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Original Article

Increasing Incidence of Inflammatory Bowel Disease, with Greatest Change Among the Elderly: A Nationwide Study in Finland, 2000–2020

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Abstract

Background and Aims: The incidence of inflammatory bowel disease [IBD] is stabilising in many Western countries. Some still show increasing incidence. Our objective was to determine the latest trends in IBD incidence and prevalence in Finland and to compare these among different age groups and between different geographical areas.

Methods: We used the nationwide registry of the Social Insurance Institute of Finland to identify new IBD cases during the period 2000–2020. Crude, age-specific, and age-standardised incidence rates were calculated. Prevalence was estimated using valid reimbursements from the same database in 2000–2020.

Results: We identified 42 498 new IBD cases. The crude annual incidence increased in ulcerative colitis [UC] from 20 to 35 (incidence date ratio [IRR] 1.03, 95% confidence interval [CI] 1.02-1.03), in Crohn's disease [CD] from 8 to 13 [IRR 1.02, CI 1.02-1.03] and in IBD overall from 28 to 48 per 100 000 person-years [IRR 1.02, CI 1.02-1.03]. Men had higher incidence than women in UC, but in CD the incidences were equal. The incidence of IBD increased in all age groups except for small children. The increase in both UC and CD was most marked among the elderly aged over 70. A north-south gradient was discernible. The crude prevalence of IBD increased from 376 to 972 per 100 000 (prevalence rate ratio [PRR] 1.05, CI 1.05-1.05).

Conclusions: The incidence of IBD, UC, and CD is increasing in Finland. The increase is most notable in the elderly. Current prevalence of IBD is 1%.

Key Words: Inflammatory bowel disease; incidence; prevalence

1. Introduction

The incidence of inflammatory bowel disease [IBD] and its subtypes ulcerative colitis [UC], Crohn's disease [CD], and inflammatory bowel disease unclassified [IBDU], increased rapidly in Western countries in the 20th century.[1] In the current millennium, reports indicate a plateau phase or even decreasing incidence in many industrialised countries, whereas incidence in several Asian and developing areas continues to rise.[2,3] Some Western countries still show an increase.[4,5]

Finland has one of the highest incidence and prevalence rates of IBD in the world.[6,7] In 2000–2007, the reported incidence of UC was 25/100 000, of CD 9/100 000, and of IBD 34/100 000 person-years. The IBD prevalence was 595 per 100 000 residents in 2008. Recent nationwide studies from other Nordic countries show incidence rates [IRs] of 17–28 in UC, 7–16 in CD, and 28–37 in IBD per 100 000 person-years.[4,8–11] Prevalence rates from Denmark, Norway, and Sweden vary from 294 to 505 in UC, from 151 to 262 in CD, and from 445 to 767 per 100 000 persons in IBD altogether.[2]

The general definition of elderly-onset IBD is disease onset at the age of 60 years or older.[12] As populations in Western countries age, an increase is expected in late-onset IBD. In newly diagnosed IBD patients, the proportion of elderly varies between 7% and 24%.[13] Although some studies suggest that elderly IBD patients present with a milder clinical course, the surgery rates seem to be higher.[8,14]

The aim of this study was to determine current IBD incidence and prevalence in Finland. We also aimed to assess the incidence trends in all ages and also between genders and different geographical areas.

2. Materials and Methods

2.1. Data source

We collected our data from the Social Insurance Institution of Finland [SII]. The insurance scheme of SII covers all permanent residents in Finland and each person is identified by a unique identification code. IBD patients are entitled to special reimbursement for medicine expenses. Granting the IBD special reimbursement in SII is a two-step process. A

limited number of specialists can issue a written certificate. The certificate must contain sufficient details on patient's IBD diagnosis including clinical presentation, findings in endoscopy, histology, and a treatment strategy, at minimum. The certificates are revised and criteria for reimbursement verified in SII by its medical examiners or specialists. The SII Special Reimbursement Registry on IBD has been operational since 1986, and previous studies confirm that it has excellent coverage and validity.[7,15]

For this study, we included all patients having IBD reimbursement granted for the first time from January 1, 2000, until December 31, 2020. The SII data made no reliable distinction between inflammatory bowel disease unclassified [IBDU] and UC; therefore, the IBDU cases were analysed with UC cases. The SII also provides publicly available data online on valid reimbursements, which we used to calculate prevalence rates.[16]

Finland has a population of 5.5 million and five university hospital regions.[17] The northernmost university hospital is in Oulu, with a catchment area of 736 563 inhabitants, and the southernmost in Helsinki, with 2 198 182 inhabitants in 2020. Population data were drawn from the official statistics producer, Statistics Finland.[17]

2.2. Statistical methods

The incident cases per year were divided by population at risk at the end of the same calendar year. The point prevalence rates were calculated by dividing the number of living IBD patients entitled to reimbursement at the end of each year by the population at risk. Results were presented per 100 000 person-years. Age-standardisation was done using European Standard Population 2013.[18] Poisson regression models were fitted to obtain incidence rate ratios [IRRs]; *p*-values <0.05 were considered significant. Data management was performed by Microsoft Excel and analyses using Stata 17.0.

2.3. Ethical considerations

The data retrieved from SII were summary data without identifiable personal data. Under the regulations, no consent from patients nor approval of an ethics committee is required for a registry-based study.

3. Results

We identified 42 498 new IBD cases during the years 2000–2020. Of these, 31 372 had UC and 11 126 CD, resulting in a UC:CD ratio of 2.8. Of the new IBD diagnoses, 15% [6 476 cases] were elderly-onset and 12% [5137 cases] were diagnosed in patients under 20 years old.

3.1. Incidence

The incidence of IBD and its subtypes increased from 2000 to 2020. The crude annual IR rose in UC from 20 to 35, in CD from 8 to 13, and in IBD altogether from 28 to 48 (IRR 1.02, 95% confidence interval [CI] 1.02-1.03) per 100 000 person-years. This translates into an average annual increase of UC, CD, and IBD incidence by 2.5%, 2.2%, and 2.4%, respectively [Table 1]. The age-standardised incidences are shown in Figure 1. Men had higher incidence than women in UC, but there was no difference between genders in CD. The incidences stratified by IBD subtype, gender, and age group are detailed in Supplementary data, [Table 1 and Table 2].

3.2. Incidence by age

The incidence of IBD increased in most age groups [Figure 2]. The increase was most notable among the elderly aged over 70 in both UC and CD [Figure 3]. The peak incidence occurred in the age group 25–29 in UC and in the age group 20–24 in CD. A smaller second peak was perceptible only in CD in the age group 45–49, caused by a peak in the incidence among women. The crude incidence of the elderly increased in UC from 10 to 20 [IRR 1.03, CI 1.03-1.04], in CD from 3 to 10 [IRR 1.05, CI 1.04 - 1.05], and in IBD overall from 14 to 31 [IRR 1.03, CI 1.03-1.04] per 100 000 person-years in IBD.

3.3. Incidence by geographical location

In CD, the incidence increased evenly from south to north with a mean incidence of 9/100 000 in Helsinki and of 11/100 000 person-years in the Oulu area. In UC, the incidence was highest in Oulu, with a mean incidence of 31/100 000 person-years. [Table 1].

3.4. Prevalence

During the study period 2000–2020, the crude prevalence of IBD increased from 376 to 972, with an average increase of 4.7% per year [prevalence rate ratio 1.05, CI 1.05-1.05]. At the end of 2020, there were 53 800 patients entitled to IBD special reimbursement in Finland, corresponding to an

Table 1 Incidence rate ratios [IRRs] 2000–2020.

	Ulcerative colitis		*p*-value	Crohn's disease		*p*-value
	IRR	95% CI		IRR	95% CI	
Overall	1.03	1.02-1.03	<0.001	1.02	1.02-1.03	<0.001
Female	1.02	1.02-1.03	<0.001	1.02	1.02-1.03	<0.001
Male	1.03	1.02-1.03	<0.001	1.02	1.02-1.02	<0.001
Male vs female	1.26	1.23-1.28	<0.001	1.02	0.98-1.06	0.349
Age group vs >75 years						
0–4	0.22	0.18-0.27	<0.001	0.38	0.28-0.50	<0.001
5–9	0.50	0.43-0.57	<0.001	0.87	0.71-1.06	0.158
10–14	1.43	1.30-1.58	<0.001	3.17	2.74-3.66	<0.001
15–19	3.81	3.51-4.13	<0.001	5.26	4.60-6.03	<0.001
20–24	5.58	5.17-6.03	<0.001	6.46	5.66-7.37	<0.001
25–29	6.47	6.00-6.98	<0.001	6.11	5.35-6.97	<0.001
30–34	5.98	5.54-6.45	<0.001	5.12	4.47-5.86	<0.001
35–39	4.94	4.57-5.34	<0.001	4.39	3.83-5.04	<0.001
40–44	4.20	3.88-4.54	<0.001	3.85	3.35-4.42	<0.001
45–49	3.68	3.39-3.98	<0.001	4.04	3.52-4.64	<0.001
50–54	3.06	2.82-3.31	<0.001	3.53	3.07-4.06	<0.001
55–59	2.90	2.68-3.15	<0.001	3.15	2.74-3.63	<0.001
60–64	2.71	2.49-2.94	<0.001	3.04	2.63-3.50	<0.001
65–69	2.46	2.26-2.69	<0.001	2.67	2.30-3.10	<0.001
70–74	1.89	1.71-2.08	<0.001	2.22	1.89-2.60	<0.001
Hospital area vs Helsinki						
Turku	0.97	0.94-1.00	0.062	1.21	1.15-1.28	<0.001
Tampere	1.02	0.98-1.05	0.299	1.07	1.01-1.13	0.020
Kuopio	0.95	0.91-0.98	0.002	1.08	1.02-1.14	0.010
Oulu	1.13	1.09-1.17	<0.001	1.27	1.20-1.35	<0.001

CI, confidence interval.

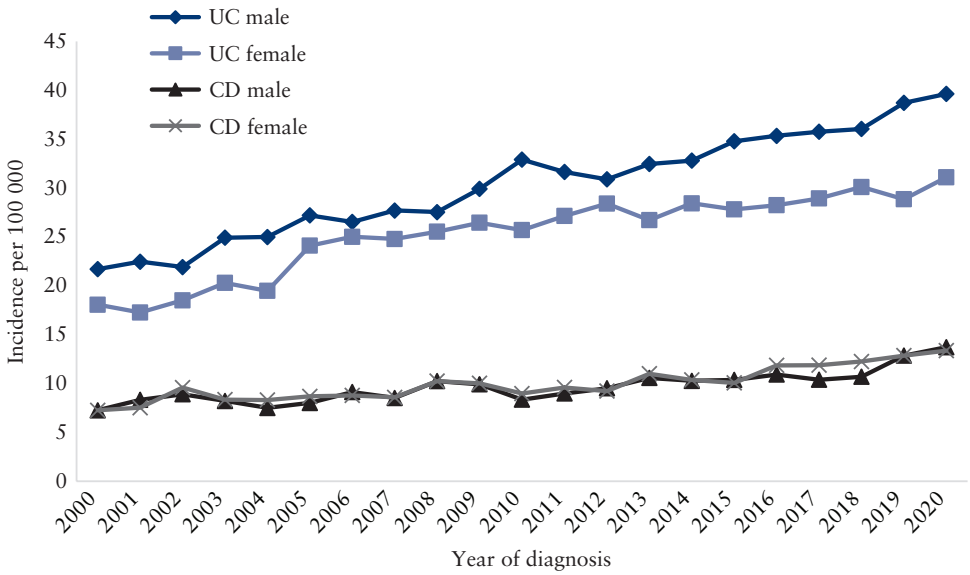

Figure 1. Age-standardised incidence of ulcerative colitis [UC] and Crohn's disease [CD] in Finland.

age-standardised prevalence of 975/100 000 persons. The crude prevalence of IBD among men reached 1035 [95% CI 1023-1047] and among women 911 [95% CI 900-922] per 100 000 persons. The prevalence was highest in the age group 40–54, and 33% of the prevalent cases were in the elderly group. Point- and age-specific prevalences are reported in Supplementary data, [Table 3] and [Figure 1].

4. Discussion

In this nationwide study we showed that during the years 2000–2020 the incidence of IBD continued to increase in Finland. The crude IR of UC increased up to 35, in CD up to 13, and in IBD up to 48 per 100 000 person-years. The increase was most substantial among the elderly. In UC, men had significantly higher incidence than women, but there was no difference in CD. We detected a clear north-to-south gradient with incidences highest in the northern parts of Finland. The crude prevalence of IBD increased from 376 to 972 per 100 000 persons.

The ongoing increase in incidence can only be explained by environmental factors. The diagnostics of IBD and the accessibility of diagnostic services in Finland have remained stable during the past two decades. Genetics play a role in the aetiology of IBD, but this change is too rapid to be explained by genetic alterations.[19] Several environmental factors have been associated with elevated risk of IBD, including urban living, exposure to antibiotics, use of oral contraceptives, tonsillectomy, smoking, consumption of soft drinks, and vitamin D deficiency.[20] Other factors seem to lower the risk, such as breastfeeding, high levels of folate, bed sharing and *Helicobacter pylori* infection. Many of these factors are related to the hygienic and modern lifestyle common in industrialised countries. Finland is no exception to Westernisation, and for years Finland's living conditions have been ranked among the top five globally.[21] This standard of living may explain the rise in incidence. Finland's northern location, and hence scarce sun exposure, also predisposes to vitamin D deficiency. A recent systematic review demonstrated an association between obesity and CD, but not UC.[22] An even more recent report suggests morbid obesity as an independent risk factor for both UC and CD.[23] Obesity in Finland is a common and growing problem among children and adults.[24,25] More studies are needed to determine whether there is a causal relationship between obesity and IBD, or if they are affected by the same factors, such as the consumption of processed foods.

Several reports have demonstrated the stabilising incidence of IBD in Western countries.[2,26,27] A recent Norwegian incidence study showed a stable incidence of IBD in 2010–2017 and a Swedish study demonstrated a decline in the incidence of IBD, CU, and CD in the period 2002–2014.[9,10] There are also reports from Europe showing constantly increasing incidence.[4,5,28] In our study, the rise in incidence was continuous. Since Norway, Sweden, and Finland have similar societies and geographical locations, it is hard to find the underlying reason for this difference.

Our study is consistent with several Nordic subtype reports stating that the incidence of UC is higher than of CD.[4,9,10] In these studies from Denmark, Sweden, and Norway, the incidence of UC is approximately twice as high as that of CD. In our study, the ratio was even higher at 2.8. There are also numerous reports from all over the world demonstrating the predominance of CD.[2] The same Nordic studies show CD to be more common in women, whereas our study demonstrated equal incidence between genders in CD. However, in our data the incidence of CD peaked in young women. It is hypothesised that sex hormones and oral contraceptives are associated with development of IBD and may alter the disease progression in CD.[29,30]

Young adulthood is commonly reported to be the peak age of IBD incidence, and accordingly, we found the incidence of UC to peak in the age group 25-29 and that of CD in the age group 20–24. Often a second peak is seen in UC, but our data did not show any such.[4,31–33] The cause of this second peak in older patients has sometimes been speculated to be misdiagnosis. Since microscopic colitis, diverticulosis with its complications, and ischaemic colitis are more common in the elderly, they may be misdiagnosed as IBD. In our data, the incidence decreased evenly in older age groups, thereby supporting the idea of accurate diagnosis.

We found the incidence to increase most markedly among the elderly. The results of IBD incidence reported

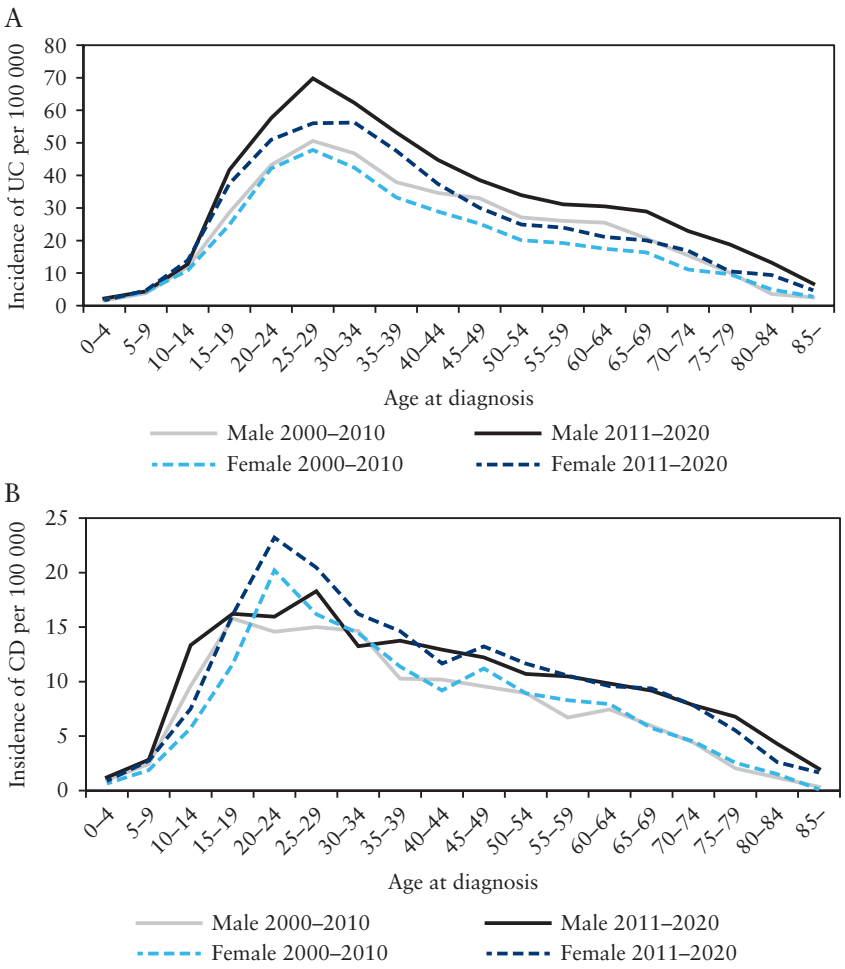

Figure 2. Age-specific incidence of [a] ulcerative colitis [UC] and [b] Crohn's disease [CD].

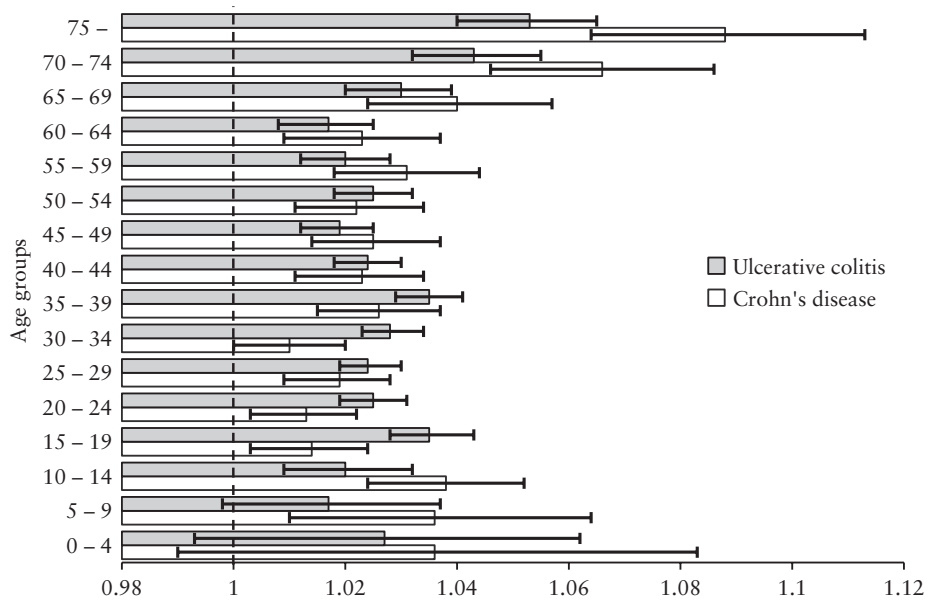

Figure 3. Age-specific incidence rate ratios [IRR] of ulcerative colitis and Crohn's disease with 95% confidence intervals, in 2000–2020.

in the literature among the elderly are inconsistent; some show increase and some decrease.[5,27] It is possible that the SII registry contains some misdiagnosed elderly IBD cases. However, our IRs are comparable to Swedish results from the same era.[8] A few studies report elderly-onset IBD to have distinctive phenotypical characteristics.[14] The exceptional features and their causes in the elderly-onset IBD need further investigation.

IBD incidence is highest in the northern parts of Finland. There are neither known genetic differences nor ethnic subgroups in the Finnish population that could explain the north-south gradient. The northern parts of Finland are also more rural, which according to studies should protect from IBD.[20]

IBD prevalence in Finland has reached 1% of population. This is no surprise, since the incidence is increasing and the IBD-associated mortality rate is low.[34] As a result, the growing group of IBD patients burdens health care services unprecedentedly. In addition, elderly IBD patients with their comorbidities and polypharmacy also pose a treatment challenge. Novel approaches are needed to manage the patient volumes and to keep the costs affordable. For example, digital solutions to monitor patients remotely are being increasingly introduced. Moreover, IBD nurses are taking more responsibility in the management and follow-up of patients.[35,36] Certainly, more research is needed to identify causative agents behind IBD and to improve disease prevention.

The strength of this study is the comprehensive nationwide coverage of IBD patients. SII policy of granting lifetime reimbursement for medicine costs, and the application without effort from patients' side, are drivers that are rarely disregarded. Therefore, virtually all IBD patients are listed in the SII IBD registry. The rare exceptions occur with patients never expected to need IBD medication, for example if UC is diagnosed and colectomy performed during the same admission.

A major limitation in our data is lack of follow-up. In the SII Special Reimbursement Registry, all data are recorded at the time of diagnosis. Misdiagnoses becoming apparent later and changes in IBD subtypes will therefore remain uncorrected. This may have caused our data to overestimate both incidence and prevalence. A study using the same SII registry revealed reclassification in 9% of IBD cases,[7] and a Swedish study showed reclassification in 18% of IBD cases after a follow-up of 4 years.[37] In addition, the SII data on UC and CD subtypes for the 1990s are incomplete; hence the prevalences of UC and CD cannot be calculated separately.

To summarise, we report an increasing incidence of UC and CD, and of IBD prevalence of 1% in Finland. Our incidence and prevalence rates in this nationwide population-based registry study are among the highest in the world. The increase in incidence is most marked among the elderly. The reason behind the rising incidence is unclear.

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Conflict of Interest

KK has received personal fees from Pfizer, Takeda, and Janssen-Cilag. PO, HH, and AJ have no conflict of interest to declare.

Author Contributions

All authors participated in the study design and read and approved the final version. KK performed data management and HH statistical analyses. KK wrote the manuscript. PO, HH, and AJ were involved in manuscript editing. Conference presentation: ECCO'22 Congress, virtual, 2022, digital oral presentation DOP02.

Data Availability Statement

The data underlying this article are available in online Supplementary material.

Supplementary Data

Supplementary data are available at *ECCO-JCC* online.

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