Inflammatory Bowel Disease in Children, an Evolving Problem in Kuwait

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ABSTRACT

Background/Aims: Inflammatory bowel disease (IBD) was previously thought a rare disease among children in Kuwait since most diarrhea cases were attributed to infections. In the past few years we observed an increase in the number of patients presenting with IBD. In this study we aimed to determine the epidemiology of IBD among children in the State of Kuwait. Patients and Methods: The charts of all children with IBD who were referred to the pediatric gastroenterology unit during the period February 1998 to January 2008 were retrospectively reviewed. Results: Out of a total of 130 children with IBD, 92 (71%) had Crohn’s disease, 36 (28%) had ulcerative colitis and two (1%) had indeterminate colitis. The estimated annual incidence for IBD was 2.16/10⁵/year. The age range was nine months-15 years (median: 11 years). Fifty-three percent of all patients were females and 77% were Kuwaiti nationals. Positive family history was found in 23%. The commonest presenting symptoms were abdominal pain (87%) and diarrhea (82%). Failure to thrive was detected in 35% and short stature in 20% at presentation. The ileocolonic region was the most common presentation site affected in Crohn’s patients and pancolitis was the commonest in ulcerative colitis. Conclusion: Inflammatory bowel disease is not uncommon in our children. We found no differences regarding disease presentation and clinical features compared to the Western world.

Key Words: Children, Crohn’s disease, inflammatory bowel disease, Kuwait, ulcerative colitis

Received 26.09.2010, Accepted: 17.11.2010

How to cite this article: Al-Qabandi WA, Buhamrah EK, Hamadi KA, Al-Osaimi SA, Al-Ruwayeh AA, Madda J. Inflammatory bowel disease in children, an evolving problem in Kuwait. Saudi J Gastroenterol 2011;17:323-5.

The incidence of inflammatory bowel disease (IBD) in children has increased over the recent years in Europe,[1,2] the United States,[11] and Australia.[10] The disease was reported to have a low incidence in Asia, however, a rising secular trend in both incidence and prevalence was noted over the past decade.[16]

In Kuwait, an increasing number of children were referred to the pediatric gastroenterology service for chronic diarrhea without an infective etiology. In this paper, we report our experience with IBD in children in Kuwait and compare its epidemiology and clinical features with those reported in the rest of the world.

PATIENTS AND METHODS

The study was carried out in the pediatric gastroenterology and hepatology unit in Kuwait. This unit is the only centre providing pediatric gastroenterology service and covers all governmental and private health sectors in the country.

Patients diagnosed with IBD from February 1998 to January 2008 were enrolled in this study. The medical records of those patients were retrospectively reviewed and the diagnosis of IBD, whether Crohn’s disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC) was established. The study was approved by the ethical committee of the Ministry of Health.

The diagnosis of IBD was based on the clinical presentation plus biochemical, radiological, endoscopic and histopathological examinations. The differentiation of disease into CD, UC or IC was based on the criteria of the IBD working groups of both the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN)[7] and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition.
Patients were labeled to have IC if there was an isolated colonic disease and the histopathology was inconclusive of either CD or UC. The data collected included the age at diagnosis, sex, nationality and presence of family history of IBD. The presenting symptoms, clinical findings and laboratory tests, on presentation, were verified. Failure to thrive (FTT) and short stature were defined as weight and height below the fifth percentile respectively. Certain laboratory cutoff values were defined such as anemia (hemoglobin <12 g/dl), thrombocytosis (platelets >400 × 10^9/L), elevated erythrocyte sedimentation rate (ESR >20 mm/h) and hypoalbuminemia (serum albumin <35 g/L).

All patients underwent colonoscopic examination with attempted ileoscopy. Upper endoscopy was performed in patients who had upper gastrointestinal (GI) symptoms such as nausea, vomiting and upper abdominal pain. Contrast study of the small bowel (SBFT) was done in patients who showed one or more of the following features: Evidence of FTT or short stature at presentation, hypoalbuminemia, terminal ileal disease on colonoscopy or histopathological features of CD. Stool samples were examined by microscopy and culture in all patients who presented with diarrhea. Tuberculosis was excluded prior to steroids or biological treatment. Different treatment modalities were used in managing the patients during both induction and maintenance therapy.

**RESULTS**

One hundred and thirty children were diagnosed with IBD during the study period, 92 (71%) had CD, 36 (28%) had UC and two (1%) had IC. The average number of children under 15 years over the study period was 600,500 representing 20% of the total population of Kuwait which was around 3 million according to the Kuwait population census in 2007. This gives an estimated annual incidence of 2.16/10^5/year (CI 95%, 1.68-2.64) for IBD, whereas the incidence for CD is 1.53/10^5/year (CI 95%, 1.12-1.93), for UC is 0.6/10^5/year (CI 95%, 0.34-0.85) and for IC is 0.03/10^5/year (CI 95%, 0-0.09).

The age at diagnosis ranged between nine months and 15 years (mean: 10.3 years, median: 11 years). As shown in Table 1, the majority of the group was ≤ 12 years and a higher percentage of young children (≤ 5 years) fall in the UC group. Most of these abnormalities were encountered in the CD group.

Although all children had colonoscopic examination, terminal ileum intubation was achieved in 88 patients of whom 69 had CD. Upper endoscopy was performed in 65 (48%) patients. The findings ranged between esophagitis, gastritis, duodenitis and duodenal ulcers. The most common disease was a manifestation in 13% of patients. The lesions varied between anal fissures, skin tags, perianal fistulae and abscesses. The UC patient had an anal fissure. Other skin lesions encountered included mouth ulcers and erythema nodosum.

As shown in Figure 1, the most common laboratory abnormality was anemia followed by thrombocytosis. Most of these abnormalities were encountered in the CD group.

Our patients presented with a mixture of symptoms and signs of gastrointestinal and extraintestinal manifestations as shown in Table 2. Abdominal pain was the most common presentation symptom followed by diarrhea. Perianal involvement was seen in 13% of patients. The lesions varied between anal fissures, skin tags, perianal fistulae and abscesses. The UC patient had an anal fissure. Other skin lesions encountered included mouth ulcers and erythema nodosum.

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**Table 1: The demographic features of IBD patients**

|                | CD (%) | UC (%) | IC (%) | Total (%) |
|----------------|--------|--------|--------|-----------|
| Sex: F         | 43 (47)| 25 (69)| 1 (50) | 69 (53)   |
| M              | 49 (53)| 11 (31)| 1 (50) | 61 (47)   |
| Age range (years) |        |        |        |           |
| 0.9-15         | 66 (72)| 27 (75)| 2 (100)| 95 (73)   |
| ≤12 years      | 10.5   | 10     | 11     | 10.3      |
| ≤5 years       | 5 (5)  | 6 (17) | -      | 11 (8)    |
| Nationality: K*| 75 (82)| 23 (64)| 2 (100)| 100 (77)  |
| NK †           | 17 (18)| 13 (36)| 30     | 30 (23)   |
| FH‡ of IBD     | 18 (20)| 11 (31)| 1 (50) | 30 (23)   |
| Total          | 92 (71)| 36 (28)| 2 (1)  | 130 (100) |

*K: Kuwaiti; †NK: non-Kuwaiti; ‡FH: Family history

**Table 2: Clinical presentations at the time of diagnosis**

|                | CD (%) | UC (%) | IC (%) | Total (%) |
|----------------|--------|--------|--------|-----------|
| Abdominal pain | 83 (90)| 28 (78)| 2 (100)| 113 (87)  |
| Diarrhea       | 70 (76)| 36 (100)| 1 (50) | 107 (82)  |
| Bloody diarrhea| 31 (34)| 34 (94)| 1 (50) | 66 (51)   |
| Lethargy       | 24 (26)| 8 (22) | -      | 32 (25)   |
| Fever          | 29 (32)| 3 (8)  | -      | 32 (25)   |
| FTT*           | 41 (45)| 5 (14) | -      | 46 (35)   |
| Short stature  | 20 (22)| 5 (14) | 1 (50) | 26 (20)   |
| Perianal disease| 16 (17)| 1 (3)  | -      | 17 (13)   |
| Skin lesions   | 10 (11)| 3 (8)  | -      | 13 (10)   |

*FTT: Failure to thrive
abnormality was gastroduodenal disease. In CD patients, non-caseating granuloma was found in 44 (48%) patients. SBFT was done in 57 (44%) patients of whom 38 showed small bowel disease. Abnormalities included bowel wall thickening, ulcerations, luminal narrowing and irregularity and cobblestone appearance.

CD was ileocolonic in the majority of patients as shown in Figure 2 while pancolitis was the commonest lesion in UC patients [Figure 3].

The follow-up period ranged between two months to ten years (median: Six years). Seven (5%) patients were lost to follow-up (non-Kuwaiti: Four, Kuwaiti: Three). Most of the complications were encountered among the CD group (gut perforation, 4 patients; gut strictures, 3 patients; and intra-abdominal abscess, 3 patients). Surgical management was provided to those patients with perforations and strictures but those with intra-abdominal abscesses were treated conservatively. In the UC group, two patients experienced fulminant colitis and were treated conservatively. One patient developed a spontaneous and unexplained intracranial bleed and recovered fully. Another patient developed a myelodysplastic syndrome (MDS) for which she was treated with chemotherapy followed by bone marrow transplant, but died two years after the transplant. The IC patients continued to be indeterminate until writing this report.

DISCUSSION

There are few published reports describing IBD in the Arabian Gulf region, which is located in Western Asia.[9-13] These described a lower rate of the disease in this part of the world. The incidence in Kuwait was reported to be 2.27/105/year for UC and 0.45/105/year for CD in the period 1977-82.[14] The UC incidence showed a slight rise (2.8/105/year) in the period 1985-99 but there are no recent reports describing CD.[15] All previous studies described the disease mainly in adults with few pediatric series.[16-18] Kalaoui et al., reported the colonoscopic findings in 159 children in Kuwait over a period of nine years and 21% of those had IBD.[17] The only study which reported IBD epidemiology among children in the region was by El Mouzan et al., who reported 50 IBD children seen in Riyadh, Saudi Arabia during 1993-2002.[18] The incidence rate was estimated to be 0.5/105/year and the prevalence was 5/105/year.

We believe that the present paper reports the largest series so far, of pediatric IBD in the Arabian Gulf, if not in the Middle East as a whole as we are unaware of any published data reporting a higher figure in the region. We followed 130 children with IBD during the study period in which we diagnosed CD in the majority of cases. This was similar to other reports from the Western world that reported CD to be more common in children.[19] Among the adult population of Kuwait, UC was reported to be the main category.[14] The pediatric gastroenterology unit serves the whole country and hence receives all suspected IBD cases. This makes the estimated annual incidence to be more representative of IBD among the children in the country.

Table 3 shows a comparison between the incidence rates among children in different populations. Although the age

| Country | Year     | Age | Incidence/105/year |
|---------|----------|-----|-------------------|
| Canada  | 1997-2006| ≤17 | 12.4              |
| Norway  | 2005-2007| <18 | 10.9              |
| Sweden  | 1990-2001| <15 | 7.4               |
| USA     | 2000-2001| <18 | 7.05              |
| UK      | 1998-1999| <16 | 5.2               |
| Scotland| 1981-1995| ≤15 | 3.4               |
| France  | 1988-1999| <17 | 3.1               |
| Kuwait  | 1998-2008| ≤15 | 2.16              |
| Italy   | 1996-2003| <18 | 1.39              |
| Australia| 1971-2001| ≤16 | 2.0               |
| Saudi Arabia | 1993-2002 | <18 | 0.5              |

*Present paper
group and the way those studies were conducted are not the same, it does give a rough idea about the epidemiology of IBD among different populations. The incidence in Kuwait is considered to be very low compared to Canada,[29] the Scandinavian countries,[2,21] the USA[3] and UK[22] but not that low if compared to Scotland[25] and France.[24] Our reported incidence is actually higher than Italy,[23] which is a South European country. It was also interesting to find that our estimated incidence was more than triple that reported in a neighboring country, Saudi Arabia.[18] We could not find reported incidence rates per 10^5 children population in other Asian or African countries for comparison.

In our series, the frequency of IBD was almost the same in both sexes. In the USA, males account for 54-60% of IBD children.[3,19] The majority of our patients were younger than or equal to 12 years at diagnosis. This data is partly skewed by the fact that only children less than 15 years old were included because most of the adolescent cases are referred to our adult gastroenterology colleagues. We anticipate that our IBD incidence would be higher than the one reported in this paper if the 16-19 years group of children were included in the calculation. IC was reported to be more frequent in younger patients[19,26] which was not the case in our group probably because we had a small number of IC cases that do not represent the typical features of that category. Seventy-seven percent of patients were Kuwaiti nationals confirming the existence of IBD in our native population. Family history of IBD was found in 23% of our series, mainly in the UC group. Familial association of IBD is recognized by many authors, especially in younger patients, with a great variability in the percentage of affected family members.[27]

The most common presenting symptoms in our patients were abdominal pain and diarrhea, which were consistent with other IBD populations elsewhere.[23,26] Failure to thrive and growth failure were documented in our CD patients [Table 2]. Growth failure is unique to pediatric IBD and was reported by Motil et al., to be present in 10-40% of affected children, especially in CD.[29] It was already a problem in our patients at presentation, therefore, effective treatment of active inflammation should lead to a growth-promoting remission. We encountered perianal disease in 13% of our patients, all but one were in the CD group. This problem was well-recognized in CD children of other populations with almost similar figures.[16]

With regards to laboratory results, anemia and thrombocytosis were detected in the majority of our patients. Cabrera-Abreu et al., reported that the presence of anemia or thrombocytosis was associated with a diagnostic sensitivity of 90.8%, a specificity of 80% and a positive predictive value of 94.4% for IBD.[31]

The disease localization in our patients was similar to that reported in other pediatric populations but with a lower rate of upper gastrointestinal (GI) involvement.[25,28,32] This might be attributed to the fact that not all patients were subjected to upper GI endoscopy. Castellana et al., found that upper GI lesions were present in 26% of asymptomatic IBD children.[33] Therefore, we recently adopted a strategy in which an upper endoscopy is performed in all children suspected of IBD.

Few rare and serious complications were encountered in our patients. One UC patient developed an intracranial bleed. Cerebrovascular accidents are well-recognized complications in IBD ranging from peripheral venous thrombosis to central stroke syndromes and pseudo-tumor cerebri.[14] Those are mainly a concern in adults with few reports in children.[35] Another UC patient developed MDS which was also reported to be associated with IBD.[16] We recommend that IBD patients with persistent anemia, without an apparent cause, should be evaluated for MDS.

In conclusion, we reviewed our experience with pediatric IBD in Kuwait, a disease that once was believed to be a rarity in our community; however, it should not be regarded as such any more. We found no differences regarding disease presentation, clinical and biochemical characteristics as well as disease localization and complications compared to the rest of the world. Combining the efforts with our general pediatric and adult gastroenterology colleagues is mandatory to establish the true incidence and prevalence rates of IBD in children and adolescents in Kuwait.

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Source of Support: Nil. Conflict of Interest: None declared.