

# Presenting features of childhood-onset inflammatory bowel disease in the central region of Saudi Arabia

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## ABSTRACT

**الأهداف:** وصف أعراض مرض التهاب الأمعاء المزمن (داء كرون والتهاب القولون التقرحي) لدى الأطفال السعوديين.

**الطريقة:** أُجريت هذه الدراسة الاسترجاعية التي شملت ملفات المرضى الذين كانت أعمارهم أقل من 18 عاماً عند بداية أعراض المرض. ولقد أتي هؤلاء المرضى إلى عيادة الأطفال والجهاز الهضمي التابعة لمستشفى الملك خالد الجامعي، ومجمع عيادات الدكتور المفرج، الرياض، المملكة العربية السعودية خلال الفترة من يناير 1993م إلى ديسمبر 2010م. ولقد قمنا بجمع المعلومات الخاصة بالعمر، والجنس، وتاريخ العائلة المرضي، وأعراض المرض السريرية ونتائج المختبر في هذين المركزين الطبيين.

**النتائج:** تم تشخيص مرض التهاب الأمعاء المزمن لدى 218 طفلاً خلال الفترة من 1993م إلى 2010م، وكان داء كرون أكثر شيوعاً لدى 68%. لقد كانت نسبة الإناث أكثر من الذكور لدى مرضى التهاب القولون التقرحي (59%). ولم يوجد فرق كبير من الناحية الإحصائية في أعمار الأطفال عند بداية أعراض داء كرون والتهاب القولون التقرحي ( $p=0.347$ ), إلا أن هناك فرقاً معنوباً بين داء كرون والتهاب القولون التقرحي بالنسبة للعمر عند مراجعة الطبيب العام ( $p=0.027$ ) وعند التشخيص النهائي ( $p=0.008$ ). كذلك كانت حالات داء كرون الأكثر انتشاراً في جميع الأعمار ما عدا لدى الأطفال أقل من 8 سنوات. وكان هناك ارتفاع كبير في عدد الحالات التي تم تشخيصها خلال الفترة من 2002-2010 مقارنة بالفترة 1993-2001م. وكان التاريخ المرضي إيجابياً لدى 15.3% من الأسر. وكانت أعراض المرض في بدايته وكذلك نتائج المختبر مشابهة لمرضى البلدان الأخرى.

**خاتمة:** تشير هذه الدراسة إلى انتشار مرض التهاب الأمعاء المزمن لدى الأطفال السعوديين وأن علاماته لا تختلف عن مرضى البلدان الأخرى مما يشير إلى احتمال وجود نفس الأسباب وبالتالي هناك حاجة إلى مزيد من الأبحاث في معدل انتشار هذا المرض في جميع مناطق المملكة وكذلك دور الاستعداد الوراثي والميكروبوي والأسلوب الحياتي في حدوث هذا المرض.

**Objectives:** To investigate the presenting features of childhood-onset inflammatory bowel disease (IBD) in

the central region of Riyadh, Saudi Arabia and to compare with those reported in the literature.

**Methods:** This is a retrospective review of medical records of children below 18 years of age at onset of symptoms with confirmed diagnosis of IBD for age, gender, family history, presenting clinical and laboratory findings in the Divisions of Pediatric and Adult Gastroenterology, King Khalid University Hospital (which provides free health care) and the Department of Gastroenterology Al Mofarreh Poly Clinic, Riyadh, Saudi Arabia, between January 1993 and December 2010.

**Results:** Two hundred and eighteen children diagnosed with IBD with predominance of males in Crohn's disease (CD) (56%) and females in ulcerative colitis (UC) (59%). There was no significant difference between UC and CD regarding age of onset of symptoms ( $p=0.347$ ); however, the difference in the age at presentation and age at final diagnosis were significant ( $p=0.027$  and  $p=0.008$ ). There was a significant increase of IBD diagnosis from the period 1993-2001 to 2002-2010 ( $p<0.0001$ ). The family history was positive in 15.3%.

**Conclusion:** The presenting clinical features and laboratory abnormalities are similar to those reported in other populations. Further studies are needed to establish the incidence and prevalence.

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Inflammatory bowel diseases (IBDs) in the form of Crohn's disease (CD) and ulcerative colitis (UC) are more common in Caucasians of the western world and less common in Asian countries including Japan.<sup>1,2</sup> In the United States of America (USA) for example, the estimated overall prevalence of IBD was 400 per 100,000 populations, with a prevalence of 2 cases per 100,000 for UC, and 4.5 cases per 100,000 for CD in children from 1-17 years.<sup>3</sup> The disease is more common in Jews than in other non-Caucasian ethnic groups.<sup>1,4</sup> In Saudi Arabia, IBD which was rarely diagnosed few decades ago, were increasingly reported in adults and children from almost all regions. However, such data were single hospital reports with a limited number of children.<sup>5-8</sup> Information regarding the presenting features of these diseases in children is scarce. In this report, the presenting features of childhood-onset of IBD in the region of Riyadh, Saudi Arabia were investigated and compared with those reported in the literature. It is hoped that this report will increase the index of suspicion of physicians for early diagnosis of IBD and stimulate further research.

**Methods.** This is a retrospective review of medical records of all children with confirmed diagnosis of IBD whose symptoms started before 18 years of age, between January 1993 and December 2010. The children were diagnosed and treated in 2 major medical centers in Riyadh; King Khalid University Hospital (KKUH), Divisions of Pediatric and Adult Gastroenterology which provides free health care at the primary and tertiary levels, and Department of Gastroenterology, Al Mofarreh Poly Clinic (MPC), Riyadh, Saudi Arabia, which is one of the leading private gastroenterology outpatient clinic. The study was approved by the Institutional Review Board of the College of Medicine and KKUH, King Saud University, Riyadh, Saudi Arabia.

The inclusion criteria were all Saudi children below 18 years of age and exclusion criteria were non-Saudi children and adult patients. According to KKUH policy, children below 13 years of age must be managed by the pediatric gastroenterologists and those above 13 must be managed by adult gastroenterologists.

The final diagnosis of IBD and differentiation of UC from CD were based on a combination of clinical, laboratory, imaging, endoscopic, and histopathology features according to the recommendations of the working groups of the European Society for Pediatric Gastroenterology Hepatology and Nutrition<sup>9</sup> and North American Society for Pediatric Gastroenterology

Hepatology and Nutrition.<sup>10</sup> The data retrieved included the final diagnosis, gender, age at presentation, age at first primary physician consultation, age at final diagnosis by gastroenterologists, presenting symptoms and signs as well as laboratory test results. Results of imaging, endoscopy and histopathology were recorded to confirm the final diagnosis. Information on the family history of IBD was obtained from the medical record and double checked by phone call to the family whenever possible. The number of cases of UC and CD diagnosed each year in the 2 centers were calculated to describe the time trend of patients diagnosed from 1993 to 2010. All variables were recorded on a database form specially designed for this study and entered into the computer.

Statistical analysis included descriptive statistics, and we used chi-square test to compare the proportions. Because the data were not normally distributed, Mann-Whitney test was used to assess the difference between UC and CD in the age at onset of symptoms, age of first primary physician consultation, and age at final diagnosis by gastroenterologists. The z-test for percentages was used to assess the significance of time trend between 1993-2001 and 2002-2010 periods. A *p*-value less than 0.05 was considered statistically significant.

**Results.** Two hundred and eighteen children with onset of symptoms below 18 years of age and confirmed diagnosis of IBD were identified in the computerized medical records. The demographic characteristics are presented in Table 1 indicating a predominance of CD (67.4%), with a male gender of 56%, but a predominance of female gender in UC (59%). Of the 218 medical records, 181 (83%) were suitable for

**Table 1** - Demographics of inflammatory bowel disease (N=218).

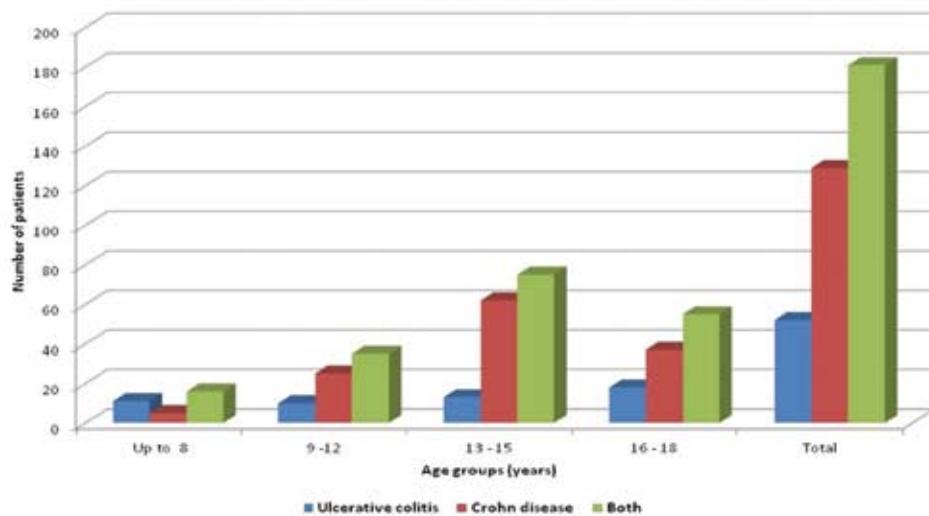
Variables	Ulcerative colitis n=71	Crohn's disease n=147
<i>Gender (%)</i>		
Males	29 (41)	82 (56)
Females	42 (59)	65 (44)
<i>Age at onset (years)</i>		
Median (minimum, maximum)*	14.40 (0.5, 18)	14.48 (3, 18)
<i>Age at primary MD consult (years)</i>		
Median (minimum, maximum)†	15.00 (0.7, 18)	16.00 (6, 19.3)
<i>Age at final diagnosis (years)</i>		
Median (minimum, maximum)‡	15.00 (1.4, 18.3)	16.00 (7, 19.3)

\**p*=0.347, †*p*=0.027, ‡*p*=0.008

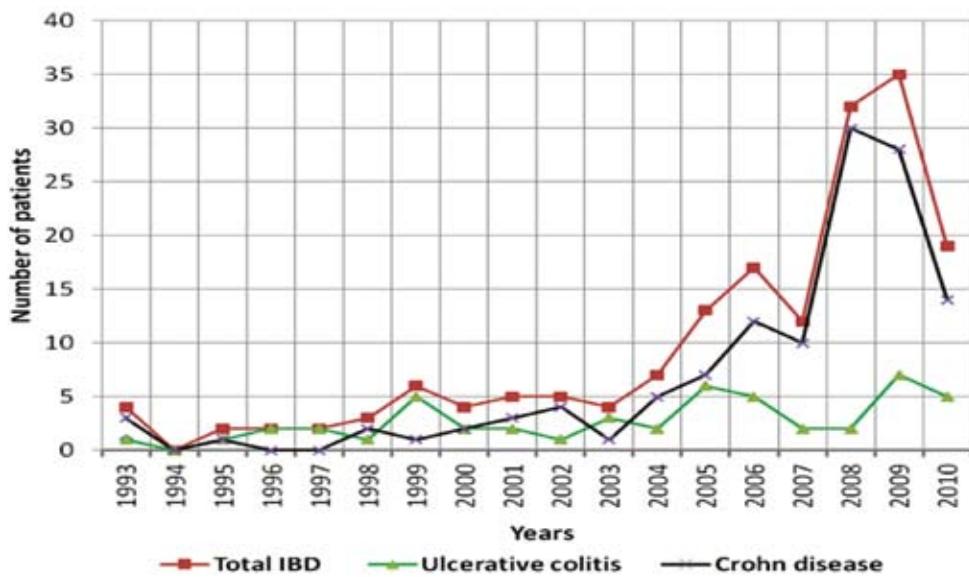
analysis and the remaining 37 records were excluded because of incomplete data on presentation despite confirmed final diagnosis on follow-up. The median, minimum and maximum age at onset of symptoms, presentation to primary physician, and final diagnoses by gastroenterologists are shown in Table 1. No significant difference between UC and CD on age at onset of symptoms ( $p=0.347$ ). However, the difference in age at presentation to primary physician and age at final diagnosis by gastroenterologists were all statistically significant ( $p=0.027$  and  $p=0.008$ ).

The age distribution of the children with IBD are shown in Figure 1, indicating more common occurrence of UC in children below 8 years of age than in older children. This difference was not statistically significant ( $p=0.114$ ).

Figure 2 illustrates the time trend of occurrence of IBD in the 2 institutions, which demonstrates increasing diagnoses of IBD represented by CD more than UC. There was an increase in IBD diagnoses in both KKUH and MPC from the period 1993-2001 to the period 2002-2010. This increase was more significant in CD



**Figure 1** - Age distribution of the children with inflammatory bowel diseases.



**Figure 2** - Time trend of occurrence of inflammatory bowel diseases (IBD) in 2 medical centers in Riyadh, Saudi Arabia.

( $p<0.0001$ ) than UC ( $p=0.0127$ ). The family history was positive in 18/118 patients (15.3%).

The most common presenting clinical features are shown in Table 2, indicating that abdominal pain was the most common presenting symptom in both CD (91%) and UC (88%). Blood in stools was significantly more common in UC ( $p=0.001$ ) and although weight

**Table 2** - Clinical presentation of 181 children diagnosed with inflammatory bowel diseases.

Clinical features	Type of inflammatory bowel diseases		
	Ulcerative colitis n=52	Crohn's disease n=129	Total n=181
Abdominal pain	46 (88.5)	117 (91.0)	162 (90.0)
Diarrhea	43 (81.0)	89 (69.0)	132 (73.0)
Blood in stools	43 (81.0)	43 (33.3)	86 (47.5)
Weight loss	23 (44.2)	98 (76.0)	121 (67.0)
Bloating/flatulence	16 (31.0)	70 (54.0)	86 (47.5)
Nausea	3 (5.8)	39 (30.2)	42 (23.2)
Vomiting	15 (28.8)	45 (35.0)	60 (33.2)
Pallor	21 (40.0)	34 (26.4)	55 (30.3)
Anorexia	10 (19.2)	45 (35.0)	55 (30.4)
Fever	8 (15.4)	23 (17.8)	31 (17.1)
Perianal disease	0 (0)	17 (13.0)	17 (9.4)
Constipation	0 (0)	18 (14.0)	18 (10.0)
Fatigue	6 (11.5)	10 (5.5)	16 (8.8)
Joint pain	2 (3.8)	11 (8.5)	13 (7.2)
Arthritis	1 (1.9)	6 (4.7)	7 (4.0)

loss was more common in CD, the difference was not significant ( $p=0.058$ ). Perianal disease was not present in any child with UC whereas it was a presenting feature in 17% of the children with CD. The most common laboratory abnormalities were low hemoglobin in UC (79%) and high erythrocyte sedimentation rate (52%) in CD (Table 3). Finally, the most common phenotype of CD at presentation was inflammatory in 56%, followed by stenosing (19%), fistulizing (16%), and combined stenosing-fistulizing (9%).

**Discussion.** Riyadh region, including the metropolitan Riyadh city, is the second most populated region in the Kingdom of Saudi Arabia. Although the population census and the annual population growth rate of this region are known from 2001 and onward.<sup>11</sup> It was not possible to accurately express our results in terms of incidence or prevalence because of the lack of IBD registry and unavailability of data from the other pediatric gastroenterology centers in Riyadh. However, this analysis combining private patients (MPC) and those attending free medical care hospital (KKUH) not only represents the largest sample of children with confirmed diagnosis of IBD, but also reflects a spectrum of patients of different socio-economic status. Therefore, this report so far, provides the most representative description of the pattern of childhood-onset IBD in Riyadh region.

This report documents the presenting features of IBD in Saudi children and supports the expected lower occurrence of UC and CD in Saudi Arab

**Table 3** - Laboratory presenting features of children with inflammatory bowel diseases.

Tests	Ulcerative colitis n (%)	Crohn's disease n (%)	Total n (%)
Hemoglobin	38/48 (79)	49/121 (40)	87/169 (51)
Hematocrit	38/48 (79)	50/120 (42)	88/168 (52)
White blood cells	14/48 (29)	20/121 (17)	34/169 (20)
Platelets	24/48 (50)	43/121 (37)	67/169 (40)
ESR	31/48 (65)	57/109 (52)	88/157 (56)
Total serum protein	5/48 (10)	8/121 (7)	13/169 (8)
Serum albumin	13/48 (27)	20/121 (17)	33/169 (20)
Alanine transferase	2/47 (4)	3/119 (3)	5/166 (3)
Total bilirubin	0/48 (0)	8/120 (7)	8/168 (5)
Alkaline phosphatase	3/48 (6)	10/121 (8)	13/169 (8)
ESR - erythrocyte sedimentation rate			

than in Western children.<sup>12</sup> The predominance of CD (67.4%) in this series and the pattern of gender distribution with more common occurrence of CD in boys and UC in girls is similar to the reports from most countries including UK and USA.<sup>4,13</sup> The lack of significant difference in age at presentation and the gradually increasing significance of the difference between UC and CD in the age at primary physician consultation and final diagnosis suggests a lower index of suspicion and more difficult diagnosis of CD than UC. The more common occurrence of UC in young children, although not reaching statistical significance probably because of small sample size, is consistent with reports in 2 large samples of North American children.<sup>14,15</sup> Although not reflecting incidence, there is an increase in diagnosis of IBD in these 2 centers, represented by CD more than UC. Comparison of the time trend between 2 periods (1993-2001 and 2002-2010) indicated a more significant increase of CD ( $p<0.0001$ ) than UC ( $p=0.0127$ ). Although this pattern may be explained by increased referrals of IBD patients, other gastroenterologists in other institutions have reported a similar trend of increasing diagnosis (personal communications), suggesting the possibility of increase in incidence in addition to increased index of suspicion and referrals, a trend similar to reports from most countries.<sup>2,16,17</sup> However, the steady increase in IBD diagnosis starting in 2004 in this report is difficult to explain as no known changes in the environment or lifestyle could be identified at that time. This pattern is unlikely to be due to a change in genetic susceptibility or in lifestyle and suggests that other factors such as the role of intestinal microbiome should be considered. The peak between 2008-2009 and the drop in 2010 may represent a spurious change in incidence or an artifact. Follow-up of this pattern after 2010 may provide better definition of future trends. The family history of IBD was positive in 15.3% of cases which are higher than the 11% reported from Wisconsin, USA<sup>3</sup> and the 12.8% reported in non-Jewish children in Toronto, Canada,<sup>14</sup> but much lower than proportions of 29% reported from a consortium population of US children.<sup>15</sup> This relatively low prevalence of positive family history in Saudi Arab children with IBD, a population with high prevalence of consanguinity and family size,<sup>18</sup> is surprising and provides more support for a greater role of environmental than genetic factors. However, this observation requires further investigations.

The presenting clinical and laboratory features indicate that IBD in Saudi children may present at any age and that certain features are more common than others in both UC and CD. These findings are consistent with classical descriptions in other populations<sup>19,20</sup> and should increase the index of suspicion among physicians caring for children in all regions of KSA. It is mentioned that the variation in the numbers of cases for each clinical or laboratory test is due to the fact that some patients presented and were investigated in other hospital and data at presentation were not available.

The implications of the results of this study are important. Description of the presenting features of IBD in Saudi children helps increase the index of suspicion of these diseases among physicians leading to early diagnosis and treatment. In addition, identification of increasing diagnosis, despite its limitation indicates the need for further prospective research to define the epidemiology and etiology of these "new" diseases in Saudi Arabia.

**Study limitations.** The retrospective nature of the study, the limited study population to 2 centers in one city, the unavailability of data from other centers in Riyadh, and the lack of denominator precludes accurate prevalence estimation.

It can be concluded that the presenting features of IBD in Saudi children are similar to the descriptions from other populations, suggesting similar disease etiology, and pattern. In addition, the trend of increasing diagnosis indicates the need for further prospective research in the epidemiology and etiology of this "new" disease in Saudi Arabia.

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