Does inflammatory bowel disease have different characteristics according to stage of adolescence?

Kata Judit Szántó [iD], Tamás Balázs, Dóra Mihonné Schrempf, Klaudia Farkas* and Tamás Molnár* [iD]

Abstract

Background: There is a lack of data about demographic and treatment characteristics of adolescent patients with inflammatory bowel disease (IBD). The aim of this retrospective, epidemiological study was to evaluate characteristics and therapeutic features of Hungarian adolescents with IBD.

Methods: We analysed the social security databases of the National Health Insurance Fund. Adolescent patients with IBD for whom data from 2009 to 2016 were observable in the database were enrolled. Patients aged 14 to 17 years and 18 to 21 years were defined as middle and late adolescent patients.

Results: The incidences of IBD were 20.12 per 100,000 middle adolescent patients and 29.72 per 100,000 late adolescent patients. Admission to gastroenterology department was higher in both groups compared with admissions to surgery department. Mesalazine was used by a high proportion of Crohn's disease and ulcerative colitis patients. Rates of corticosteroid use were similar in both groups, with a tendency to decrease over time. The need for biologic agents was higher in the middle adolescent patients. The proportion of patients in the middle adolescent group who received anti-TNF therapy showed an increasing tendency.

Conclusion: Our data suggest differences in the treatment strategies of gastroenterologists for these age groups. The greater need of anti-TNF therapy among the middle adolescent group indicates that adolescent patients before the transition to adult care may have a more severe disease phenotype. We expect that a strategy of early, effective treatment will significantly ameliorate the subsequent disease course, which is manifested in adult care.

Keywords: adolescence, anti-tumour necrosis factor therapy, corticosteroid, inflammatory bowel disease, transition

Introduction

The incidence of paediatric inflammatory bowel disease (IBD), such as Crohn's disease (CD) and ulcerative colitis (UC), is increasing worldwide; up to 20% of cases of IBD are diagnosed before the age of 18. A recent analysis from Canada revealed that the incidence of IBD is 9.7 per 100,000 children and the prevalence is 38.2 per 100,000 per children.[1] Adolescence is a period of life with unique developmental and psychosocial changes, and is also characterised by the growing autonomy and psychological vulnerability of the patients. Adherence to medical regimens is often poor because of forgetting, lack of time, other activities (school, extracurricular activities) or cosmetic changes caused by medications; therefore, continuous guidance and support of these patients is crucial for improving adherence.[2,3] Moreover, behaviour and the course of chronic diseases in this population may differ from those in other age groups. The phenotype of childhood-onset IBD is more severe disease with a higher risk of complications, such as higher rates of hospital admission, greater use of immunosuppressants and greater need of biologic therapy.[4–6] In this study, we aimed to

Correspondence to:
Klaudia Farkas
Department of Medicine, University of Szeged, Kálvária sgt. 57, Szeged, 6725, Hungary
farkas.klaudia@gmail. com

Kata Judit Szántó
Tamás Molnár
Department of Medicine, University of Szeged, Szeged, Hungary

Tamás Balázs
Dóra Mihonné Schrempf
Healthware Consulting Ltd., Budapest, Hungary

*contributed equally as co-senior authors

evaluate the clinical phenotype and therapeutic features of the Hungarian adolescent population with IBD to fill the gaps in knowledge about clinical and treatment characteristics of such patients. We also aimed to assess whether patients with a chronic condition in this psychologically vulnerable age group have a more serious disease phenotype at the time of transition than do patients who have already transitioned to adult care.

Patients and methods

The data source for this retrospective observational analysis was the nationwide, longitudinal database of the National Health Insurance Fund of Hungary (NHIF). The database contains demographic information such as age, gender, date of birth/death and, most importantly, all reimbursed health care events in in/outpatient care, medications and imaging technology. Results of laboratory tests, examinations or operations are not directly available. For the purpose of the study, a historical database was made available in a time span between 1 January 2009 and 31 December 2016. Between this time period newly diagnosed CD and UC patients aged between 14–17 or 18–21 years were enrolled. Patients aged between 14–17 or 18–21 years and diagnosed before 1 January 2009 were also enrolled if the patients met the inclusion criteria.

CD and UC patient groups were defined by K50 and K51 International Classification of Diseases (ICD-10) codes. All patients were classified uniquely to one subtype of IBD by using the following algorithm:

If a patient had only one type of ICD-10 code (just K50 or just K51) during the whole follow-up time, then the patient was represented in that IBD subtype. If a patient had both types of ICD-10 codes, then the relevant registrations were analysed by the type of care (inpatient care/outpatient care/medical care/biological medical care). In order to categorise a patient in a given type of care into CD or UC, an 80% code incidence rate was demanded. After that, a patient was categorised into the CD or UC group, if the patient had at least one type of care category where the given ICD-10 code was dominant, and at the same time, the other code was not dominant in either care category.

Only those patients were who dispensed at least one biological therapy or had at least one surgery or received at least two relevant therapies by year were analysed in the study. Beside IBD subtype, patients were categorised into middle adolescent (age between 14 and 17) and late adolescent (age between 18 and 21) age groups, where the age was defined by the time of diagnosis (first relevant ICD-10 code registration).[7]

Extraintestinal manifestations were defined based on ICD-10 codes.

During the study the IBD subtypes and age groups were compared by the following endpoints: incidence and prevalence rate, frequency of extraintestinal manifestations (dermatologic, rheumatologic, hepatic and ocular), therapy usages [immunosuppressive and anti-tumour necrosis factor (anti-TNF; infliximab: IFX, adalimumab: ADA) therapies], hospital admissions (gastroenterology and surgical departments) and diagnostic methods (endoscopy and non-invasive diagnostic methods).

Age- and gender-standardised annual incidence and prevalence per 100,000 population were obtained by direct standardisation method using the European population between 2009 and 2016. Those patients who had the diagnosis after 31 December 2011 were considered as incident patients. In order to calculate the proportion of patients using or starting with a given therapy, only incident patients were analysed in the therapy usage part. Conditional elapsed time for the first medical therapy was calculated only for those patients who started with the given therapy. The proportions were compared by the Chi-squared test. The frequency of anti-TNF therapy usage, hospital admissions and diagnostic methods were also analysed by calendar year. After a graphical illustration of the proportions, if a tendency occurred on the figure then the proportion in 2009 and in 2016 were statistically compared using conservative Wald test. Due to the violation of independence (one patient may appear in multiple calendar years), the standard error of the difference of the two proportions was overestimated by the sum of the separately calculated standard errors of the rates. Data with value less than 10 cannot be published according to the NHIF regulation.

Ethical approval

The study was approved by the Hungarian Medical Research Council (ethical approval number:

8885-1/2019/EKU). The Ethics Committee has granted exemption from obtaining informed consent of the participants as this is an analysis of a retrospective databank of de-identified data.

Results

Incidence, prevalence and demographic data

With the above-mentioned criteria, we analysed data of 2520 patients from the period of 1 January 2009 to 31 December 2016; of those patients, 912 were middle adolescent patients (aged 14–17 years) and 1608 were late adolescent patients (aged 18–21 years). The incidence of IBD was 20.12 per 100,000 among middle adolescent patients (CD: 13.15 per 100,000 and UC: 6.96 per 100,000) and 29.72 per 100,000 among the late adolescent patients (CD: 16.27 per 100,000 and UC: 13.44 per 100,000). Of the incident middle and late adolescent patients 34.5% and 45.1% had a diagnosis of UC ($p = 0.001$). The prevalence of IBD was 144.11 per 100,000 middle adolescent patients (CD: 97.95 per 100,000 and UC: 46.15 per 100,000) and 233.57 per 100,000 late adolescent patients (CD: 140.76 per 100,000 and UC: 92.80 per 100,000). The proportion of prevalent UC patients was 32.6% and 41.6%, respectively ($p = 0.001$). The most common extraintestinal manifestations were dermatologic manifestation, followed by rheumatologic involvement. Detailed information about the extraintestinal manifestations is presented in Table 1.

Hospital admissions

In all, during the observational period, 40.4% of the middle adolescent patients and 14.4% of the late adolescent patients were hospitalised. Of those hospitalised, 87.7% of the middle and 68.5% of the late adolescent patients were admitted to the gastroenterology departments. The proportions of middle and late adolescent patients admitted to surgical departments were 18.5% and 37.5%, respectively. Hospital admissions to gastroenterology and surgery departments are presented in Table 2. Decreasing tendency was observed regarding admissions to gastroenterology departments in both groups (middle adolescent patients: $p = 0.12$; late adolescent patients: $p < 0.001$).

Use of endoscopy and non-invasive diagnostic methods

The proportion of patients underwent computed tomography (CT), magnetic resonance imaging (MRI) examinations and endoscopy is presented in Table 2. The number of CT examinations did not decrease significantly in the middle adolescent group. On the other hand, the number of MRI examinations did not reflect changes over the observational period in either group. The number of endoscopies decreased in the late adolescent group from 2009 to 2016 ($p < 0.001$).

Immunosuppressive and anti-TNF therapy

The proportion of patients and conditional median elapsed days to the first medical therapy after diagnosis was calculated among the incident patients. Detailed proportions of patients on each therapy and conditional median elapsed days are shown in Tables 3 and 4.

Mesalazine was the most frequently prescribed first medical therapy after the diagnosis of CD and UC. Of the middle and late adolescent patients, 62.8% and 73.4%, respectively, took mesalazine. Some 55.9% and 74.7% of the middle and late adolescent CD patients, respectively, received it as first medical therapy, and 76.6% and 71.8% of middle and late adolescent UC patients.

Sulphasalazine as first medical therapy for IBD was prescribed for 11.5% and 17.1% of the middle and late adolescent patients; 8.3% and 18% of the middle adolescent CD and UC patients, and 9.4% and 26.5% of the late adolescent CD and UC patients received sulphasalazine as first therapy.

Azathioprine was prescribed for 25.7% and 9.5% of the middle and late adolescent patients, mainly for CD patients.

The proportion of incident patients that received corticosteroid or first-line anti-TNF therapy at some point was calculated. Corticosteroids were used at least once by 69.4% of the middle adolescent patients and by 68.9% of the late adolescent patients. The proportion of patients that received corticosteroid therapy decreased significantly in both groups from 2009 to 2016 ($p < 0.001$; Figure 1). In all, 20% of the incident middle adolescent patients and

Table 1. Characteristics of the prevalent patients.

	Middle adolescent patients	Late adolescent patients	*p*-value
Number of patients	912	1608	
Prevalence (per 100,000 population)			
IBD	144.11	233.57	
CD	97.95	140.76	
UC	46.15	92.8	
Patients with UC (%)	297 (32.6%)	669 (41.6%)	0.001
Extraintestinal manifestations			
Dermatologic	178 (19.5%)	266 (16.5%)	0.067
Rheumatologic	119 (13%)	173 (10.8%)	0.097
Hepatic	25 (2.7%)	54 (3.4%)	0.46
Ocular involvement	NA	20 (1.2%)	–
Hospital admissions			
Gastroenterology or Surgical department	368 (40.4%)	232 (14.4%)	<0.001
Gastroenterology department	323 (87.7%)	159 (68.5%)	<0.001
Surgical department	68 (18.5%)	87 (37.5%)	<0.001
Diagnostic methods			
Computed tomography	47 (5.2%)	103 (6.4%)	0.234
Magnetic resonance imaging	94 (10.3%)	39 (2.4%)	<0.001
Endoscopy	254 (27.9%)	744 (46.3%)	<0.001

CD, Crohn's disease; IBD, inflammatory bowel disease; UC, ulcerative colitis

12.8% of the late adolescent patients received anti-TNF therapy at some point ($p = 0.002$). IFX was initiated in 54.9% of the middle adolescent patients and in 58.4% of the late adolescent patients as first-line anti-TNF therapy. Of the patients with CD, the proportion of middle adolescent patients receiving anti-TNF therapy (26.1%) was higher than that of the late adolescent patients (17%; $p = 0.006$).

Azathioprine and ADA combination therapy was prescribed in 53.7% of the incident middle adolescent patients and in 30.4% of the late adolescent patients ($p = 0.02$). Azathioprine and IFX combination therapy was prescribed in 64.6% and 56.4%, respectively ($p = 0.51$). The proportion of patients who received anti-TNF therapy showed an increasing tendency from 2009 to 2016 ($p = 0.06$, Figure 2).

Discussion

We conducted a population-based, retrospective survey of the social security databases of the NHIF to analyse baseline characteristics, treatment patterns, hospitalisation among adolescent patients with IBD in Hungary and to assess whether patients around the transition have a more severe disease phenotype and need early and more common immunosuppressive therapy.

The incidence of IBD is increasing among paediatric, adolescent and young adult populations.

The European Crohn's and Colitis Organisation Epidemiological Committee inception cohort study revealed that the overall age- and gender-adjusted annual incidence per 100,000 was 5.4 for CD and 8.2 for UC in Europe. The annual incidence of CD and UC combined in all Western European centres was shown to be twice as high as that in all Eastern European centres.[8] In a recent systematic study, researchers analysed the global trends of paediatric-onset IBD. The incidence of paediatric-onset IBD was 0.5–23 per 100,000; that for paediatric-onset CD was 0.1–13.9 per 100,000, and that for paediatric-onset UC, 0.3–15.0 per 100,000. Researchers in North America and Europe have reported the highest incidences of CD and UC.[9]

However, incidence rates within adolescent populations are not well known. According to our analysis, the incidence of IBD was 20.12 per 100,000 people in middle adolescence (13.15 with CD per 100,000 and 6.96 with UC per 100,000) and 29.72 per 100,000 people in late adolescence (16.27 with CD per 100,000 and 13.44 with UC per 100,000). Because the incidence and prevalence of IBD among the adult population in our region have also been reported to be outstandingly high, our findings are not surprising.[10] Also, the incidence and prevalence of CD were higher among the middle and late adolescent patients than those of UC.

The rising incidence of IBD has created challenges for health care services and for governmental budgets. Moreover, adolescence is the most vulnerable period in life, both physically and emotionally, which can lead to complications in the process of transition to adult care. Therefore, we call the period between the ages of 18 and 25 years 'emerging adulthood'.[11]

Adequate and effective therapy in adolescent patients with IBD is mandatory to prevent the development of complications, which occur as a consequence of the progressive nature of the disease. In this study, we analysed the proportions of patients who received the first conventional, immunosuppressive and anti-TNF therapy. Despite the known indications of aminosalicylates in IBD, mesalazine was used by both middle and late adolescent patients with CD and UC, usually as first-line therapy; this finding is similar to global data.[12] Thiopurines are generally recommended after corticosteroid therapy in cases of CD.

Table 2. Proportion of patients who underwent imaging examinations and hospital admissions.

	CT		MRI		Endoscopy		Admission to gastroenterology		Admission to surgery	
	Middle adolescent patients (%)	Late adolescent patients (%)	Middle adolescent patients (%)	Late adolescent patients (%)	Middle adolescent patients (%)	Late adolescent patients (%)	Middle adolescent patients (%)	Late adolescent patients (%)	Middle adolescent patients (%)	Late adolescent patients (%)
In all	5.2	6.4	10.3	2.4	27.9	46.3	87.7	68.5	18.5	37.5
2009	5.5	6.8	3.9	NA	15.5	31.5	10	10.6	6.7	4.9
2010	6.3	4.7	4.1	1.3	22.5	28.6	9.7	8.1	6.1	3.9
2011	3.8	4.3	5.4	2.0	17.3	25.0	7.6	8.9	6.6	5.3
2012	4.3	4.9	3.6	2.4	19.0	22.1	8.7	5.9	4.6	3.8
2013	5.0	4.1	5.6	2.9	18.5	22.5	9.6	3.9	6.7	4.6
2014	4.0	3.8	4.1	1.4	20.1	22.7	6.8	4.2	5.2	3.3
2015	3.2	3.1	4.4	1.9	17.3	20.7	5.8	4.1	3.8	3.1
2016	3.7	2.5	5.3	2.6	17.4	17.4	6.3	3	3.2	3.2
p	0.36	*0.002	0.45	0.13	0.55	*<0.001	0.12	*<0.001	0.07	0.19

Proportions of the first and last observed year were compared.
*p = 0.05.
CT, computed tomography; MRI, magnetic resonance imaging; NA, not available.

Table 3. Proportion of incident patients on different type of medical therapy.

	Middle adolescent patients	Late adolescent patients	*p*-value
Number of patients	409	698	
Incidence (per 100,000 population)			
IBD	20.12	29.72	
CD	13.15	16.27	
UC	6.96	13.44	
Patients with UC (%)	141 (34.5%)	315 (45.1%)	0.001
Therapy usage (%), and median elapsed days			
IS	382 (93.4%) 9 days	651 (93.3%) 3 days	1
Mesalazine	335 (81.9%) 10 days	592 (84.8%) 4 days	0.238
Sulphasalazine	73 (17.8%) 20 days	174 (24.9%) 7 days	0.008
Azathioprine	245 (59.9%) 60 days	289 (41.4%) 94 days	<0.001
Corticosteroid	284 (69.4%) 22 days	481 (68.9%) 13 days	0.908
Anti-TNF	82 (20%) 248 days	89 (12.8%) 263 days	0.002
Adalimumab	54 (13.2%) 481 days	56 (8.0%) 544 days	0.007
Infliximab	48 (11.7%) 238 days	55 (7.9%) 263 days	0.043
First therapy registration (%) and median elapsed days			
IS			
Mesalazine	240 (62.8%) 7 days	478 (73.4%) 2 days	<0.001
Sulphasalazine	44 (11.5%) 8 days	111 (17.1%) 2 days	0.021
Azathioprine	98 (25.7%) 14 days	62 (9.5%) 10 days	<0.001
Anti-TNF			
Adalimumab	37 (45.1%) 333 days	37 (41.6%) 338 days	0.754
Infliximab	45 (54.9%) 232 days	52 (58.4%) 253 days	0.754
Combination therapies			
Azathioprine + Adalimumab	29 (53.7%)	17 (30.4%)	0.02
Azathioprine + Infliximab	31 (64.6%)	31 (56.4%)	0.51
CD, Crohn's disease; IBD, inflammatory bowel disease; IS, immunosuppressive agents; UC, ulcerative colitis.			

Azathioprine was used as first therapy after the diagnosis of IBD mainly in CD patients; in the case of UC, the low number of patients (less than 10 patients) cannot be published according to the NHIF's regulation. Corticosteroid therapy is effective in inducing remission. Approximately two-thirds of both age groups in our study received at least one course of corticosteroid therapy during the observational period. However, the use of corticosteroids decreased in both groups, which

Table 4. Medical therapies of the incident UC and CD patients.

	CD			UC		
	Middle adolescent patients	**Late adolescent patients**	*p*-value	**Middle adolescent patients**	**Late adolescent patients**	*p*-value
Number of patients	268	383		141	315	
Therapy usage (%), and median elapsed days*						
IS	254 (94.8%) 12 days	360 (94%) 5 days	0.801	128 (90.8%) 4 days	291 (92.4%) 1 day	0.694
Mesalazine	218 (81.3%) 14 days	330 (86.2%) 6 days	0.121	117 (83.0%) 5 days	262 (83.2%) 3 days	1
Sulphasalazine	34 (12.7%) 29 days	54 (14.1%) 11 days	0.687	39 (27.7%) 16 days	120 (38.1%) 5 days	0.04
Azathioprine	197 (73.5%) 42 days	220 (57.4%) 79 days	<0.001	48 (34%) 158 days	69 (21.9%) 225 days	0.009
Corticosteroid	192 (71.6%) 28 days	302 (78.9%) 11 days	0.043	92 (65.2%) 16 days	179 (56.8%) 18 days	0.112
Anti-TNF	70 (26.1%) 248 days	65 (17%) 285 days	0.006	12 (8.5%) 220 days	24 (7.6%) 253 days	0.89
Adalimumab	48 (17.9%) 487 days	41 (10.7%) 541 days	0.012	6 (4.3%) 287 days	15 (4.8%) 607 days	1
Infliximab	38 (14.2%) 238 days	36 (9.4%) 284 days	0.078	10 (7.1%) 288 days	19 (6.0%) 256 days	0.825
First therapy registration (%) and median elapsed days						
IS						
Mesalazine	142 (55.9%) 11 days	269 (74.7%) 4 days	<0.001	98 (76.6%) 3 days	209 (71.8%) 1 day	0.373
Sulphasalazine	21 (8.3%) 10 days	34 (9.4%) 4 days	0.719	NA	NA	–
Azathioprine	91 (35.8%) 14 days	57 (15.8%) 13 days	<0.001	NA	NA	–
Anti-TNF						
Adalimumab	35 (50%) 344 days	30 (46.2%) 342 days	0.784	NA	NA	–
Infliximab	35 (50%) 232 days	35 (53.8%) 263 days	0.784	NA	NA	–

CD, Crohn's disease; IS, immunosuppressive agents; UC, ulcerative colitis.
*p = 0.05.

may reflect the wider access to and use of biologic therapy for adolescent patients, and also may reflect the successful induction of remission and the effective maintenance treatment with either immunosuppressive or biological therapy.

Anti-TNF therapy is reserved for patients who are corticosteroid dependent or whose disease is refractory to steroid or immunosuppressive therapy, as well as patients with penetrating CD. IFX and ADA are approved for paediatric-onset CD and UC in Hungary by individual fairness claim. We found that anti-TNF therapy was introduced significantly more frequently for the middle adolescent patients. These data correspond to those from the Inflammatory Bowel Disease Epidemiology Database of the University of Manitoba, which also documented that the use of biologic drugs was more common among patients who received diagnoses before the age of 18.[13] Paediatric-onset IBD may have a more aggressive course than adult-onset disease, and this probably drives the need for biologic therapy, as well as the desire to avoid the potential side effects of recurrent corticosteroid use and to avoid delay in growth or puberty.[14,15]

In Hungary the proportion of biologically treated patients is still low, but our results show that anti-TNF use is increasing. According to the data from the Inflammatory Bowel Disease Epidemiology
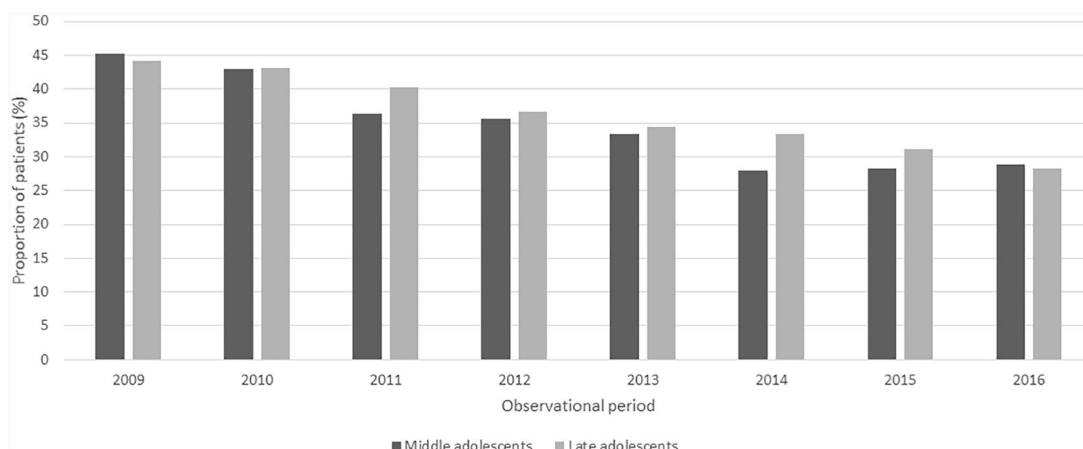
Figure 1. Proportion of patients who received corticosteroid therapy decreased ($p < 0.001$).
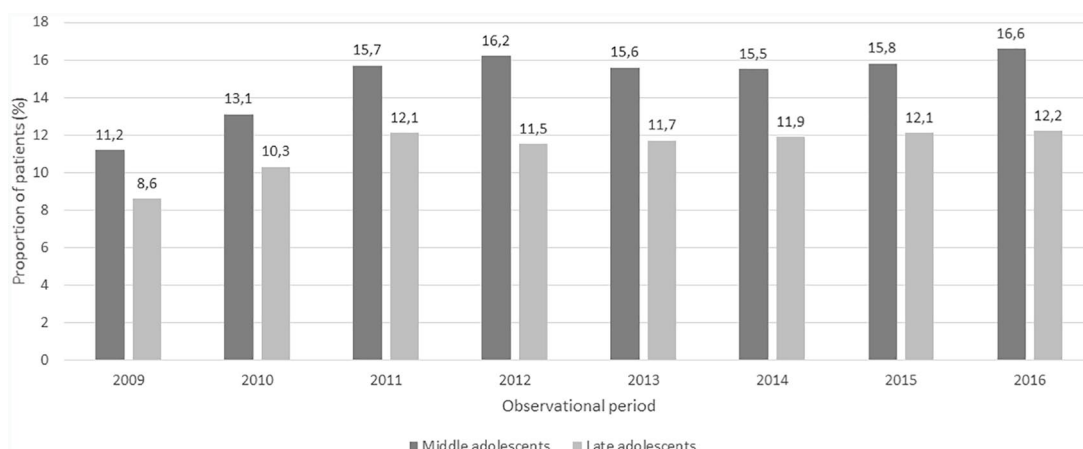

Figure 2. Proportion of patients who received anti-TNF therapy.

Database at the University of Manitoba, the cumulative prevalence of current or prior anti-TNF exposure in 2014 was 20.4% of patients with CD and 6.0% of patients with UC. In 2014 these values within 5 years of diagnosis were 23.4% of patients with CD and 7.8% of patients with UC.[13] In our analysis, a higher proportion of CD patients in both age groups received anti-TNF therapy compared with UC patients.

Decreasing hospitalisation rates were observed in both age groups, mainly among late adolescents; however, middle adolescent patients had a higher rate of admission to gastroenterology departments. This could be attributable to the fact that paediatric patients who undergo endoscopy under anaesthesia must receive inpatient care in Hungary. We did not reveal any statistically significant changes in admissions to surgery departments during the

observational period in either group. IBD at a young age has been shown to be a risk factor for radiation exposure.[16,17] The number of CT examinations decreased significantly among late adolescent patients; a slight decreasing tendency can be observed among middle adolescent patients. The number of MRI examinations was slightly increased among middle adolescent patients; however this did not reflect changes over the observational period. We assumed a decrease in endoscopies, resulting from the widespread use of faecal calprotectin, although it is not financially supported in Hungary. However, the number of endoscopies decreased significantly only in the late adolescent patient group.

Our study has some strengths and limitations that should be mentioned. The nationwide database used in this study was based on the sole insurance

fund in Hungary, which has almost full population coverage. Group selection was artificial so as to symbolise two adolescent age groups. With the inclusion criteria of patients' selection detailed in the Methods section, a certain number of IBD patients may not have been included in the analysis. A major limitation is the retrospective nature of the study. No data were available with regard to clinical outcomes, such as laboratory values, disease severity indices or patient-reported outcomes. Information about dose of conventional and biologic therapy and about switching of biologic therapy was limited. Despite these limitations, data were available from a huge number of adolescent patients with IBD, and we were able to obtain information about the epidemiological and treatment characteristics of these patients.

According to our data, physicians who take care of adolescent patients, in both paediatric and adult care, have a huge responsibility in the management of IBD. Our data suggest differences in the treatment strategies of gastroenterologists for this age group. We expect that a strategy of early effective treatment will significantly ameliorate the subsequent disease course, which is manifested in adult care.

Authors' contributions
Kata Judit Szántó has a role in data collection, analysis and interpretation of the data, drafted the manuscript and approved the final version of the manuscript.

Tamás Balázs conceptualised and designed the study, has a role in data collection, statistical analysis and interpretation of the data and drafted and revised the manuscript, approved the final version of the manuscript.

Dóra Mihonné Schrempf has a role in data collection, statistical analysis and interpretation of the data, approved the final version of the manuscript.

Klaudia Farkas conceptualised and designed the study, drafted and revised the manuscript, approved the final version of the manuscript.

Tamás Molnár conceptualised and designed the study, drafted and revised the manuscript, approved the final version of the manuscript.

Conflict of interest statement
The authors declare that there is no conflict of interest.

Disclaimers
The manuscript, including related data, tables and figures, has not been previously published, and the manuscript is not under consideration elsewhere.

ORCID iDs
Kata Judit Szántó https://orcid.org/0000-0003-0749-5061

Tamás Molnár https://orcid.org/0000-0002-4913-7599

References
1. Benchimol EI, Bernstein CN, Bitton A, *et al.* Trends in epidemiology of pediatric inflammatory bowel disease in Canada: distributed network analysis of multiple population-based provincial health administrative databases. *Am J Gastroenterol* 2017; 112: 1120–1134.

2. Greenley RN, Stephens M, Doughty A, *et al.* Barriers to adherence among adolescents with inflammatory bowel disease. *Inflamm Bowel Dis* 2010; 16: 36–41.

3. Ingerski LM, Baldassano RN, Denson LA, *et al.* Barriers to oral medication adherence for adolescents with inflammatory bowel disease. *J Pediatr Psychol* 2010; 35: 683–691.

4. Van Limbergen J, Russel RK, Drummond HE, *et al.* Definition of phenotypic characteristics of childhood-onset inflammatory bowel disease. *Gastroenterology* 2008; 135: 1144–1122.

5. Vernier-Massouille G, Balde M, Salleron J, *et al.* Natural history of pediatric Crohn's disease:

a population-based cohort study. *Gastroenterology* 2008; 135: 1106–1113.

6. Goodhand J, Dawson R, Hefferon M, *et al.* Inflammatory bowel disease in young people: the case for transitional clinics. *Inflamm Bowel Dis* 2010; 16: 947–952.

7. Allen B. Stages of adolescence. American Academy of Paediatrics, https://www.healthychildren.org/English/ages-stages/teen/Pages/Stages-of-Adolescence.aspx (2019, accessed 10 May 2020).

8. Burisch J, Pedersen N, Čuković-Čavka S, *et al.* East–West gradient in the incidence of inflammatory bowel disease in Europe: the ECCO-EpiCom inception cohort. *Gut* 2014; 63: 588–597.

9. Sýkora J, Pomahačová R, Kreslová M, *et al.* Current global trends in the incidence of pediatric-onset inflammatory bowel disease. *World J Gastroenterol* 2018; 24: 2741–2763.

10. Ng SC, Shi HY, Hamidi N, *et al.* Worldwide incidence and prevalence of inflammatory bowel disease in the 21st century: a systematic review of population-based studies. *Lancet* 2017; 390: 2769–2778.

11. Trivedi I and Keefer L. The emerging adult with inflammatory bowel disease: challenges and recommendations for the adult gastroenterologist. *Gastroent Res Pract* 2015; 2015: 260807.

12. Yu H, MacIsaac D, Wong JJ, *et al.* Market share and costs of biologic therapies for inflammatory bowel disease in the USA. *Aliment Pharmacol Ther* 2018; 47: 364–370.

13. Targownik LE, Tenakaroon A, Leung S, *et al.* Temporal trends in anti-TNF initiation among persons with IBD: a population based analysis. *Clin Gastroenterol and Hepatol* 2017; 15: 1061–1070.

14. Romberg-Camps MJ, Dagnelie PC, Kester AD, *et al.* Influence of phenotype at diagnosis and of other potential prognostic factors on the course of inflammatory bowel disease. *Am J Gastroenterol* 2009; 104: 371–383.

15. Beaugerie L, Seksik P, Nion-Larmurier I, *et al.* Predictors of Crohn's disease. *Gastroenterology* 2006; 130: 650–656.

16. Zakeri N and Pollok RC. Diagnostic imaging and radiation exposure in inflammatory bowel disease. *World J Gastroenterol* 2016; 22: 2165–2178.

17. Sauer CG. Radiation exposure in children with inflammatory bowel disease. *Curr Opin Pediatr* 2012; 24: 621–626.

Visit SAGE journals online
journals.sagepub.com/
home/tag

⑤SAGE journals