DOI: 10.4176/081210

Childhood Inflammatory Bowel Disease in Libya: Epidemiological and Clinical features

Ahmaida AI[1] and Al-Shaikhi SA[2]

1 Department of Pediatrics, Faculty of Medicine, Al-Arab Medical University
2 Al-Fateh Children's Hospital, Benghazi, Libya

Abstract

Background & Aims: Inflammatory bowel disease is thought to be rare in Libya. The aim is to determine the prevalence of juvenile onset inflammatory bowel disease in Libya. Setting: Al-Fateh childrens' hospital, Benghazi, Libya. **Methods:** This is a retrospective study of all cases diagnosed over 10 years (1997-2006) with either ulcerative colitis, Crohn's disease or indeterminate colitis. Inclusion criteria were age <15 years at time of presentation who were resident in the eastern part of the country and who diagnosed with inflammatory bowel disease. Clinical features were outlined using a proforma. **Results:** Sixteen cases were diagnosed with inflammatory bowel disease, of whom 11 were males (M:F ratio of 1.5:1). The prevalence and incidence rates in the year 2006 were 3.6 and 0.9 per 100,000 children, respectively. The incidence rate increased from 0.2 in 2002 to 0.9 in 2006 (Z score of 39.87, p= 0.00). The age at presentation ranged from 5 months to 14 years. Nine had Crohn's disease (6 males) and 6 had ulcerative colitis (4 males). One patient had indeterminate colitis. The most common clinical features were diarrhea in 10 (62.5%), abdominal pain, anorexia and weight loss in 9 (56.2%), anemia in 7 (43.75%) and vomiting in 6 (37%). Ileopancolitis was found in 3 patients whereas 6 patients had ileocecal disease. **Conclusions:** Childhood inflammatory bowel disease in this population is not so rare and it is increasing. The clinical pattern is similar to that reported by others.

Abbreviations

IBD= inflammatory bowel disease
CD= Crohn's disease, UC= Ulcerative colitis
IC= Indeterminate colitis
GIT= gastrointestinal tract.

Key words: *Inflammatory bowel disease, Ulcerative colitis, Crohn's disease, Indeterminate colitis, Juvenile onset inflammatory bowel disease*

Introduction

Inflammatory bowel disease (IBD) includes a heterogeneous group of immunologically mediated inflammatory conditions of the gastrointestinal tract (GIT) with or without extraintestinal manifestations. Major members of this group are Crohn's disease (CD) and ulcerative colitis (UC). Both of these disorders are chronic diseases characterized by remissions and relapses. Crohn's disease can directly involve any part of the gastrointestinal tract, whereas ulcerative colitis involves only the colon. The clinical manifestations of Crohn's disease in particular are varied and include poor growth, abdominal pain, diarrhea, constipation, rectal bleeding, fever, and anaemia. Ulcerative colitis, on the other hand, is characterized by bloody diarrhea and abdominal pain among other symptoms. However, CD can present with colitic features similar to those of UC. Indeterminate colitis (IC) is another less common member of the group and its diagnosis rests on the exclusion of other causes of colitis. Some believe that it is a temporary stage towards the development of CD or UC [1]. However, others find it a clearly distinct member of the group [2].

The aetiology of IBD is still a mystery in spite of extensive research in the field. It is thought that environmental factors play an important role as evidenced by a relatively low concordance rate among identical twins. However, the higher frequency of IBD in first degree relatives indicates a role for genetics in its etiology [3].

Inflammatory bowel disease occurs with a variable frequency in different parts of the world. It is a common observation that IBD is prevalent in industrialized countries as it is seen in Europe and USA but much less common in the southern part of the globe [4-6]. Twenty to twenty five percent of CD and UC cases, respectively, present during childhood [7].

Neither the prevalence of childhood-onset IBD nor its clinical profile has been described, and only a few reports have been published on IBD in Arab and Middle Eastern countries. These reports show that IBD is not common in this part of the world [8-10].

The importance of environmental factors in the development of IBD is further substantiated by the increasing frequency of IBD in areas that used to have a distinctly low prevalence [11]. Westernization of the life style in these areas is thought to be a contributing factor to this rise in IBD frequency in spite of lack of a hard causal relationship. We see in our practice that there has been an increase in the number of cases referred to us for possible IBD in the last decade. We therefore carried out a retrospective descriptive study on IBD in Eastern Libya to know the prevalence of childhood IBD and its clinical profile.

Material and methods

A retrospective study was performed on the children diagnosed as having either CD or UC or indeterminate colitis (IC). Benghazi is the second major city in Libya and its hospitals function as referral hospitals for the rest of the eastern part of the country. As a rule, all children with suspected and /or diagnosed IBD are evaluated and followed up at the gastroenterology-hepatology clinic of Al-fateh Childrens' Hospital (AFCH), which is a major teaching hospital and the only pediatric referral hospital in the whole eastern region. However, since some adolescents might as an exception looked after by adult

DOI: 10.4176/081210

physicians, we looked at the records of adult gastroenterology clinics in Benghazi area as well (one at El-Keish polyclinic and another one at Al-jamhouriya hospital). Inclusion criteria were as follows: presence of IBD, age ☐15 years at the time of presentation, presentation within the last 10 years (1997-2006), and residence in the east of Libya. More common differential diagnoses, such as amoebiasis, bacterial infections, tuberculosis and allergy, were for all practical purposes ruled out by conventional methods, such as stool examination, culture techniques, imaging, tuberculin testing, radioallergosorbent tests, elimination and challenge dietary maneuvers, and therapeutic trials, as needed. The usual workout of these patients included history taking, clinical examination (including screening for signs of vitamin deficiency) and anthropometric assessment (height, weight and mid-upper arm circumference). Local growth charts were used to assess growth [12, 13]. Puberty was graded according to the well known Tanner's staging [14]. All patients were subjected to the following investigations: full blood count, erythrocyte sedimentation rate (ESR), serum calcium, phosphorus, alkaline phosphatase and albumin, in addition to blood urea and serum creatinine. C-reactive protein and serum ferritin were done only in the more recent cases. The diagnosis was based on clinical, endoscopic, radiological and histopathologic findings. All patients were endoscoped, except for one in whom the diagnosis was based on post-operative histopathology of an excised ileocaecal mass. Data on the structure of the population were obtained from a census carried out in 2006 by the National Data and Documentation Bureau. According to this census, the annual growth rate over the period 1996-2006 is 1.83%. We used this figure to estimate the population size over the years of our study. Prevalence and incidence rates were expressed as the number of cases per 100,000 children under 15 years old. Results were expressed as ranges, means ± standard deviation (SD) and percentages. A z-test at a confidence level of 95% was used to test the statistical significance of any possible change in prevalence or incidence. EpiCalc-2000 version 1.02 software was used for this purpose.

Results

The number of people aged < 15 years in the catchment area was 441,371. Sixteen patients had IBD giving a total prevalence and incidence rates of 3.6 and 0.9 per 100,000 in the year 2006, respectively. Fifteen patients were registered at AFCH and one at Al-jamhouriya hospital. The incidence rate increased 4-folds from 0.2 per 100,000/year in the year 2002 to 0.9 per 100,000/year in 2006 with a Z score of 39.87 (p= 0.00) (table 1). The prevalence rate increased from 1.2 per 100,000 in 2002 to 3.6 per 100,000 in 2006, with a Z score of 71.33 (p = 0.00). IBD prevalence in Benghazi governorate in the year 2006 was 6 per 100,000. Table 2 shows the individual prevalence rates of CD and UC in the studied governorates. Eleven of our patients were males (M:F ratio =1.5:1). The age at presentation ranged from 5 months to 14 years with a mean of 10.3 ± 2.8. Nine patients had CD (males =6) with a mean age of 8.3± 4.2 years (range: 9 months-14 years). Six patients had UC (4 males) with a mean age of 8±4 years (range 2.5-13 years). One patient who was 5 months old at the time of presentation had indeterminate colitis. One patient was initially diagnosed as UC and few years later turned out to be CD. Time elapsed between onset of symptoms and diagnosis mostly ranged from 2 months to 4 years, but in one case this took 8 years.

Diarrhea was the most common clinical feature and seen in 10 (62.5%) of IBD cases particularly in those with CD (77%). One patient with Crohn's disease had constipation as a prominent chronic symptom. Anorexia, abdominal pain, weight loss and rectal bleeding were each found in 9 patients in various combinations. However, all patients with UC had rectal bleeding whereas just 3 out of 9 CD patients had it (100% vs 33%). Linear growth was impaired in 5 patients with pubertal delay in 2 of them. Perianal disease including fistulas, abscesses, tags and nodules was seen in 4 CD patients (44% of Crohn's). Well defined extraintestinal manifestations were seen in one patient in the form of mono-articular arthritis and the same patient had extensive aphthous ulceration of the mouth. Less well defined symptoms such as arthralgias and muscle pains were seen in four IBD patients. Two patients were subjected to operation for a right iliac fossa mass. Three patients with CD and one with UC were classified as having severe illness.

Table 1 Incidence and prevalence rates of IBD over the study period

Year	of children <15 years	cases of IBD	Incidence per 100,000/year	Cumulative No. of cases	Prevalence per 100,000
1997	368677	0	0	0	0
1998	376754	2	0.53085	2	0.53085
1999	384831		0	2	0.519708
2000	392909	1	0.254512	3	0.763537
2001	400986	1	0.249386	4	0.997542
2002	409062	1	0.244461	5	1.222307
2003	417139	2	0.479456	7	1.678095
2004	425217	2	0.470348	9	2.116567
2005	433294	3	0.692371	12	2.769483
2006	441,371	4	0.906267	16	3.625068

Investigations

Hemoglobin level at presentation ranged from 7-13.5 (10.4±1.75) gm/dl. Anaemia at presentation was found in seven patients (43.8%). ESR was high in 7 out of all patients and C-reactive protein in 2 out of 7 cases subjected to the test. All UC patients had distal colitis. The localization of the disease among CD patients was as follows: ileopancolitis in 3 and ileocecal in 6. Two patients have upper GIT involvement. Five patients were given multiple empirical treatments for amebiasis prior to referral to our hospital. None of these patients was investigated before receiving the anti-amoebic treatment.

Treatments

In addition to supportive therapy patients were treated with systemic steroids, salazopyrine, 5-ASA derivatives and metronidazole in various combinations. Azathioprine was used for 3 patients. Budesonide enema was highly

DOI: 10.4176/081210

effective in 3 patients with colitis. Nutritionally defined formula was available for use only on 2 occasions.

Table 2 total and individual prevalence rates of different forms of juvenile onset IBD in the studied governorates*.

Governorate	No. of children <15 years	UC no. (prevalence)	CD no. (prevalence)	IC no. (prevalence)	IBD no. (prevalence)
Benghazi	198547	6 (3)	6 (3)	0 (0)	12 (6.0)
Batnan	55200	0 (0)	0 (0)	1 (1.8)	01 (1.8)
Derna	55254	0 (0)	01 (1.8)	0 (0)	01 (1.8)
Al-Jabal	70358	0 (0)	2 (2.84)	0 (0)	02 (2.84)
Al-Marj	62012	0 (0)	0 (0)	0 (0)	0 (0)
Total	441371	6 (1.36)	9 (2.0)	1 (0.2)	16 (3.6)

*Values between brackets represent prevalence rates per 100,000 children

Discussion

We show that juvenile onset IBD is not so rare in the eastern part of Libya, with a prevalence rate of 3.6 per 100,000 in 2006. Though our clinic at AFCH looks after most children with suspected and/or diagnosed IBD, we can not assume that all IBD cases are referred to AFCH, particularly those with milder forms of the disease. However, even on keeping this limitation in mind the prevalence and incidence rates of IBD are obviously lower than the rates in Western countries, where rates of 2.2-7/100,000 per year were reported [15-18]. A similar study from Saudi Arabia reported a prevalence of 5 per 100,000 [10] which is quite similar to ours. In addition, another study from Saudi Arabia pointed to a low rate of IBD, though no exact prevalence figures were reported. In their report, Isbister and Hubler described just 101 IBD cases from Saudi Arabia during almost two decades (1976-1994) [19]. A relative exception to this comes from a study on adult Kuwaiti patients, in which 91 patients with UC and 14 with CD were diagnosed over 6 years in a hospital serving 55% of the population of Kuwait [20]. The authors in this study suggested that IBD is likely to be common in Kuwait.

Eastern Libya is characterized by having a more ethnically homogeneous population than that encountered in most of the Gulf countries which may account, at least partially, for the observed differences in prevalence rates. However, rest of Libya is ethnically less homogeneous and our results might not be applicable to the rest of it. Though most Libyans are of Arab ancestry, some have African roots, particularly in the south of the country. Ethnic heterogeneity in the epidemiology and phenotype of IBD is well known. For example, ethnic differences have been observed in the multiracial Asian countries. In addition, NOD2/CARD15 variants have not been found in Asian CD patients, indicating a different genetic background from Western CD patients [11]. The effect of race extends to involve the phenotype of IBD. In a report on characteristics of IBD among African Americans, Hispanics and non-Hispanic whites in north America, African American CD patients were more likely to have gastroduodenal, colorectal and perianal disease and less likely to have ileal involvement [21]. Some European countries reported a relatively low incidence of IBD in children [18]. From the above we could see that the rates of occurrence of IBD have no consistent pattern among western countries and it would be an oversimplification to generalize statements on the prevalence of IBD in developed and under-developed areas of the world.

The prevalence of IBD has been increasing in western and non-western countries [10,22,23]. Since our clinic is for all practical purposes the only one looking after pediatric IBD cases in the eastern part of Libya, we have the unique position of knowing most children with IBD in our area. We had the impression that IBD locally is increasing. Our study showed that the incidence of IBD has increased fourfold in 2006 compared to 2002. We feel that this increase in the occurrence rate is most probably a real one since the diagnostic facilities have not changed much over these 5 years. This rise in occurrence might be a result of the westernization of the local life style. It has been observed that IBD incidence has increased in urban areas [24]. Urbanization of lifestyle embodies changes in diet and environment. For example, non-nutritive microparticles such as titanium dioxide are found in the diet. These microparticles are believed to combine with other substances found in the intestine to form antigens capable of mediating inflammatory immune responses. Patients with IBD were also shown to consume higher amounts of sucrose and refined carbohydrates [25]. Table sugar is subsidized by the Libyan government, resulting in high consumption rates. Such dietary changes might have contributed to the observed rise in IBD incidence in our area. On the other hand, IBD is more likely to occur in people exposed to dirt and helminthes [26,27]. However, we can not eliminate the possibility of increased awareness of the disease as a contributing factor to the rise in the incidence.

Though AFCH is the only hospital at which young children from eastern Libya with suspected IBD are evaluated, we can not claim that every child with IBD is referred to us. It is possible that some patients did not find their way to us either because of less awareness of

DOI: 10.4176/081210

the disease in governorates other than Benghazi or because they managed to get medical advice in nearby countries. For all these reasons, it is likely that the actual prevalence and incidence figures are higher than those we got.

Table 3 comparison between percent frequencies of some of the clinical features of IBD in Great Britain and Ireland 29 and those seen in our patients

	Ulcerative colitis		**Crohn's disease**	
	UK (n=172) n (%)	**Libya** (n=6) n (%)	**UK** (n=)379 n (%)	**Libya** (n=9) n (%)
Abdominal pain	106 (62)	4 (66)	274 (72)	5 (56)
Diarrhea	127 (74)	3 (50)	214 (56)	7 (77)
Rectal bleeding	145 (84)	6 (100)	84 (22)	2 (22)
Weight loss	53 (31)	4 (66)	220 (58)	5 (56)
Anorexia	11 (06)	3 (50)	94 (25)	5 (56)
Perianal disease	Not mentioned	0	17 (6.6)	4 (44)

Interestingly, the prevalence rates of CD and UC in Benghazi were equal (3 per 105). This is in contrast to reports from western countries which show that UC is significantly more common [18,22]. This opposite trend is increased further if we include patients from other governorates where CD outnumbers UC. It is known that dietary factors and intestinal microflora play an important role in IBD. The different dietary habits prevalent locally and the higher rate of early childhood infections might have something to do with this difference between ulcerative colitis and Crohn's disease [28]. The predominance of UC is not universal in industrialized countries. A report from France shows predominance of CD over UC, a trend similar to ours. However, because of the small number of cases in our study we stress that such comparisons need to be taken with caution.

The clinical features of Crohn's disease and ulcerative colitis in the Libyan patients were similar to those reported from western and non-western countries. Common presenting features in our patients were diarrhea, abdominal pain, weight loss, anorexia and bleeding. A study carried out on presenting features of IBD in Great Britain and Ireland showed a very similar pattern to ours [29]. This was somewhat unexpected finding in view of our small sample size and in view of the epidemiological differences between these European countries and Libya. Table 3 compares our finding with theirs.

Because IBD in Libya is considered by the local medical community as a rare disease, doctors tend to label patients with more common diagnoses. In this cohort, 5 patients received blind treatment for amebiasis on a number of occasions. Such an empirical treatment might delay the diagnosis particularly if metronidazole is used. Though it is crucial to rule out more common diseases in developing countries, it is important not to miss IBD. Tuberculosis is seen in Libya more frequently nowadays than it was a decade ago and it has to be kept in mind as a differential diagnosis. Recently, a group of pediatric gastroenterologists released a report on the criteria for diagnosis of IBD. In this report, it was stressed that every child suspected of having IBD should be subjected to a complete diagnostic work up. This work up is composed of history, clinical examination, ileocolonoscopy, upper GIT endoscopy and in all cases a contrast small bowel study (with possible exception of obvious ulcerative colitis) [30]. Understandably, these recommendations are universal and need to be implemented locally as well.

Conclusion

In conclusion, we have shown that juvenile onset IBD is not that rare in Libya and its clinical features resemble those reported in other countries. It is also clear that childhood IBD is on the rise in Libya. Though it is important to exclude common infections, it is crucial to keep the possibility of IBD in mind. Studies on juvenile onset IBD in other parts of the country are highly needed as well.

References

1- Geboes K, De Hertogh G. Indeterminate colitis. Inflamm Bowel Dis 2003; 9: 324–31.

2- Carvalho RS, Abadom V, Dilworth HP, Thompson R, Oliva-Hemker M, Cuffari C. Indeterminate colitis: a significant subgroup of pediatric IBD. Inflamm Bowel Dis 2006; 12: 258–62.

3- Halfvarson J, Bodin L, Tysk C, Lindberg E, Järnerot G. Inflammatory bowel disease in a Swedish twin cohort: a long-term follow-up of concordance and clinical characteristics. Gastroenterology 2003; 124: 1767–1773.

4- Auvin S, Molinie F, Gower-Rousseau C et al. Incidence, clinical presentation and location at diagnosis of pediatric inflammatory bowel disease: a prospective population-based study in northern France (1988-1999). J Pediatr Gastroenterol Nutr 2005; 41: 49-55.

5- Kolek A, Janout V, Tichy M, Grepl M. The incidence of inflammatory bowel disease is increasing among children 15 years old and younger in the Czech Republic. J Pediatr Gastroenterol Nutr 2004; 38:362-3.

6- Hildebrand H, Finkel y, Grahnquist L, Lindholm J, Ekbom A, Askling J. Changing pattern of paediatric inflammatory bowel disease in northern Stockholm 1990-2001. Gut 2003; 52:1432-4.

7- Mamula P, Markowitz JE, Baldassano RN. Inflammatory bowel disease in early childhood and adolescence: special considerations. Gastroenterol Clin North Am 2003; 32:967-95.

8- Elloumi H, Sfar S, Ben Abdelaziz A, Arfaoui D, Mouna G, Ajmi S. Crohn's disease: influence of age at diagnosis on clinical type of disease. Tunis Med 2007; 85: 862-5.

9- Abdul-Baki H, ElHajj I, El-Zahabi LM et al. Clinical epidemiology of inflammatory bowel disease in Lebanon. Inflamm Bowel Dis 2007; 13: 475-80.

10- El Mouzan, MIE, Abdullah AM, Al Habal MT. Epidemiology of Juvenile-onset Inflammatory Bowel

Disease in Central Saudi Arabia. J Trop Pediatr;2006 ;52:69-71.

11- Ouyang Q, Tandon R, Goh K L, Pan G-Z, Fock K M, Fiocchi C, Lam S K, Xiao S-D. Management Consensus of Inflammatory Bowel Disease for the Asia-Pacific Region. J Gastroenterol Hepatol. 2006; 21:1772-1782.

12- Abounaja S, Gilmour WH. Standards for height and weight of Libyan children aged 6-17 years [Dissertation]. Glasgow Univ.; 1985.

13- Tajouri RF, Prader A.Cross sectional study of growth in urban Libyan children 0-5 years [Dissertation]. Zurich Univ.; 1978.

14- Marcell AV. Adolescence. In: Kliegman RM, Behrman RE, Jenson HB, Starton BF, editors. Nelson Textbook of Pediatrics. 18th ed. Philadelphia: Sanders Elsevier; 2007. p.60.

15- Kugathasan S, Judd RH, Hoffmann RG et al. Epidemiologic and clinical characteristics of children with newly diagnosed inflammatory bowel disease in Wisconsin: a statewide population-based study. J Pediatr 2003; 143:525-31.

16- Sawczenko A, Sandhu BK, Logan RF et al. Prospective survey of childhood inflammatory bowel disease in the British Isles. Lancet 2001; 357:1093-4.

17-Bentsen BS, Moum B, Ekbom A. Incidence of inflammatory bowel disease in children in southeastern Norway: a prospective population-based study 1990-94. Scand J Gastroenterol 2002;37:540-5.

18- Langholz E, Munkholm P, Krasilnikoff PA, Binder V. Inflammatory bowel diseases with onset in childhood. Clinical features, morbidity, and mortality in a regional cohort. Scand J Gastroenterol1997; 32: 139-47.

19- Isbister WH, Hubler M. flammatory bowel disease in Saudi Arabia: presentation and initial managemen. J Gastroenterol Hepatol. 1998; 13:1119-24

20- Al-Nakib B, Radhakrishnan S, Jacob GS, Al-Liddawi H, Al-Ruwaih A. Inflammatory bowel disease in Kuwait. Am J Gastroenterol 1984;79:191-4.

21- Nguyen GC.; Torres EA.; Regueiro M. et al. Inflammatory Bowel Disease Characteristics Among African Americans, Hispanics, and Non-Hispanic Whites: Characterization of a Large North American Cohort. Am J Gastroenterol. 2006;101:1012-1023.

22- Vind I, Riis L, Jess T et al.Increasing incidences of inflammatory bowel disease and decreasing surgery rates in Copenhagen city and County, 2003-2005: a population-based study from the Danish Crohn colitis database. Am J Gastroenterol 2006; 101: 1274-82.

23- Lok KH, Hung HG, Ng CH, Li KK, Li KF, Szeto ML. The epidemiology and clinical characteristics of Crohn's disease in the Hong Kong Chinese population: experiences from a regional hospital. Hong Kong Med J 2007;13: 436-41.

24- Ekbom A, Helmick C, Zack M, et al.: The epidemiology of inflammatory bowel disease: a large, population-based study in Sweden. Gastroenterology 1991, 100:350-358

25- Mahmud N, Weir DG. The urban diet and Crohn's disease: is there a relationship? Eur J Gastroenterol Hepatol. 2001; 13:93-95.

26- Sonnenberg A: Occupational distribution of inflammatory bowel disease among German employees. Gut 1990, 31:1037-1040.

27- Elliott DE, Summers RW, Einstock JV. Helminths and the modulation of mucosal inflammation. Curr Opin Gastroenterol. 2005; 21:51-58.

28- Sartor RB. Review article: Role of the enteric microflora in the pathogenesis of intestinal inflammation and arthritis. Aliment Pharmacol Ther 1997; 11(Suppl.3): 17.

29- Sawczenko, A. and Sandhu BK. Presenting features of inflammatory bowel disease in great Britain and Ireland. Arch Dis Child. 2003; 88: 995-1000.

30- IBD Working Group of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). Inflammatory Bowel Disease in Children and Adolescents: Recommendations for Diagnosis-The Porto Criteria . J Pediatr Gastroenterol Nutr 2005;41:1-7