

**Incidence, Paris Classification, and Follow-up in a Nationwide
Incident Cohort of Pediatric Patients With Inflammatory Bowel Disease**

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Abstract

Objectives: Our aim was to evaluate the incidence, baseline disease characteristics, and disease location based on Paris Classification in pediatric inflammatory bowel disease (IBD) in the Hungarian nationwide inception cohort. In addition, one-year follow-up with therapy was analyzed also.

Methods: From January 1, 2007 to December 31, 2009, newly diagnosed pediatric patients with inflammatory bowel disease were prospectively registered. Twenty-seven pediatric gastroenterology centers participated in the data collection ensuring the data from the whole country. Newly diagnosed patients with IBD younger than 18 years were reported. Disease location was classified according to Paris Classification.

Results: A total of 420 patients were identified. The incidence rate of pediatric inflammatory bowel disease was $7.48/10^5$ (95% CI $6.34/10^5$ - $8.83/10^5$). The incidence for Crohn's disease (CD) was $4.72/10^5$ (95% CI 3.82 - 5.79), for ulcerative colitis (UC) $2.32/10^5$ (95% CI 1.71 - 3.09), and for IBD-unclassified (IBD-U) $0.45/10^5$ (95% CI 0.22 - 0.84). Most common location in CD was L3 (58.7%); typical upper gastrointestinal abnormalities (ulcer, erosion and aphthous lesion) were observed in 29.9%. Extensive colitis in UC patients (E4, proximal to hepatic flexure) was the most common disease phenotype (57%), while only 5% of children had proctitis. 18.6% of patients had ever severe disease (S1). Frequency of azathioprine administration at diagnosis was 29.5% in CD patients, and this rate increased to 54.6% (130/238) at one year follow-up. In UC only 3.3% received azathioprine initially, and this rate elevated to 22.5% (25/111). Use of corticosteroid decreased from 50% to 15.3% in patients with UC. Rate of bowel resection in CD patients during the first year of follow-up was 5%.

Conclusions: The incidence of pediatric inflammatory bowel disease in Hungary was among the higher range reported. This is the first large, nation-wide incident cohort analyzed according to Paris classification which is a useful tool to determine the characteristic pediatric CD phenotype.

Keywords: pediatric inflammatory bowel disease; Crohn's disease; ulcerative colitis; epidemiology; therapy

Introduction

Increasing numbers of pediatric and adolescent patients with Crohn's disease (CD) and ulcerative colitis (UC) have been reported. It is estimated that 15-25% of patients experience the onset of their symptoms under 20 years of age (1). In addition, reports have shown an increasing incidence of pediatric CD in the last decades (from 1.3-2.3 to 3.1-4.2/10⁵), whereas the incidence of UC has remained stable (range: 0.1-0.7/10⁵) (2,3). On the other hand, a recent study has shown that this phenomenon is not caused by a trend towards disease onset at a younger age, but this may rather be a consequence of the overall increasing incidence of chronic inflammatory bowel disease (IBD) (4).

Data from epidemiological pediatric IBD studies have shown special features unique to pediatric IBD, including disease location. With a specific focus on facilitating research an international group of IBD experts developed a new classification, the Paris Classification (5), which reflects currently available evidence and clinical practice of pediatric IBD. Important modifications include classifying age at diagnosis as A1a (0 to <10 years), A1b (10 to <17 years), A2 (17 to 40 years) and A3 (>40 years). Furthermore, upper GI (gastrointestinal) involvement proximal to ligament of Treitz (L4a) has been distinguished from upper GI involvement distal to ligament of Treitz (L4b). The new criteria system allows for classifying both stenosing and penetrating disease in the same patient (B2B3), and denoting the presence of growth failure in the patient at any time as G1 versus G0. In ulcerative colitis E4 indicates extent of the disease proximal to the hepatic flexure, and S1 designates ever severe ulcerative colitis during disease course.

Data on clinical course of pediatric IBD is scarce. There are only few population-based, short-term follow-up studies that involved medical and surgical management (6,7,8,9). Eleven to 44% of CD patients had undergone intestinal resection and total colectomy rate was 17.6% to 24% of children with UC (7,9). Of note, the prevalence of AZA use was as high as 25% at the end of the one-year follow-up. Moreover, an increasing use of immunomodulators and decreasing 1-year surgery rates in pediatric patients with IBD were observed in a 12 year-prospective population-based cohort study from Eastern Denmark 2007-2009 (10).

Despite the increasing number of epidemiological studies conducted in pediatric IBD, there are only few reports available from Eastern Europe, and to our knowledge no nationwide study investigated the early disease course. Therefore, our aim was to determine the incidence of pediatric IBD in Hungary in a prospective nationwide epidemiological study and to evaluate disease location according to Paris Classification.

Materials and Methods

On behalf of the Hungarian Pediatric Gastroenterology Society, a prospective registry of pediatric inflammatory bowel disease was launched on the 1st of January, 2007. Cooperation of 27 institutes has ensured the coverage of the whole country (HUPIR, Hungarian Pediatric IBD Registry). The participating institutes include all 4 academic (university) centers in Hungary, 17 tertiary hospitals, where pediatric gastroenterology is present, 4 secondary hospitals with pediatric gastroenterologists, and 2 pediatric gastroenterology outpatient offices. Private pediatric gastroenterology offices with endoscopy are not available in Hungary. Furthermore, coordinators are in contact with the main adult IBD centers to find adolescents diagnosed in adult centers. We contacted regularly the centers via email or phone calls (every months). The coordinators contacted the gastroenterologist if there had been any discrepancies in the survey (e.g. confirm the proper diagnosis of IBD; discuss the discrepancies between macroscopic and microscopic endoscopic findings etc.).

Questionnaires are filled out by gastroenterologists who made the IBD diagnosis. Newly diagnosed IBD patients younger than 18 years are reported. Exclusion criteria were: age at diagnosis older than 18 years, missing information on ileocolonoscopy and ileocolonic histology, and a diagnostic workup without endoscopic, histologic, and radiologic abnormalities. We contacted regularly the centers via email or phone calls (every month). The questionnaires are collected via email and original data were validated by the KEM and GV. The coordinator contacts the gastroenterologist if there is any discrepancies in the survey (e.g. confirm the proper diagnosis of IBD; discuss the discrepancies between macroscopic and microscopic endoscopic findings etc.). If data had been still lacking (no time to fulfill the questionnaire), we visited the centers and personally collected data from medical records. We also organized personal meetings to discuss difficult cases, mostly IBD-U patients.

We analyzed the data of patients recorded from the 1st of January 2007 to 31st of December 2009 (36 months). Age, gender, weight, height, presenting symptoms, concomitant diseases, extraintestinal manifestations (EIM), familiarity (first-degree) and complications were recorded. Furthermore, characteristics of diagnostic procedures including endoscopy, radiology, histology, surgical interventions, and were documented. The survey obtained the data anonymously.

The diagnosis of IBD was based on the Porto criteria, though, EGD and SBFT were not always performed despite the recommendation (11). Every child was re-evaluated 12 months

following the diagnosis. Physicians had to confirm the diagnosis and report the applied therapy, as well as surgical interventions at one-year follow-up.

Location and phenotype of disease were based on the Paris classification criteria (5). The site of the disease was evaluated only for those patients who underwent a complete bowel investigation (colonoscopy and esophagogastroduodenoscopy and/or small and large bowel were visualized for CD; large bowel was visualized up to the cecum for UC).

The therapeutic strategy in pediatric IBD in Hungary was based on international guidelines. Available therapies at diagnosis for induction of remission include corticosteroids, exclusive enteral nutrition, sulfasalazine or mesalazine, antibiotics and for maintenance azathioprine. Calcineurin inhibitors or methotrexate are used as a second-line immunosuppressive therapies. Infliximab has been available for children with CD in Hungary since 2007. It is used for both induction and maintenance (PCDAI>30, despite immunosuppression therapy for minimum 3 months). Indications for surgery included intractable disease, perianal disease, and complications of intestinal disease, such as abscess, stricture, intestinal obstruction, and intraabdominal fistulas.

The age- and gender-specific demographical data for calculating incidence were obtained from the Hungarian Central Statistical Office. The population, a total of 10.04 million, is predominantly white in Hungary. In 2007, 1.8 million of the inhabitants were <18 years old. Height, weight and BMI (body mass index) results were converted into standard deviation z scores using nomogram of the Hungarian Longitudinal Survey of Children's Growth. Impaired growth was defined as z score lower than -2.

The study was approved by the National Ethical Committee.

Statistics

Normality of the data was tested by Kolmogorov-Smirnov tests. Data are expressed mean (\pm SD) and for statistical analyses parametric tests were used. Univariate comparisons were among different subgroups (type of diagnosis, genders, extraintestinal manifestation, familiarity, initial therapy) with regard to disease phenotype, anthropometrical data. We used Fisher's exact tests or χ^2 tests to compare binominal variables, while t-test with separate variance estimates was used to compare continuous variables. To assess the correlation of two parameters in case of dichotomous and continuous outcomes, logistic and linear regression models were used, respectively. Kaplan–Meier survival curves were plotted to analyze need for surgery. A $p < 0.05$ was considered as significant. Statistical analyses were performed using the SPSS® statistical

package, version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Kaplan-Meier analysis was calculated by StatsDirect, version 2,7,8.

Results

Incidence of newly diagnosed pediatric IBD in Hungary

A total of 420 children with IBD were diagnosed between January 1, 2007 and December 31, 2009 in Hungary. Twice as many CD cases were registered as UC cases; CD, 265 patients (63%), UC, 130 patients (31%); and 25 patients (6%) inflammatory bowel disease type unclassified (IBD-U). The clinical characteristics of patients are presented in **Table 1**.

The overall incidence of IBD was $7.48/10^5$ per year (95% CI 6.34-8.83) in children <18 years. The incidence of CD was $4.72/10^5$ per year (95% CI 3.82-5.79), in UC, $2.32/10^5$ (95% CI 1.71-3.09), and in IBD-U, $0.45/10^5$ per year (95% CI 0.22-0.84). There was no significant difference in incidence rate in the three following years (data not shown).

A male predominance was observed in all patients with CD (male:female ratio 1.43:1), in contrast we found a slight female predominance in UC (1:1.15) (**Table 1**). Mean age was 12.9 ± 3.47 years for all IBD patients; 12.7 ± 3.51 years in UC, 13.2 ± 3.54 years in CD, and 12.7 ± 4.28 years in IBD-U (**Table 1**). **Figure 1** shows the age-specific incidence of IBD.

Clinical presentation at diagnosis

Anthropometry

Height z score lower than -2SD was reported in 6.5% of patients with CD while only in 0.8% of children with UC. Mean z score of BMI was significantly lower in CD than in UC (-0.64 vs. -0.26, $p=0.005$). Growth retardation in UC was less severe by increasing age ($r=-0.296$, $p=0.013$). Gender distribution and normal growth were comparable in CD and UC.

There was no association between family history, gender, location and growth failure.

Paris Classification

Most CD patients belonged to the age-group A1b ($n=197$, 74.3%). Thirteen percent of the patients (33/247) showed L1 (involvement of terminal ileum and/or cecum) location (**Table 2**). Isolated colonic disease (L2) was seen in 27.5% ($n=68$) of children with CD, and ileocolonic disease (L3) occurred in 58.7% ($n=145$) of CD patients.

Esophagogastroduodenoscopy was performed in 184 (68%) of pediatric CD patients. Upper GI was based on macroscopic lesions (erosion, ulcer, aphthous lesion) or on radiological

findings (MRI/CT/SBFT). Upper GI abnormality was found in 74 (29.9%) of all children with CD, and there was only one patient of 247 (0.4%) with isolated upper GI disease. Esophagogastroduodenal involvement (L4a) was present in 30.4% (n= 56) of pediatric CD, while L4b (jejunal/proximal ileal) disease occurred in 13.6% (n=25) of children.

Most CD patients had inflammatory disease at diagnosis (B1+B1p 84.4%), while 12.1% CD patients had stricturing disease (B2), 2.3% had fistulizing disease (B3), and 1.2% belonged to B2/B3 phenotype. Frequency of perianal disease (abscess, fistula) was 14.5% (37/247). There was no significant correlation between gender, phenotype, familiarity, and location.

Fifty-seven percent of UC patients had disease location E4, and 13 of 121 children have ever had severe disease (S1) at diagnosis (**Table 3**). Disease location did not differ neither by age at diagnosis nor by sex. Familiarity, anthropometrical parameters did not show any association with location either in CD or in UC.

Extraintestinal manifestation

EIMs were present in 10.9% of IBD patients at the time of the diagnosis (**Table 1**). It was more common in patients with CD than in children with UC (12.9% vs. 7%), though the difference was not statistically significant. The most common EIM was joint involvement (42.5%), followed by cutaneous manifestations (31.9%). Multiple EIM was observed in 10.6% of patients with EIM. There were no associations between gender, age, family history and EIM.

Therapy at diagnosis and after one year follow-up

Medical therapy

Onehundredseventy-seven CD patients (177/259, 68.3%) were treated with systemic corticosteroid as initial therapy (**Table 4**). 19.3% (46/238) of patients received corticosteroid at one-year follow-up. Azathioprine was started directly after diagnosis in 32.8% (85/259) of children with CD (42.5% within 3 months after diagnosis), and in 54.6% (130/238) at one-year follow-up. Infliximab was administered in 14% (33/238) of CD patients after one year of diagnosis. Exclusive enteral nutrition was applied in 6 CD patients.

In UC, the rate of corticosteroid use was 50% (62/124) at diagnosis, and it decreased to 15.3% (17/111) at one-year follow-up. Immunomodulator as an initial therapy was reported in only four patients (3.2%, 4/124) and 22.5% (25/111) received azathioprine after one year. Infliximab was not available in pediatric UC during this period.

Surgery

In CD, the need for surgery for any indication was 11.3% (27/238) within one year from diagnosis. Surgical intervention was performed due to perianal abscess in ten cases, three fistulectomies occurred, and appendectomy related to diagnosis happened in two cases.

Cumulative incidence of intestinal resection (small bowel resection or/with partial colectomy) was 5.04% (12/238) at one year. Intestinal resection within the first 3 months after diagnosis was performed in seven cases. One patient with IBD-U (1/19) had an operation due to perianal abscess. There was no need for surgical intervention in 111 patients with UC during the first year of the disease course.

Discussion

The present study is the first prospective nationwide cohort - based on Paris Classification - reporting on the incidence and management in the first year after the diagnosis in pediatric IBD.

The incidence rate ($7.5/10^5$ per year) of pediatric IBD in Hungary is comparable to that reported from high incidence areas (Wisconsin (12), Ontario (13)) within the same age- group (under 18 years) (**Figure 2**). Increasing incidence rates were reported in IBD in the last decades in Western Europe in both children and adults (12,14,15). The same trend was reported from Eastern European adult studies; however, data on pediatric incidence is limited. According to a population-based inception cohort from Veszprem province in Hungary the incidence in adult patients has been rising steadily in the last 25 years (incidence 1977-2001: UC: from 1.66 to $11.01/10^5$ per year, in CD from 0.41 to $4.68/10^5$ per year) (16). Even higher incidence rates were reported between 2002-2006 (17), similarly to those observed in high incidence Western European and Nordic countries.

Previous studies have suggested a difference in location between pediatric and adult onset IBD patients, since pediatric patients have more frequently extensive small- and large bowel disease; while the prevalence of limited ileal disease is lower (2.65% vs. 31.5%) (18,19), and panenteric disease is more common in children (20). Disease extension in CD (L1, L2, L3) in the present study was comparable to disease location in other studies (21,22). Another important feature of pediatric CD is the frequent upper GI involvement (30-70%) (21,23). The wide range of upper GI abnormality may be explained by the different definition of upper GI disease (any abnormalities or specific abnormalities: erosions, aphthous lesions, ulcers at endoscopy) in some reports. Diagnostic yield of upper endoscopy was 9% as it was described in details in our recent paper (24).

Paris Classification was applied in the report of Eurokids Registry (22). Location in CD and UC were comparable to the results of the present study. However, isolated upper GI disease was less frequent in our cohort. This discrepancy is probably due to the different population of the two studies. Eurokids registry is not a population-based cohort, but a selection of centers with special interest in IBD, meanwhile the HUPIR is a population-based incident cohort involving less severe cases. This phenomenon emphasize the importance of nation-wide registeries, that enrolles all pediatriac patients with IBD including less severe cases also.

In addition, isolated colonic disease was significantly more often in A1a age- group than in A1b in Eurokids Registry (22). A similar trend was found in the Hungarian cohort, though the difference was not significant. In this population we could not describe any significant difference in the subgroups of Paris Classification. The reason for that is probably the small sample size of the subgroups, however tendencies were similar to other studies (22).

Disease behavior has shown to progress during the disease course. Penetrating/stricturing phenotype and perianal disease are associated with more aggressive disease course and increased risk of surgery. Approximately, one third of newly diagnosed adults presented with complicated CD (17). In contrast, the majority of pediatriac IBD patients had inflammatory behavior in a previous study (91.25%) (20,22), in concordance with figures in the present study (85.3%). The rate of perianal disease was comparable with earlier studies (16.9% vs. 14.9%) (22,25).

Need for surgery is often regarded as the marker of disease severity. Only few pediatriac studies report the incidence of surgery after one year of diagnosis. The surgical rate (5.04%) in our cohort is comparable with the finding of the Pediatriac Consortium (6%) (26). It should be noted, this is the first nationwide pediatriac IBD study where incidence of surgery after one year is shown.

Colectomy among patients with UC was not detected. Similarly, Jakobsen et al described no need for surgical intervention in children with UC within the first 2 years after diagnosis (27). In contrast, the probability of colectomy in UC was 8% at 1 year, 11% at 2 years, and 20% at five years in an earlier study of Gowers-Rousseau et al (9).

Cumulative probability of surgery after one year in adult CD patients was 10-19% in recent reports (17,28). Reduction in surgery rates was reported in population-based adult studies in the last 20 years, which is probably due to increasing use of immunomodulation (10). Cumulative incidence of surgery during the first year was 15-35% in studies before the era of immunomodulators (29,30). The role of immunomodulators in the reduced need for surgery during the first year is questionable. In a population-based pediatriac cohort (1962-1987), reported by Langholz et al, mean yearly operation rate was 13%. In a population-based cohort of children

with IBD enrolled between 1984 and 1995 in Sweden, 38 of 639 patients (5.9%) were operated within 1 year (31). Interestingly, surgical rates during the first year after diagnosis in pediatric population are lower than in adults both in recent and earlier studies. The slight decrease (from 13% to 4.4-7%) in operation rate in pediatric population in the last decades may be explained as a consequence of increased use of azathioprine also (20,21).

Administration of 5-ASA is high in this CD cohort, however, this phenomenon is not restricted to our registry. Initial use of 5-ASA was 95% in a pediatric CD cohort collected between 1998-2009 (32). In addition, in a Finnish study 96% of 97 pediatric CD patients still used 5-ASA during the first year after diagnosis of CD (33).

Although we applied a nationwide approach, the study has some limitations. A relatively large proportion of the CD patients (62/265) did not have small bowel investigations (CT, MRI, SBFT) or EGD, thus upper GI location may be underestimated. The decrease in the incidence in the 16-18 year-olds is virtual and associated with the fact that adolescents more frequently tend to receive medical care from adult gastroenterologists (40). As a result the incidence in older age-groups is probably underestimated.

In summary, the data of our study are remarkable since this is a nationwide incident cohort; participants are not only from a few tertiary centers. Important observations of pediatric IBD based on the Hungarian Pediatric IBD Registry include (1) incidence of pediatric IBD is comparable in Eastern European countries to Western countries, (2) after one year of follow-up surgical rate in pediatric patients with CD is 5%, (3) a large population-based cohort has been analyzed according to Paris Classification which is a useful tool to determine the characteristic pediatric CD phenotype.

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Figure Legends

Figure 1 Incidence (/10⁵) of pediatric patients with Crohn's disease, ulcerative colitis and inflammatory bowel disease type of unclassified by age-groups (2007-2009).

Figure 2 Incidence of pediatric inflammatory bowel disease (/10⁵) in different geographic area.

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Figure 1 Incidence (/10⁵) of pediatric patients with Crohn's disease, ulcerative colitis and inflammatory bowel disease type of unclassified by age-groups (2007-2009).

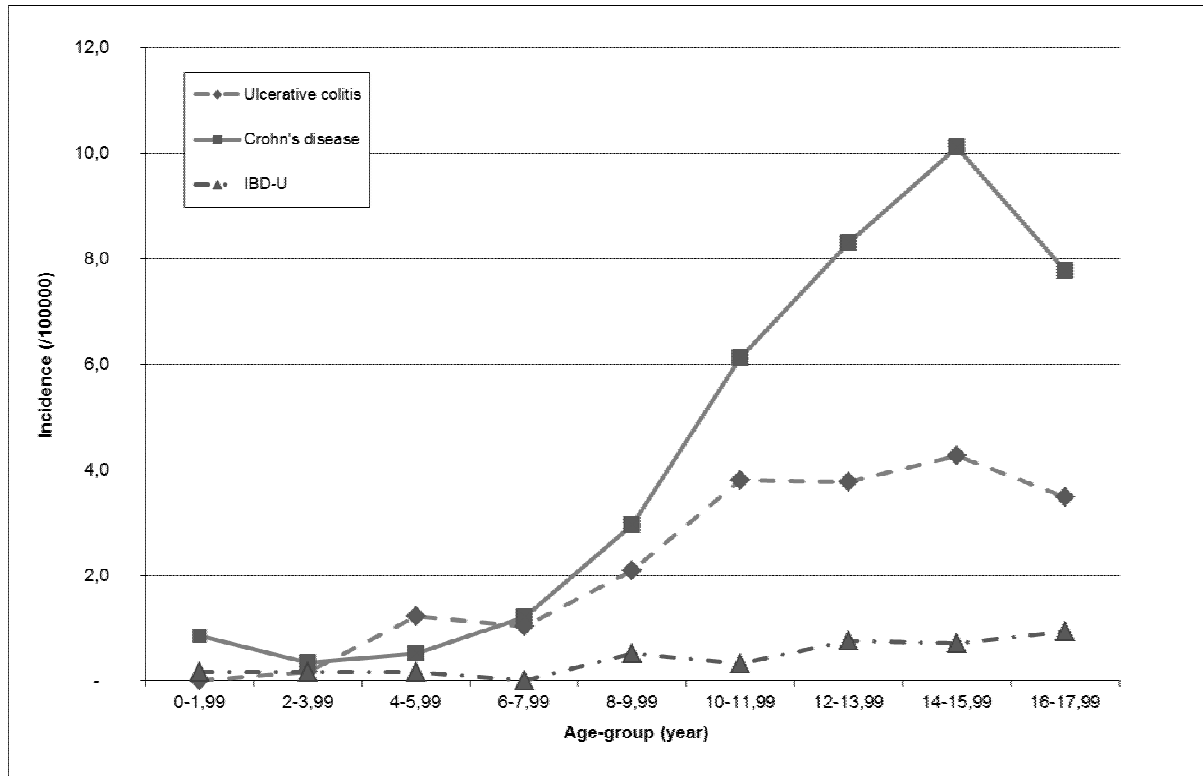


Figure 2 Incidence of pediatric inflammatory bowel disease (/10⁵) in different geographic area.

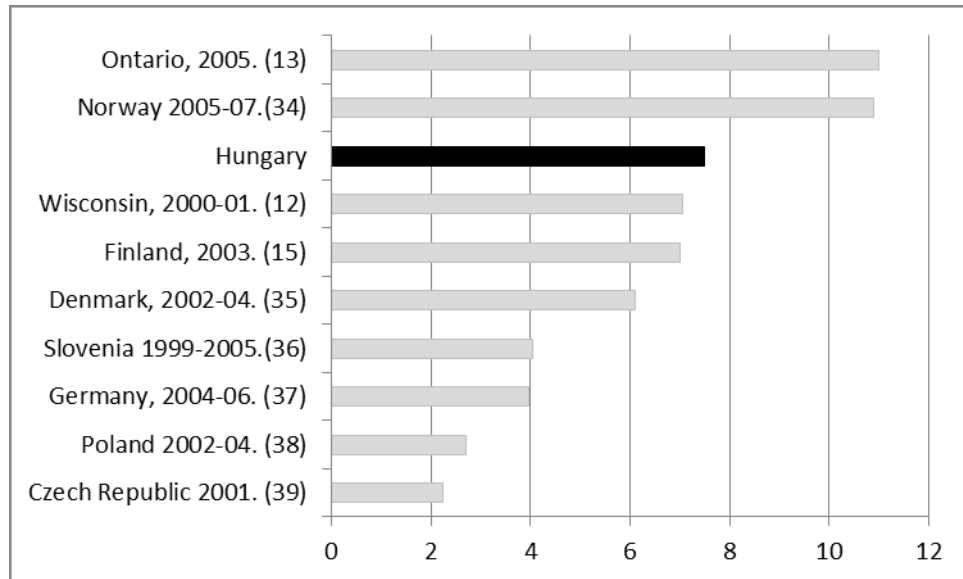


Table 1 Demographic characteristics of pediatric patients with inflammatory bowel disease diagnosed 2007-2009 in Hungarian Pediatric IBD Registry at diagnosis

^a IBD, inflammatory bowel disease

^b IBD-U, inflammatory bowel disease type of unclassified

| | All IBD ^a | Ulcerative colitis | Crohn's disease | IBD-U ^b |
|---------------------------------------|----------------------|--------------------|-----------------|--------------------|
| Number of patients (%) | 420 | 130 (31.0%) | 265 (63.1%) | 25 (6.0%) |
| Gender | | | | |
| Male | 227 (54.0%) | 60 (46.2%) | 156 (58.9%) | 11 (44%) |
| Female | 193 (46.0%) | 70 (53.8%) | 109 (41.1%) | 14 (56%) |
| Male:Female | 1.18:1 | 1:1.15 | 1.43:1 | 1:1.27 |
| Age | | | | |
| Mean | 12.9 | 12.7 (±3.51) | 13.2 (±3.54) | 12.7 |
| (range, year) | (±3.47) | | | (±4.28) |
| Familial disease | 41 (10.6%) | 12 (10.3%) | 25 (10.1%) | 4 (18.2%) |
| Extraintestinal manifestations | 44 (10.6%) | 9 (7%) | 34 (12.9%) | 1 (4%) |
| Arthropathy | 20 (42.5%) | 2 | 18 | 0 |
| Primary sclerosing cholangitis | 6 (1.4%) | 6 | 0 | 0 |
| Cutaneous | 15 (27.6%) | 1 | 14 | 0 |
| Ocular | 1 (2.1%) | 0 | 1 | 0 |

Table 2 Disease location and behavior in Crohn's disease according to Paris

Classification

*UGI, upper gastrointestinal involvement

A1a: 0-<10 years, A1b: 10-<17 years, A2:17-<40 years.

L1: distal 1/3 ileal disease ((±limited cecal disease). L2: colonic disease. L3: ileocolonic disease. L4: upper gastrointestinal tract disease. L4a: esophagogastrroduodenal disease proximal to ligament of Treitz. L4b: distal to ligament of Treitz.

B1: nonstricturing-nonpenetrating, B2: stricturing, B3: penetrating, B2B3: both penetrating and stricturing.

p: perianal disease modifier

G1 evidence of growth delay

| | All CD | A1a | A1b | A2 |
|-------------------------|----------------|---------------|----------------|---------------|
| | (n=247) | (n=27) | (n=197) | (n=23) |
| L1 | 33 (13.4%) | 3 | 26 | 4 |
| L1+L4 | 7 | 1 | 6 | |
| L2 | 68 (27.5%) | 9 | 55 | 4 |
| L2+L4 | 17 | 2 | 14 | 1 |
| L3 | 145 (58.7%) | 14 | 116 | 15 |
| L3+L4 | 49 | 3 | 40 | 6 |
| L4b only | 1 (0.4%) | 1 | 0 | 0 |
| B1 | 216 (84.4%) | 26 | 170 | 20 |
| B2 | 31 (12.1%) | 1 | 28 | 2 |
| B3 | 6 (2.3%) | 1 | 4 | 1 |
| B2B3 | 3 (1.2%) | - | 2 | 1 |
| Perianal disease | 37 (14.5%) | 1 | 34 | 2 |
| G1 (n=244) | 16 (6.6%) | 3 | 12 | 1 |

Table 3 Disease location in ulcerative colitis according to Paris Classification

E1, ulcerative colitis; E2, left-sided ulcerative colitis (distal to splenic flexure); E3, extensive (splenic flexure distally); E4, Pancolitis (proximal to hepatic flexure); S0, never severe; S1, severe at some stage.

| Ulcerative colitis | |
|---------------------------|------------|
| (n=121) | |
| E1 | 6 (5.0%) |
| E2 | 30 (24.8%) |
| E3 | 16 (13.2%) |
| E4 | 69 (57.0%) |
| S0 | 57 (81.4%) |
| S1 | 13 (18.6%) |

Table 4 Initial therapy in pediatric patients with inflammatory bowel disease at diagnosis.

*Number of cases with ulcerative colitis at diagnosis 123, number of cases at one year follow-up was 111.

** Number of cases with Crohn's disease at diagnosis was 258, number of cases at one year follow-up was 238.

| | Initial therapy | Therapy at one year follow-up |
|----------------------------------|------------------------|--------------------------------------|
| Ulcerative colitis* | | |
| 5-ASA (oral) | 110 (89.4%) | 90 (81%) |
| Corticosteroid (systemic) | 62 (50.4%) | 17 (15.3%) |
| Azathioprine | 4 (3.3%) | 25 (22.5%) |
| Antibiotics | 37 (30%) | 1 (0.9%) |
| Crohn's disease** | | |
| 5-ASA (oral) | 227 (87.9%) | 207 (86.9%) |
| Corticosteroid (systemic) | 177 (68.6%) | 46 (19.3%) |
| Azathioprine | 76 (29.5%) | 130 (54.6%) |
| Antibiotics | 93 (36%) | 13 (5.5%) |