

Inflammatory bowel diseases at Vilnius University Hospital Santariškių Klinikos, 2004–2008

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Background. Inflammatory bowel diseases (IBD) ulcerative colitis (UC) and Crohn's disease (CD) are of great interest in nowadays gastroenterology. The aim of our study was to describe the demographic and clinical characteristics of IBD at Vilnius University Hospital Santariškių Klinikos (VUHSK).

Materials and methods. VUHSK IBD case histories were examined retrospectively covering the period from 2004 to 2008.

Results. Case histories of 288 patients were analyzed: 28.1% CD, 71.9% UC. Men / women 45.7%/54.3% CD; 44.9%/55.1% UC, $p > 0.05$. Mean age diagnosing CD was 38.6, UC, 41.1 years, $p > 0.05$. The extent of UC was as follows: proctitis 25.6%, proctosigmoiditis 28.5%, left side colitis 9.2%, pancolitis 30.9%, and normal mucosa 2.4%. UC was mild in 30.5%, moderate in 55.5%, and severe in 24% cases. The location of CD was: ileal 27.2%, colonic 48.1%, ileocolonic 9.9%, isolated upper disease 0%, normal mucosa 11.1%. Behaviour of CD: non-stricturing, non-penetrating 72.8%, stricturing 16%, penetrating 8.6%, perianal 2.5%. Forms of CD: remission 23.5%, moderate 56.8%, severe 19.8%. Corticosteroids were used for 45.7% CD and for 43.5% UC patients. Use of immunomodulators was: 33.3% in CD and 19.8% in UC group, $p < 0.05$. Intestinal operations were performed: 32.1% in CD and 6.8% in UC group, $p < 0.05$.

Conclusions. CD is a rarer diagnosis than UC; the ratio is 1 : 2.6. The main course of UC is mild and moderate proctitis and proctosigmoiditis. The main type of CD is mild non-stricturing, non-penetrating colonic type of the disease. Immunomodulators and surgery because of the complicated course of the disease are more frequent in CD than in UC. The proportion between men and women, their age at diagnosing IBD, use of corticosteroids are comparable between CD and UC patients.

Key words: inflammatory bowel diseases, ulcerative colitis, Crohn's disease

INTRODUCTION

Inflammatory bowel diseases (IBD) ulcerative colitis (UC) and Crohn's disease (CD) are of great interest in nowadays gastroenterology because of their increasing rates worldwide, domination in young employable population, disabling course of the diseases. The incidence of these diseases is assumed to be highest in the developed countries and lowest in the developing regions of the world (1, 2). 10–15 years ago the diagnosis of CD was very rare in Lithuania. However, it must be observed that in the last 15 years our country is undergoing huge changes in socioeconomic life. This may have influence not only on the life style, but also on the changes in the prevalence and clinical presentation of IBD. Therefore, it is natural to expect the trends

that are already visible in the developed countries. IBD, although becoming more common, are not widely studied in Lithuania, except for one paper from Kaunas University Hospital, where retrospective data of IBD patients were evaluated for the period 1995–2001 (3). The aim of our study was to describe the demographic and clinical characteristics of UC and CD at Vilnius University Hospital Santariškių Klinikos during the calendar year period 2004–2008.

MATERIALS AND METHODS

Vilnius University Hospital Santariškių Klinikos case histories of IBD inpatients and outpatients were examined retrospectively during the 4 year calendar period from January 1, 2004 to January 2008.

Information on sex, age, date of the onset of symptoms, date of confirming diagnosis, extent of disease, histological findings, and treatment for IBD, data and type of intestinal operations, anamnesis of colorectal cancers were collected.

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The extent of disease for UC was defined as proctitis (proximal extent to the sigmoid colon), proctosigmoiditis (to the descending colon), left-sided (to the splenic flexure), or pancolitis (beyond the splenic flexure). The severity of the disease was determined as follows: mild, moderate or severe ulcerative colitis, using Truelove and Witts classification (4). For CD, the Montreal classification was used to classify the localization in ileal, colonic, ileo-colonic, and isolated upper type of the disease.

The small bowel was tested by small bowel follow through (SBFT) and fibrogastroduodenoscopy. The type of behaviour of CD was distributed to: non-stricturing non-penetrating, stricturing, penetrating, peri-anal disease (5). The severity of Crohn's disease (remission, moderate, severe disease) was assessed using Harvey-Bradshaw index (6). IBD histology was examined in the National Center of Pathology using standardized grading scores for histological assessment of CD and UC (7, 8).

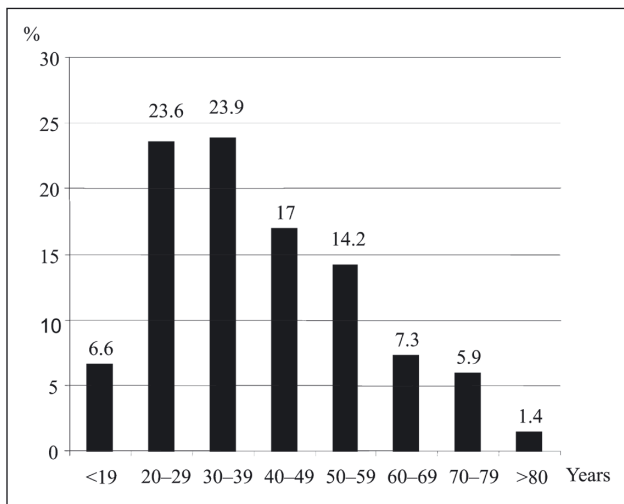
The statistical analysis was performed with SPSS software (16.0). Student's t-test and χ^2 test were used to continuous and non-continuous variables. P values < 0.05 were considered to be statistically significant.

RESULTS

Demographic characteristics

288 patients were analyzed, 81 (28.1%) with Crohn's disease and 207 (71.9%) with ulcerative colitis. Relation between men and women was comparable: 130 (45.1%) vs 158 (54.9%). Current age of the patients was 18–89 years (mean age 46.2 years ± 16.8 years). Age of the patients at diagnosing IBD was 8–86 years (mean age 40.4 years ± 16.5 years). Most of the patients became ill, when they were 20–40 years old (Table 1).

Table 1. Age of the patients at diagnosing IBD



The duration of IBD of these patients lasted from 0 to 47 years (mean age 5.6 years ± 6.7 years).

49 patients have been ill with IBD for 10 years and more, 56 patients, from 5 to 9 years. The rest have been ill for less than 5 years. In 9 (3.1%) patients diagnoses were changed during the course of their disease: in 8 cases ulcerative colitis diagnosis was changed to Crohn's disease and in one case *vice versa*.

The mean time for diagnosing ulcerative colitis was 0.7 years (std dev 1.9 years) and 1.4 years (std dev 4.45 years) for Crohn's disease.

The main characteristics, comparing ulcerative colitis with Crohn's disease, are shown in Table 2. The proportion between men and women, their age at diagnosing IBD, use of corticosteroids did not differ between Crohn's disease and ulcerative colitis patients. However, use of immunomodulators and surgical treatment because of the complicated course of the disease were much more frequent in Crohn's disease than in ulcerative colitis.

Table 2. Main characteristics, comparing ulcerative colitis with Crohn's disease

	Crohn's disease n = 81 (28.1%)	Ulcerative colitis n = 207 (71.9%)	P
Gender:			
Men (n (%))	37 (45.7)	93 (44.9)	>0.05
Women (n (%))	44 (54.3)	114 (55.1)	
Age at diagnosing disease:	38.6 (15.9)	41.1 (16.7)	>0.05
Mean years ± std dev			
Operations: n (%)	26 (32.1)	14 (6.8)	<0.05
Use of corticosteroids: n (%)	37 (45.7)	90 (43.5)	>0.05
Use of azathioprine: n (%)	27 (33.3)	41 (19.8)	<0.05
Use of biological therapy: n (%)	6 (7.4)	2 (1)	<0.05

Extent of the diseases and clinical characteristics

Tests performed for IBD patients are listed in Table 3.

Ulcerative colitis. Proctitis and proctosigmoiditis were diagnosed in most of 207 UC patients, 53 (25.6%) cases and 59 (28.5%) cases respectively. 19 (9.2%) cases were left side colitis, while 64 (30.9%) patients suffered from pancolitis. In 5 patients (2.4%) macroscopically mucosa looked normally; ulcerative colitis diagnosis was made only after histological examination. UC extent was not detected in 7 (3.4%) patients, as incomplete colonoscopy was made because of technical interruptions. 63 (30.5%) patients were diagnosed as having mild UC, 115 (55.5%) moderate one, and 29 (24%) were ill with severe UC.

Table 3. Tests performed for IBD patients

Tests	UC patients	CD patients
Colonoscopy and histology	207	81
SBFT	-	81
Fibrogastroduodenoscopy	-	81

Crohn's disease. Location of CD was as follows: ileal in 22 (27.2%), colonic in 39 (48.1%), ileocolonic in 8 (9.9%), isolated upper disease in 0 cases. In 9 cases (11.1%) the endoscopic view of colonic mucosa was normal. In these patients CD was diagnosed by performing histology. In 3 (3.7%) cases the exact location of the disease remained unknown because of not detailed examination due to technical difficulties.

Non-stricturing, non-penetrating behaviour of CD was diagnosed in 59 cases (72.8%), stricturing in 13 (16%), penetrating in 7 (8.6%), and perianal disease modifier in 2 cases (2.5%).

19 (23.5%) cases were remission of CD, 46 (56.8%) cases had a moderate form, and 16 (19.8%) cases were a severe form of CD.

Dysplasia

Colon dysplasia histologically was detected in 9 (3.1%) IBD patients. In 2 cases dysplasia was categorized as a high grade one. 1 dysplasia case was CD, the rest 8 were UC (3 patients with proctitis, 2 with proctosigmoiditis, and 3 with pancolitis). Age at diagnosing IBD in these patients was 8–77 years (mean age 37 years). Age at diagnosing dysplasia was from 20 to 77 years (mean age 41 years.). Duration of IBD in these patients before detecting dysplasia was: more than 10 years in 4 patients, less than 10 years in 5 patients. The course of IBD in these patients was the following: 2 mild cases, 6 moderate cases, and 1 case of severe colitis.

Operations

Ulcerative colitis. Indications for operations in 14 (6.7%) UC patients were: 6 colorectal carcinomas, 2 tubulovillous adenomas, 4 stenoses (one of them together with perforation), 1 severe bleeding, and 1 proctitis. One patient (0.5%) was operated on more than 1 time because of colon stenosis and bleeding. In 3 cases carcinoma was operated before diagnosing UC, in 2 cases colorectal carcinoma and UC were diagnosed at the same time. In one case carcinoma was diagnosed and operated 2 years after diagnosing severe pancolitis without remission. The age of the patients at diagnosing colorectal carcinoma varied from 47 to 77 years (mean age 62 years). The extent of UC in patients with detected colorectal carcinoma was: pancolitis in 2 cases, left side colitis in 2 cases, proctosigmoiditis in 1 case, and proctitis in 1 case.

Crohn's disease. 26 (32.1%) CD patients were operated on. In 20 cases (76.9%) the diagnosis was made only after the operation. 2 patients were operated on within the first year of diagnosis, and 4 patients were operated on from 4 to 16 years after diagnosing CD. Indications for operations were: stenosis in 17 cases, stenosis and villous adenoma in 1 case, proctitis in 5 cases, severe bleeding in 2 cases, and megacolon in 1 case. 5/26 patients (19.2%) were operated on more than one time.

DISCUSSION

Crohn's disease according to our data is still a rarer (28.1%) diagnosis than ulcerative colitis (71.9%); the ratio is 1 : 2.6. Similar data have been obtained at Kaunas University Hospital, where 80% patients are ill with UC and 20% with CD (3). The data from Eastern Europe have shown similar trends. Among the patients from Romania the incidence of ulcerative colitis was nearly twice that of Crohn's disease (9). The data from Poland show the following rates of UC and CD: 90 and 10 percent (10).

Although both ulcerative colitis and Crohn's disease are increasing in the developing countries, the incidence of Crohn's disease lags significantly behind that of ulcerative colitis. This phenomenon has been well described in European populations, where ulcerative colitis typically increases in incidence 15–20 years ahead of Crohn's disease (11).

The data analyzing sex relation in IBD differs: some authors state that IBD incidence is slightly greater in females

than in males (12). The others propose that ulcerative colitis occurs slightly more frequently in males; whereas Crohn's disease more often in females. In our study the relation between women (54.9%) and men (45.1%) was comparable and did not reach any significant difference either in UC or in CD (13). According to the world literature IBD affects people of all ages but usually begins before the age of 30, with the peak incidence from 14 to 24 (14). Most of our patients became ill with IBD at the age between 20–40 years. These diseases may have a second smaller peak between the ages 50–70; however, this later peak may include some cases of ischemic colitis. We did not observe the second age peak in our IBD patients. We also did not detect any difference between the age of manifestation of CD and UC.

In fact, we know that it is much more difficult to recognize CD than UC. Sometimes it takes a long time to confirm a CD diagnosis. In our study, it took 1.4 years on average to confirm a CD diagnosis after the appearance of the first symptoms. For UC this time was 0.7 year. In Denmark population study through the period 2003–2005, the mean delay from the first symptoms to CD diagnosis was 8 months. In 1962–1987, this period in Denmark was 2.2 years (15). Availability of new diagnostic tools may play a role. We hope we will be able to recognize CD more quickly in future, too.

Location of CD in our study population was predominantly colonic, 48.1% cases. Comparable data are from Denmark population-based study, where the predominant extent of CD at diagnosis was colonic as well. A surprisingly low percent of colonic location of CD was found at Kaunas University Hospital in 1995–2001, only 13%. The authors observed that it was difficult to differentiate the colon location of CD from UC. We analyzed our data from 2004 when ECCO recommendations were approved (7). Following ECCO recommendations we were taking multiple biopsies from different segments of the colon. It is quite possible that it allowed us to recognize colonic forms of CD more precisely and to differentiate them from UC. One more explanation of our findings is that phenotypic presentation of CD is changing towards more distal colonic localization (15). Rates of terminal ileum and ileocolon involvement in Denmark CD population were higher: 32% and 22%, compared to our patients: 27.2% and 9.9%. We may be still missing a part of small intestinal CD lesions because of difficulties in the small bowel diagnostic techniques. The small bowel for our patients was tested using SBFT.

In Denmark study, the isolated upper CD was diagnosed in 7% cases, and no cases of such localization in our CD patients were found. The proximal form of CD is rare, anyhow, we should keep in mind that CD can occur in the upper parts of intestinal tract, and biopsies for differential diagnosis should be performed in doubtful cases.

About 20% of CD patients have penetrating course of the disease, about 33% of patients have perianal disease (especially fissures and fistulas) (16, 17). Rates of penetrating and perianal forms of CD in our patients were surprisingly low: 8.6% and 2.5%, respectively. The reasons of such findings are unknown. It may be explained by the fact, that we are not yet a highly industrialized country, and, fortunately, therefore, we still have fewer complicated forms of CD.

In most of our UC patients proctitis (25.6%) and proctosigmoiditis (28.5%) were diagnosed. 9.2% cases were diagnosed as left side colitis, and 30.9% as pancolitis.

The rates of proctitis and proctosigmoiditis were comparable with the 1995–2001 period data from Kaunas University Hospital, where 45.9% were diagnosed as proctitis and proctosigmoiditis. Pancolitis was much rarer in Kaunas University Hospital patients (13.8%) compared to our patients. There are 2 possible reasons for explanation: may be recently more difficult forms of UC are being treated at to our hospital, or UC is becoming more aggressive in the period of the last years possibly because of the industrialization progress in our country. We looked at the data from Denmark, one of the developed West European countries, located in a similar geographical position. Pancolitis was diagnosed to 27% of the newly diagnosed patients in Denmark population based study through the period 2003–2005 (15). Findings from different studies show that the clinical course of CD is more aggressive, and the quality of life with CD generally is lower than that with UC (12). In our study more aggressive treatment and more cases of surgery because of the complicated course of the disease were needed for patients with CD as well. According to literature colorectal surgery rates in CD patients reach up to 80 percent throughout their life (19).

The mean duration of IBD in our patients was 5.6 years. 32.1% CD patients were operated on. In a similar study from Norway, where CD patients were followed up for 5 years after diagnosis, 28% underwent intestinal surgery.

In most cases (76.9%), the CD diagnosis for our patients was made only after the operation. 2 patients were operated on within the first year of diagnosis. These results generate an idea that up till now CD has not been well recognized until it caused complications. In Copenhagen cohort IBD study for 2003–2005 period, an incomparably fewer number (12%) of CD patients had intestinal resection performed within one year after diagnosis. A significant reduction in early operation rates was observed compared to the previous rates from a study in Copenhagen County, 1962–1987, in which surgery was performed in 35% CD patients during the first year of diagnosis (15, 18).

Long-standing ulcerative colitis and Crohn's disease are associated with the development of colorectal dysplasia and cancer. This is one of the most serious complications of IBD and explains up to one sixth of all the deaths in UC patients and one twelfth of all the deaths from Crohn's disease (19, 20).

Rubin and colleagues conducted a retrospective review of a large registry of patients with ulcerative colitis who underwent surveillance examinations over a 10-year period. Dysplastic lesions were found in 3.2% cases during this study interval (21). A very similar rate of dysplasia – 3.1% – was detected in our study patients. According to our data, the rate of colectomy because of UC was 6%. The main reason for colectomy was colorectal cancer. The European Cohort IBD group studied 784 patients with UC for a minimum of 10 years to evaluate the colectomy rates. They found out very similar rates of colectomy in UC patients, 7.6% (22).

Patients with a young age at the onset of the disease, more extensive colitis, greater inflammatory burden, concomitant primary sclerosing cholangitis, and a family history of colorectal cancer are at a greatest risk to have a colorectal cancer. Most

cancers arise in pancolitis, and there is little or no increased risk associated with proctitis while left-sided colitis carries an intermediate cancer risk (23).

Colorectal cancer was diagnosed in 2.9% cases of UC patients in our study, and there were no cases in CD patients. Most of the colorectal cancer cases were diagnosed and operated on before or together with UC diagnosis. So it is not clear whether UC diagnosis was overlooked for many years, or the cancer in these cases was not the consequence of UC in the subgroup of our study patients. The dominating extent of UC in our study population with colorectal carcinoma was pancolitis and left side colitis (4 cases out of 6). The mean age at diagnosing colorectal carcinoma in IBD patients was 62 years.

While analyzing our data of ulcerative colitis and Crohn's diseases we observe similar trends like in other European countries concerning demographic characteristics of the patients, clinical course and prognosis of the diseases. The difference is that up till now we have less complicated forms of Crohn's disease. On the other hand, we are still lagging behind West European countries in diagnosing Crohn's disease in due time. Clinical vigilance should be enhanced for IBD, especially for Crohn's disease.

CONCLUSIONS

1. CD is a rarer diagnosis (28.1%) than UC (71.9%) in the Lithuanian patients examined, with the ratio 1 : 2.6.
2. The main course of UC is mild and moderate proctitis and proctosigmoiditis.
3. The main type of CD is mild non-stricturing, non-penetrating colonic type of the disease.
4. Uses of immunomodulators and surgical treatment because of the complicated course of the disease are more often in CD than in UC.
5. The proportion between men and women, their age at diagnosing IBD, use of corticosteroids are comparable between CD and UC patients.

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- Goda Denapienė, Aušrinė Barakauskienė, Eugenijus Ugianskis, Vytautas Kasiulevičius, Algimantas Irnias, Jonas Valantinas**
- UŽDEGININĖS ŽARNŲ LIGOS VILNIAUS UNIVERSITETO LIGONINĖS SANTARIŠKIŲ KLINIKOSE 2004–2008 M.**
- Santrauka*
- Įvadas.** Visame pasaulyje didėja uždegiminių žarnų ligų (UŽL), opinio kolito (OK) ir Krono ligos (KL) aktualumas. Mūsų studijos tikslas buvo retrospektyviai išanalizuoti Vilniaus universiteto ligoninės Santariškių klinikose gydytų UŽL pacientų demografinius duomenis ir ligų klini- kines apraiškas.
- Medžiaga ir metodai.** Retrospektyviai išnagrinėtos 288 pacientų, sergančių UŽL, Vilniaus universiteto ligoninės Santariškių klinikų as- mens sveikatos istorijos nuo 2004 iki 2008 m.
- Rezultatai.** Buvo gydyti 288 pacientai: 28,1% sirgo KL, 71,9% – OK. Vyrų ir moterų, sergančių KL, buvo 45,7% ir 54,3%; OK – 44,9% ir 55,1% ($p > 0,05$). Vidutinis amžius diagnozuojant KL buvo 38,6 m., OK – 41,1 m. ($p > 0,05$). OK išplitimas: proktitas – 25,6%, proktosi- gmoiditas – 28,5%, kairės pusės kolitas – 9,2%, pankolitas – 30,9%, norma – 2,4%. OK sunkumas: lengvas – 30,5%, vidutinis – 55,5%, sun- kus – 24%. KL lokalizacija: klubinėje žarnoje – 27,2%, storojoje žarno- je – 48,1%, klubinėje ir storojoje žarnoje – 9,9%, proksimali izoliuota forma – 0%, norma – 11,1%. KL formos: nestriktūrinė, nepenetruojan- ti – 72,8%, striktūrinė – 16%, penetruojanti – 8,6%, išanginė – 2,5%. 23,5% KL sergančių pacientų buvo remisija, 56,8% – vidutinė, 19,8% – sunki KL eiga. Kortikosteroidus teko vartoti 45,7% KL ir 43,5% OK sergantiems pacientams ($p > 0,05$). Imunomodulatorius teko var- toti 33,3% KL ir 19,8% OK sergantiems pacientams. Gastrointestininis traktas buvo operuotas 32,1% KL ir 6,8% OK sergantiems pacientams.
- Išvados.** OK serga daugiau pacientų nei KL (2,6 : 1). Tarp OK sergančių pacientų vyravo lengvas ir vidutinis proktitas bei prokto- sigmoiditas. Pagrindinis KL tipas buvo lengvos eigos nestriktūrinis, nepenetruojantis. Imunomodulatorių vartojimas ir gastrointestininės operacijos buvo dažnesnės tarp KL sergančių pacientų nei tarp sergan- čiųjų OK.
- Vyrų ir moterų santykis, amžius diagnozuojant UŽL, kortikosteroi- dų vartojimas nesiskyrė tarp sergančiųjų OK ir KL.
- Raktažodžiai:** uždegiminės žarnų ligos, opinis kolitas, Krono liga