ORIGINAL ARTICLE

Clinical Presentations of Inflammatory Bowel Disease (I.B.D.) Among Children at King Hussein Medical Center (K.H.M.C.) in Amman/Jordan

ABDALLAH M. GHANMA*, RIHAB A. GHANMA**, RUWAIDA I. HIJAZEEN***

ABSTRACT

Objectives: To describe the clinical presentations of I.B.D. in the Jordanian pediatric age group at K.H.M.C.

Methods: Specially designed Medical Record abstract forms were filled with data collected from 36 patients presented to the Pediatric Gastroenterology Clinic, between August 2005 and September 2011 at KHMC-Amman/Jordan. They were all diagnosed to have I.B.D (Crohn's disease or ulcerative colitis). Full detailed medical history, proper clinical examination, laboratory tests and histopathologic results were collected for all these patients. All underwent upper endoscopy and colonoscopy, in addition to barium studies, thrombophilia screen and DEXA scan.

Results: A total of 36 patients were diagnosed to have I.B.D..The age range was between 12 months and 14 years. The mean age was 8 years. The male to female ratio was 0.8:1 (45% were males). Ulcerative colitis was found to be more common in our study (51.6%). The most presenting symptoms were abdominal pain, weight loss and bloody diarrhea, respectively. On the other hand, the most common clinical finding was delayed growth parameters. Delayed bone age and osteoporosis were strikingly high in our study, and colonoscopic positive findings were found in 32 patients (88%).

Conclusion: The Inflammatory bowel disease (I.B.D.) usually considered uncommon in young children in our country in now being described increasingly in this age group. A female predominance was notices with abdominal pain, weight loss and bloody diarrhea being the most common presenting symptoms. The most common clinical extra-intestinal finding was delayed growth..

Key words: Inflammatory Bowel Disease, Crohn's, Ulcerative Colitis, Children.

INTRODUCTION

The inflammatory bowel disease is an immune medicated bowel injury, triggered by environmental factors, in a genetically predisposed individual[1].

Crohn's disease (C.D.) is a chronic inflammatory disease that can affect any part of bowel from to mouth and anus. The most common sites are terminal ileum, ileocolon and colon. The typical pathological features are transmural inflammation and granuloma formation which may be patchy[2] .

Ulcerative colitis (U.C.) is an inflammatory disease limited to the colonic and rectal mucosa. The characteristic histology is mucosal and submucosal inflammation with goblet cell depletion, cryptitis, and crypt abscesses but no granulomas. The inflammatory change is usually diffuse rather than patchy[2]. The disease is becoming significantly more and more common in Jordanian pediatric population.

The exact etiology of I.B.D. remains unclear, although many risk factors were studied including family history, diet, appendectomy, improved living conditions and "Hygiene Hypothesis", drugs, smoking and others[3].

The term indeterminate colitis, describes cases of I.B.D. almost always with acute or severe disease requiring urgent or emergent colectomy (fulminant colitis) in which pathologic features are ambiguous and do not permit precise separation of C.D. from U.C. On the other hand, distributional features, gross appearance, and histologic characteristics of typical cases of C.D. and U. C. have been well described.

I.B.D. appears to be multi factorial in origin and the well documented increase in the incidence and prevalence of the disease is part of the worldwide emergence of chronic autoimmune and inflammatory diseases, a phenomenon closely related to social and economic development. The most surprising finding in international studies was that the vast majority of the new gene discoveries were common to both C.D. and U.C., further reinforcing our belief that both disease entities stem from same pathogenesis but have differing clinical spectra[3]

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*Jordanian Board in Pediatrics- Pediatric Gastroenterologist Senior Specialist at KHMC.

**Jordanian board in Ophthalmology- Senior Specialist at KHMC.

***Senior consultant in Gastro-Enterology and Hepatology at KHMC.

Correspondence to Abdallah M. Ghanma

Finally, many foods have been implicated in theories about etiology of I.B.D. and for the treatment of C.D. in children, however, enteral feeding with a semi-elemental diet seems to be effective in inducing and maintaining remission, such as polyunsaturated fatty acids, butyrate, glutamine and cytokines such as transforming growth factor –beta[4,5].

We present our experience over the last six years at our pediatric gastroenterology clinic at KHMC to report clinical findings of I.B.D in our Jordanian pediatric population,and to compare it with regional and international studies.

METHODS

A specially designed Medical Record abstract form was used to collect the relevant data. Full detailed medical history, proper clinical examination, laboratory and histopathologic investigations were performed for 36 patients in the period between January 2006 and September 2011 at KHMC.

Laboratory investigations included: full blood count, liver and kidney function tests, Erythrocyte sedimentation rate, C-reactive protein, P.ANCA and ASCA, Billirubin (total and direct), Prothrombin time(PT), Partial Thromboplastin Time(PTT), International Normalized Ratio (INR),Total protein and Albumin, Stool analysis and culture, Urine analysis and culture, Thrombophilia screen, in addition to bone age, barium studies in particular cases, Ophthalmologic consultation was performed for all our patients, and finally Colonoscopy and Upper endoscopy. Simple descriptive statistics (frequency and percentage) was used to describe the study variables.

RESULTS

Thirty Six patients were diagnosed to have I.B.D with age range between 12 month and 14 year, with a mean age of 8 years, out of which 16 patients (45%) were males and 20 females (55%).

The most common presenting symptoms were shown in (table 1): abdominal pain among 26 patients (72%),weight loss in 21 patients (58%), bloody diarrhea in 20 patients (55%),non-bloody diarrhea in 17 patients (47%), pallor in 10 patients (27%), low grade fever in 10 patients (27%), and arthralgia in 7 patients(19%).on the other hand, the least presenting symptoms were, skin rash in 3 patients (8%) oral ulcers in one patient and perianal abscess in another patient.

The Extra intestinal manifestations(that are not as common as in adults) were as follows :delayed growth parameters in 16 patients (44%), osteoporosis in 12 patients (33%), anemia in 12 patients (33%), osteopenia in 9 patients(25%), hepatomegaly in 5 patients(13%),oral aphtous ulcerations in 3 patients(8%),skin findings in 3 patients (8%), and the least were uveitis, and renal stones each found in one of our patients(2.7%).

The most significant Laboratory Findings presented in (table 2) were: Thrombocytosis in 29 patients (80%), high erythrocyte sedimentation rate (ESR) in 23 patients (63%), positive stool analysis findings in 22 patients (61%), leukocytosis in 13 patients (36%) followed by anemia in 12 patients (33%).

Each patient in our study underwent Colonoscopy and upper endoscopy; 15 were found to have C.D compared to 21 cases of U.C (one single case with isolated Proctitis, one case of U.C (a 12 year male) who was presented with hepatomegaly, jaundice, ascitis, coagulopathy, high liver transaminase, and high Gamma-glutamyltransferase, associated with bloody diarrhea, who underwent ERCP that showed primary sclerosing cholangitis.

Another patient who is a 12 year old females was referred to our tertiary medical center with right iliac fossa mass, non-bloody diarrhea, abdominal pain, pallor and weight loss, was diagnosed to have C.D. (localized ilieo-colonic segment) that was excised surgically and showed very good improvement over five years' follow up.

Three cases of C.D were found to have upper gastro-intestinal tract involvement (gastro-duodenal). DEXA scan was performed for all our patients and showed high percentage of osteoporosis (33%) and osteopenia (25%).

Thrombophilia screen results showed that three patients (8%) have heterozygous Factor V- Leiden mutation and one (3%) with homozygous mutation. Four patients (11%) with homozygous MTHFR mutation, in addition to three others with heterozygous MTHFR mutation, but no cerebral thrombo-embolic events documented.

Table I: Clinical Presentations among the study group (n=36)

Clinical presentation	**=n**	**%age**
Abdominal Pain	26	72
Weight Loss	21	58
Bloody Diarrhea	20	55
Non-bloody Diarrhea	17	47
Pallor	10	27
Fever	10	27
Arthralgia	7	19
Skin Rash	3	8
Red Eyes	1	2.7
Jaundice	1	2.7
Peri-anal Abscess	1	2.7

Delayed bone age was found in 15 patients (42%) and finally during Barium studies we found that two patients (5%) with C.D. were having ileal narrowing of small bowel, in addition to one patient with narrowing of the descending colon. Another patient with U.C. was found to have sigmoid stricture.

Table II: Laboratory findings among the study group (n=36)

Laboratory test	=n	%age
Thrombocytosis	29	80
High ESR	23	63
+ Stool Analysis	22	61
Leukocytosis	13	36
Positive CRP	12	33
Anemia	12	33
+Thrombophilia Screen	11	30
Low Total Protein	4	11
Low Albumin	4	11
+P.ANCA	4	11
Prolonged P.T.	2	5
+ASCA	2	5
High ALT	1	2
Thrombocytopenia	0	0

Table III: Comparative results between our study and Gargi Shikhhare Study[3] (n=36)

Extra intestinal manifestations	Gargi Shikhhare Study	Our study
Weight Loss	80%	44%
Osteoporosis	40%	33%
Joint Involvement	25%	27%
Skin Involvement	10-15%	8%
Oral Aphthous Ulcer	5-10%	8%
Primary Sclerosing Cholangitis	3.5%	2.7%
Eye Involvement	1%	2.7%
Thrombosis	3.1%	0%

DISCUSSION

Crohn's disease (C.D.) and Ulcerative Colitis (U.C.) are both chronic inflammatory diseases of gastro-intestinal tract with periods of remission and exacerbation. C.D. is characterized by transmural inflammation and can be found any where in the gastro-intestinal tract from month to anus, with patchy inflammation process.

U.C. is chronic inflammation involving only the mucosa of the colon, the inflammation being continuous, starting in the rectum and extending proximally to varying extent[3].

Approximately one fourth of cases of I.B.D. occur during childhood and children are more prone than their adult counterparts to have severe disease at presentation[6].

Our study included 36 patients with I.B.D. with male: female ratio of 0.8:1, compared to 1.5:1 in a study conducted at Atlanta/USA (Emory Children's Hospital)[3].

The mean age of presentation in our study was eight years and the range was 12 months to 14 years. In a Kuwaiti study 53% were females with a mean age of 11 years, 71% had C.D., 28% with U.C. and 1% with indeterminate colitis[7].

A Saudi study in 2011[8] showed a female involvement of 60% in U.C., and the commonest symptoms was abdominal pain found in 93% (where as in our study abdominal pain was found in 72% of patients, weight loss in 58%, bloody diarrhea in 55% and non-bloody diarrhea in 45% of patients).

U.C. was found in 21(58.3%) of our patients and C.D. was found in 15 patients (41.7%). In a study from Portugal they found that orogastric duodenoscopy and ileal intubation contributed to a definitive diagnosis of C.D[9]. In our study, we found one case with isolated Proctitis and another case of U.C. associated with primary sclerosing cholangitis. Three cases which were diagnosed to have C.D. were found to have upper gastro-intestinal tract involvement (gastro-duodenal). Two other cases of C.D. were primarily found to have eosinophilic colitis at presentation, before finding histopathologic diagnosis of C.D. later on.

A 12 year old female patient referred to our center with right iliac fossa mass, past chronic history of abdominal pain, diarrhea and weight loss was diagnosed to have C.D. (isolated segment) that have been resected surgically with very good follow up results over 5 years.

Delayed growth parameters, presented in 44% of our patients, is considered the most common extra intestinal manifestation of I.B.D.in children. In "Johathan Teitelbaum" study [10] in May-2011 this percentage is only 16%. Gargi. S and Subra-K conducted their study[3] in 2010 and reported that weight loss is a major problem in C.D. and many children have decreased appetite/intake and decreased nutritional absorption. Growth failure is a critical concern in childhood onset I.B.D., Growth impairment can be the only presenting sign of C.D. However, the etiology of growth failure is multifactorial; likely reasons are nutritional deficits, increased nutrient losses, mal absorption, increased metabolic demands and medications.

Goulet. O from "Hospital Necker-Enfants malades" – Paris[11], found that an increasing number of children enter disease before 8 years of age, and that chronic abdominal pain associated with growth failure and inflammatory syndrome with or without intestinal transit disorders, suggest C.D. and treatment with Anti-TNF frequently relapsing disease especially those with ano-perineal disease.

Inflammatory bowel disease is not a single organ disease but a systemic disease with many "extra-intestinal" features, between 25-30% of patients will exhibit some extra intestinal manifestations during their lifetimes[3].

Table 3 compares our results of extra-intestinal manifestations and those results of Gargi Shikhare study[3] in Atlanta/USA University School of Medicine.

In our study, there is one case (2%) with peri-anal abscess (C.D.) and five cases having hepatomegaly (13%), one patient with renal stone (2.7%), 12 patients with anemia (33%). M. Castro and his colleagues in Italy[12], found kidney stones in 0.3% of their patients with C.D., 0.3% sclerosing cholangitis and no patients with cerebral vascular disorders. In our study we didn't have any documented case of thrombotic events, despite high number of thrombophilic disorders (Factor V Leiden and MTHFR mutations).

A.R. Barclay and his colleagues[13], published an article in 2009, suggested that there is a recognized association between pediatric I.B.D. and mainly U.C. and thrombo-embolic events.

A study by Michael Kappelman[14] reported and alarmed about the association of pediatric I.B.D. with other immune-mediated diseases, like Rheumatoid arthritis, Hypothyroidism, diabetes and allergic condition.

Maria Pia Paroli[15] reported a case of uveitis that preceded C.D. by 8 years and Ferreira R. from Portugal[16] presented a case of C.D. diagnosed at the age of 11 years with severe osteoporosis at onset.

Other extra-intestinal manifestations include anemia which is seen even more common in children than the older I.B.D. patients[17], and that could be due to deficiency in Iron, folate or B12.

Osteopenia and osteoporosis are commonly seen in I.B.D., vitamin D deficiency contributes to diminish bone acquisition in childhood. Alon. D. Levin and his colleagues[18] in Australia found that one in five of these children with I.B.D. were 25 (OH) D deficient.

CONCLUSION

- The Inflammatory bowel disease (I.B.D.) usually considered uncommon in young children in our country in now being described increasingly in this age group.
- A female predominance was notices with abdominal pain, weight loss and bloody diarrhea being the most common presenting symptoms.
- The most common clinical extra-intestinal finding was delayed growth. Delayed bone age and osteoporosis were strikingly high in our study.

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