Clinical characteristics of 320 pediatric Crohn's disease patients registered in the nationwide Crohn's disease registry in Poland

Charakterystyka kliniczna 320 dzieci z chorobą Leśniowskiego-Crohna zarejestrowanych w ogólnopolskim Rejestrze Choroby Crohna w Polsce

Jarosław Kierkuś[1], Małgorzata Sładek[2], Tomasz Pytrus[3], Piotr Landowski[4], Grażyna Czaja-Bulsa[5], Iwona Ignyś[6], Grażyna Mierzwa[7], Urszula Grzybowska-Chlebowczyk[8], Elżbieta Czkwianianc[9], Alicja Żabka[10], Grażyna Rydzewska[11]

[1]Department of Gastroenterology, Hepatology and Immunology, Children's Memorial Health Institute, Warsaw, Poland
[2]Department of Pediatrics, Gastroenterology and Nutrition, Jagiellonian University Medical College, Krakow, Poland
[3]2nd Department of Pediatrics, Gastroenterology and Nutrition, Wroclaw Medical University, Poland
[4]Chair and Clinic of Pediatrics, Pediatric Gastroenterology, Hepatology and Nutrition, Medical University of Gdansk, Poland
[5]Department of Pediatrics, Gastrology and Rheumatology, Children's Hospital SPS ZOZ "Zdroje", Szczecin, Poland
[6]Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Science, Poland
[7]Chair and Department of Pediatrics, Allergology and Gastroenterology, Ludwik Rydygier *Collegium Medicum* in Bydgoszcz, Nicolaus Copernicus University in Torun, Poland
[8]Department of Pediatrics, Gastroenterology Division, Silesian Medical University, Katowice, Poland
[9]Gastroenterology and Pediatric Department, Polish Mother's Memorial Hospital, Research Institute, Lodz, Poland
[10]Department of Pediatrics, Medical University of Silesia, Pomeranian Medical University, Zabrze, Poland
[11]Department of Internal Diseases and Gastroenterology, Central Clinical Hospital of Ministry of Home Affairs, Warsaw, Poland

Prz Gastroenterol 2012; 7 (4): 228–232
DOI: 10.5114/pg.2012.30507

Key words: inflammatory bowel disease, Crohn's disease, database.
Słowa kluczowe: nieswoiste zapalenia jelit, choroba Leśniowskiego-Crohna, rejestr.

Address for correspondence: Jaroslaw Kierkus MD, PhD, Department of Gastroenterology, Hepatology and Immunology, Children's Memorial Health Institute, Al. Dzieci Polskich 20, 04-730 Warsaw, Poland, phone: +48 22 815 73 84, fax: +48 22 815 73 82, e-mail: j.kierkus@czd.pl

Abstract

Introduction: Inflammatory bowel disease, particularly Crohn's disease (CD), is a rising problem in pediatric gastroenterology. Limited information is available on demographic and clinical aspects of pediatric CD in Poland.
Aim: Preliminary data on demographic and clinical characteristic of pediatric CD in Poland based on the web-based prospective registry in order to gather reliable information to identify appropriate treatment strategies.
Material and methods: In September 2005 a web-based prospective registry of CD patients was initiated in Poland. Ten institutes (9 academic centers, 1 referred regional hospital) took part in the project with the object of obtaining the demographic and clinical data of pediatric CD patients across the country. With this end in view, a computerized questionnaire was used and the collected data were sent

Streszczenie

Wstęp: Nieswoiste choroby zapalne jelit (*inflammatory bowel diseases* – IBD), zwłaszcza choroba Leśniowskiego-Crohna (*Crohn's disease* – CD), są narastającym problemem w gastroenterologii pediatrycznej. Dostępne dane dotyczące klinicznych i demograficznych aspektów choroby w Polsce są ograniczone.
Cel: Zebranie rzetelnych danych o klinicznych i demograficznych aspektach choroby Leśniowskiego-Crohna u dzieci w Polsce na podstawie utworzonego internetowo prospektywnego rejestru choroby mających pomóc w opracowaniu najbardziej optymalnych strategii terapeutycznych dla tej grupy pacjentów.
Materiał i metody: We wrześniu 2005 roku został utworzony w Internecie ogólnopolski rejestr pacjentów z chorobą Leśniowskiego-Crohna. Do projektu włączono 10 jednostek szpitalnych (9 szpitali akademickich, 1 rejonowy szpital refe-

prospectively to a central registry for analysis. The following data were analyzed: demographics, family history, location and behavior of disease, extraintestinal manifestation, coexisting diseases, diagnostic work-up, and medical treatment including surgical intervention.

Results: Through the period of 4 years, 320 patients (male : female – 191 : 129) aged below 16 years with CD diagnosed at the mean age of 9.2 ±6.8 years were incorporated in the registry. Early onset of disease (age at diagnosis below 5 years) was recorded in 68 children (21.25%). Positive family history was reported for 16 patients (5%). The predominant localization of lesions described using the Montreal classification (L1 for small intestine, L2 for colon, L3 for ileocolon, and L4 for the upper gastrointestinal tract) was ileocolon (L3) – 217 patients (67.8%). The predominant behavior of disease was non-stricturing and non-penetrating – 225 patients (70.32%). Extraintestinal manifestation was reported in 20 patients (6.25%). Coexisting diseases occurred in 35 patients (10.93%). The predominant initial therapy was mesalazine (227 patients – 70.1%). Seventeen patients (5.31%) required a surgical intervention.

Conclusions: This study provides comprehensive information on demographic and clinical aspects of pediatric CD in Poland. Our results are consistent with the previously published reports from other countries in terms of age of onset and male predominance in pediatric CD patients. Our conclusions are as follows: information needs to be well defined, validated at entry, and updated at every visit, which facilitates our work and makes the data more reliable.

rencyjny). W celu zebrania danych demograficznych i klinicznych zastosowano dostępny internetowo kwestionariusz, który następnie przesyłano do centralnego rejestru do prospektywnej analizy. Ocenie poddano następujące dane: demografia, historia rodzinna, lokalizacja i postać choroby, objawy pozajelitowe, choroby współistniejące, diagnostyka oraz leczenie (włączając w to interwencje chirurgiczne).

Wyniki: Przez 4 lata 320 pacjentów (płeć męska : płeć żeńska – 191 : 129) w wieku poniżej 16 lat ze zdiagnozowaną CD (średni wiek w momencie postawienia diagnozy: 9,2 ±6,8 roku) zostało zarejestrowanych w bazie danych. Tak zwany wczesny początek choroby (wiek przy rozpoznaniu poniżej 5 lat) stwierdzono u 68 dzieci (21,25%). Rodzinne występowanie (obciążony wywiad rodzinny) odnotowano u 16 pacjentów (5%). Główne miejsce zmian chorobowych (według Klasyfikacji montrealskiej: L1 – jelito cienkie, L2 – jelito grube, L3 – *ileocolon*, L4 – górny odcinek przewodu pokarmowego) stanowiła lokalizacja krętniczo-kątnicza (L3) – 217 (67,8,%). Postać niepenetrująca bez zwężeń była przeważającą postacią choroby – 225 (70,32%) pacjentów. Objawy pozajelitowe zaobserwowano u 20 chorych (6,25%).

Wnioski: Badanie dostarcza pełnych informacji dotyczących aspektów demograficznych i klinicznych choroby Leśniowskiego-Crohna w Polsce. Uzyskane dane są zgodne z doniesieniami z innych krajów. Wnioski z badania są następujące: zbierane informacje muszą być dobrze zdefiniowane i określone już na samym początku badania, weryfikowane oraz aktualizowane systematycznie w trakcie jego trwania, aby usprawnić pracę i uzyskać jak najbardziej wiarygodne wyniki.

Introduction

Recent evidence indicates that the incidence and prevalence of Crohn's disease (CD) varies greatly around the globe both in children and adults [1, 2]. However, the majority of data comes from studies conducted in North America and Western Europe and limited information is available from the central part of the "old continent". There is a common impression that the incidence and prevalence of CD in the Polish population have been rising in recent years, making CD one of the most prevalent chronic conditions in pediatric gastroenterology. The protracted and relapsing clinical course causes important public health problems affecting education, social life and quality of life. Epidemiological studies are important to determine factors contributing to the expression of the disease.

Aim

Therefore, for better understanding and to characterize demographic and clinical features of the pediatric CD population we established a nationwide web-based Crohn's disease registry in many centers across Poland to collect data on the demographic and clinical features of Polish patients with CD.

Material and methods

Data collection and survey period

In September 2005, a nationwide Crohn's disease registry in Poland was established to collect demographic and clinical data of patients diagnosed with Crohn's disease. A collaborative, prospective registry of consecutive CD patients conducted in 10 pediatric gastroenterology centers (9 academic, 1 regional reference hospital) across the country was initiated.

The registration period started in September 2005 and data were collected through a period of four years. Both prevalent (existing) and incident (new) CD patients diagnosed before 18 years were prospectively incorporated. Patients older than 16 years were not included in this analysis. Patients with ulcerative colitis and indeterminate colitis were not registered in the study. Table I presents a list of centers participating in the project.

Dataset

A computerized questionnaire for every CD patients was used to record age, gender, height, weight, family history, date of diagnosis, time delay between CD-related symptoms and establishing the diagnosis, pheno-

Table I. List of centers participating in the project

Tabela I. *Lista ośrodków biorących udział w badaniu*

Department of Gastroenterology, Hepatology and Immunology, Children's Memorial Health Institute, Warsaw
Department of Pediatrics, Gastroenterology and Nutrition, Jagiellonian University Medical College, Krakow
Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Science, Poznan
Chair and Department of Pediatrics, Allergology and Gastroenterology, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun
Department of Pediatrics, Gastroenterology Division, Silesian Medical University, Katowice
Gastroenterology and Pediatric Department, Polish Mother's Memorial Hospital. Research Institute, Lodz
Department of Pediatrics, Silesian Medical University, Zabrze
Department of Internal Diseases and Gastroenterology, Central Clinical Hospital of Ministry of Home Affairs, Warsaw

type and location of the disease (according to the Montreal classification), extraintestinal manifestation, coexisting disease, diagnostic work-up, and initial and current medical treatment including surgery. Collected data on demographic and clinical aspects were prospectively sent to a central registry for analysis.

Diagnostic criteria

The diagnosis of CD was based on the Porto criteria and thus confirmed by clinical presentation, upper and lower endoscopy with preferable terminal ileum intubation with multiple biopsy taken, radiological evaluation of small bowel (small bowel follow-through, enteroclysis, magnetic resonance imaging (MRI), computed tomography (CT)) or surgery. Endoscopy and biopsy were used to determine the behavior of the disease. The localization of lesions was described using the Montreal classification as follows: L1 – disease limited to lower small intestine with or without cecum involvement, L2 – any exclusively colonic location between cecum and rectum, L3 – disease of the terminal ileum and any location in colon, and L4 – any location proximal to the ligament of Treitz. Disease was classified as inflammatory (B1), structuring (B2), and penetrating (B3) with/or without perianal disease (p). Inflammatory disease (B1) denoted a non-structuring and non-penetrating disease. Structuring (B2) was categorized by presence of luminal narrowing diagnosed on radiology, endoscopy or surgery. Penetrating disease (B3) denoted radiological, endoscopic or surgical evidence of an abscess or fistula. Perianal disease was defined as a history of perianal or perineal abscess(es), fistula, skin tags and/or anal stenosis. Extra-intestinal symptoms were recognized as affecting eyes (uveitis), skin (erythema nodosum, pyoderma gangrenosum) and joints. The following coexisting diseases were reported: rheumatic joint inflammation (2.5%), celiac disease (4.37%), autoimmune hepatitis (1.25%), viral hepatitis (1.25% for both b and c virus by ratio of 3 : 1 respectively), primary sclerosing cholangitis (1.56%).

Demographics

Smoking and alcohol

Smoking status was recorded as smoker, non-smoker or ex-smoker; the kind and quantity of doses were registered. Alcohol status was recorded as drinking or not drinking; the kind and quantity of doses were noted. None of the specified habits was noted, which can be explained by the fact that our cohort comprised only pediatric patients.

Locality

Locality was divided into 3 categories: city, town and village, according to urbanization and number of inhabitants.

Current and initial therapies

Pharmacological treatment: Treatment with 5-aminosalicylic acid (5-ASA), steroids, immunosuppressive drugs (azathioprine, methotrexate, cyclosporine) and tumor necrosis α blocker was recorded. The results refer to the initial and current treatment at the time of registration.

Surgery

Surgical procedures were categorized as follows:

- Resection surgery (RS) including subtotal colectomy, segmental colectomy, small bowel resection or strictureplasty.
- Examination under anesthesia (EUA) including surgical toileting of the perineal area, seton suture insertion, perianal abscess drainage (PA).
- Others. All other procedures, e.g. percutaneous drainage of abdominal collection.

Results

During the 4-year period, 320 patients (male : female – 191 : 129) aged below 16 years with CD diagnosed at the mean age of 9.2 ±6.8 years were incorporated in the registry. Early onset of disease (age at diagnosis below 5 years) was recorded in 68 children (21.25%) with predominance of boys – 45 (66.2%) vs. 23 (33.8%) respectively. Positive family history was reported in 16 patients (5%). The most frequently found localization of lesions was the ileocolon (L3) – 217 patients (67.8%)

and the predominant behavior of the disease was non-stricturing and non-penetrating – 225 patients (70.32%). Coexisting diseases were observed in 35 patients (10.93%). Extra-intestinal manifestation was reported in 20 patients (6.25%). Initial medical therapy included mesalazine (227 patients – 70.1%), sulfasalazine (52 patients – 16.25%), azathioprine (130 – 40.62%), cyclosporine (4 – 1.25%), methotrexate (7 – 2.19%), prednisone or methylprednisolone (147 – 46%), budesonide (32 – 10%), antibiotics (131 – 41%), and infliximab (14 – 4.4%). Seventeen patients (5.31%) required surgical interventions. Characteristics of study participants are summarized in Table II.

Table II. Characteristics of study participants (n = 320)

Tabela II. *Charakterystyka pacjentów (n = 320)*

Parameter	Characteristic
Gender:	
Male	191 (59.7%)
Female	129 (46.3%)
Age at diagnosis [years]	9.2 ±6.8
Early onset (n)	68 (21.25%)
Positive family history	16 (5%)
Involved region:	
Small intestine (L1)	1.56%
Colon (L2)	3.43%
Ileocolon (L3)	67.8%
Upper gastrointestinal tract (L4)	1.25%
L1 + L4	0.625%
L2 + L4	5.62%
L3 + L4	19.7%
Behaviour of the disease:	
Non-structuring and non-penetrating	225 (70.32%)
Fistula or perianal lesion	39 (12.2%)
Stricturing	38 (11.88%)
Penetrating	18 (5.6%)
Coexisting diseases	35 (10.93%)
Extra-intestinal manifestation	20 (6.25%)

Discussion

This is the first prospective survey, based on a central registry, to assess the demographic and clinical aspects of pediatric CD in Poland. Our results are consistent with the previously published reports from other countries in terms of age of onset and gender of pediatric CD [3, 4]. According to our registry the mean age at diagnosis was 9.2 ±6.8 years and early onset of disease defined as age at diagnosis below 5 years was recorded in 68 children (21.25%) with predominance of boys (by a ratio of 1.96 : 1). The predominance of male sex in pediatric CD has been consistently observed in many studies in Europe, North America and Asia, with a male to female ratio of 1.3–1.6 : 1 [5-7]. The predominant disease localization was L3 with non-structuring and non-penetrating (56.6%) behavior, which is also consistent with the previously published reports from other countries such as UK and Denmark [8]. The issue of early onset disease requires a special comment. Our data showed that the predominant location in this subgroup in our country was the ileocolon (L3). This result is not consistent with previously published reports from other countries which reported the colon to be the predominant localization [9]. We still have not identified any reason for this difference. So far the effects of our project are satisfactory, but we did not avoid some mistakes. During the period of data collection unexpected gaps emerged (e.g. the date of first symptoms mistaken with the date of diagnosis), which makes the data less reliable. This highlights the need for clear definition, consistency and completeness of data collection. Clinical management is made easier by the 'at a glance' summary, automated clinic letters, and facilities for monitoring and audit. The CD is believed to arise as a consequence of the interaction between genetic and environmental factors. In order to confirm this statement we have analyzed family history of our patients. Epidemiological papers report that the presence of positive family history in first- and second-degree relatives of children with newly diagnosed inflammatory bowel disease (IBD) vary from 10% in Europe to 29% in America [10]. Our data showed that family history was positive in 16 patients (5%). This discrepancy may be explained by different genetic background in respective populations. According to our data, CD tends to occur with a higher frequency in urban areas, which could be most likely explained by the influence of environmental factors such as differences in dietary habits in populations, closely related to geography and environmental pollution. Smoking is also a known environmental risk factor associated with CD relapse [11]. Due to the specific character of the analyzed group, i.e. pediatric, we did not record any smokers, even in adolescents. The data on alcohol are analogous to those for smoking. However, we put forward the suspicion that patients, especially the adolescents, did not report the habits on purpose. Therefore we do not find those results very reliable and approach them skeptically. That is why further epidemiological studies in this field are needed in order to clarify the data. We are aware that this study has some limitations. The database of our registry does not include all CD pediatric patients in Poland. The data

come from reference centers of the highest diagnostic quality, and hence concern a certain specific group of patients. Nonetheless, as IBD is not a common disease and its diagnosis often requires a specialized approach and expert advice, children with suspected or diagnosed CD are predominantly treated in the academic centers. That is why we assume that our database comprises the great majority of all CD pediatric patients in our country and certainly most (if not all) difficult and severe cases. We have learned through this project as much from the data as from the process itself, principally, the data collection. Our lessons learned are as follows: information needs to be well defined, validated at entry, and updated at every visit. This guarantees the quality of data and makes them more reliable, which is the background for establishing standards and procedures and above all helps in everyday practice of CD patients' management. Our experience may also help to support national IBD standards and audit.

Conclusions

This study provides comprehensive information on demographic and clinical aspects of pediatric CD in Poland. Our results are consistent with the previously published reports from other European countries in terms of age of onset, gender of pediatric patients with CD, localization and behavior of the disease. Our experience proves that it is possible to collect data on the epidemiology and clinical characteristics of pediatric CD from centers across the country which truly reflect clinical practice and thus develop individual patient management. This project has demanded technology but even more of time and discipline.

The IBD is a worldwide problem so others may find our experience of interest, particularly as the technical aspect of creating the database is not an end in itself but a means of raising our own standards of IBD care.

References

1. Ponsky T, Hindle A, Sandler A. Inflammatory bowel disease in the pediatric patient. Surg Clin North Am 2007; 87: 643-58.
2. Yao T, Matsui T, Hiwatashi N. Crohn's disease in Japan: diagnostic criteria and epidemiology. Dis Colon Rectum 2000; 43: S85-93.
3. Molinié F, Gower-Rousseau C, Yzet T, et al. Opposite evolution in incidence of Crohn's disease and ulcerative colitis in Northern France (1988-1999). Gut 2004; 53: 843-8.
4. Jess T, Riis L, Vind A, et al. Changes in clinical characteristics, course, and prognosis of inflammatory bowel disease during the last 5 decades: a population-based study from Copenhagen, Denmark. Inflamm Bowel Dis 2006; 13: 481-9.
5. Kim ES, Kim WH. Inflammatory bowel disease in Korea: epidemiological, genomic, clinical, and therapeutic characteristics. Gut Liver 2010; 4: 1-14.
6. Williams JG, Cheung WY, Russell IT, et al. Open access follow up for inflammatory bowel disease: pragmatic randomised trial and cost effectiveness study. BMJ 2000; 320: 544-8.
7. Luo CH, Wexner SD, Liu QS, et al. The differences between American and Chinese patients with Crohn's disease. Colorectal Dis 2009; 30.
8. Bardhan KD, Simmonds N, Royston C, et al. A United Kingdom inflammatory bowel disease database: making the effort worthwhile. JCC 2010: published online Feb 22. DOI: 10.1016/j.crohns.2010.01.003.
9. Lindberg E, Lindquist B, Holmquist L, Hildebrand H. Inflammatory bowel disease in children and adolescents in Sweden, 1984-1995. J Pediatr Gastroenterol Nutr 2000; 30: 259-64.
10. Calkins B M, Mendeloff AI. Epidemiology of inflammatory bowel disease. Epidemiol Rev 1986; 8: 60-91.
11. Carlens C, Hergens MP, Grunewald J, et al. Smoking, use of moist snuff, and risk of chronic inflammatory diseases. Am J Respir Crit Care Med 2010; 181: 1217-22.