investigated in many hospitals, and some laboratory tests at presentation were not available.

The implications of this descriptive study are very important, as these help increase the index of suspi-cion among physicians caring for children in all regions of Saudi Arabia, leading to early diagnosis and treatment of patient with UC.

In conclusion, the presenting features of pediatric UC in Saudi Arabia are similar to descriptions from other populations, suggesting similar disease etiology and pattern. A prospective research is needed to study the role of lifestyle, microbiome, and genetics of UC in this population.

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