

Incidence of inflammatory bowel disease in the area of Liège : a 3 years prospective study (1993-1996)

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Abstract

A first prospective epidemiological study of IBD was conducted in the area of Liège. The duration of the study was short taking into account the small size of the population (1 million inhabitants). Therefore we carried out a 3 years prospective study.

Method. Private and public gastroenterologists completed a questionnaire for each new case they diagnosed between 01.06.1993 and 31.05.1996.

Results. During that period 270 IBD patients were identified : 137 (51%) had Crohn's disease (CD), 111 (41%) had ulcerative colitis (UC) including 32 proctitis (29% of UC) and 22 (8%) had unclassified colitis. The mean annual incidence per 10⁵ was 4.5 for CD and 3.6 for UC. The female/male ratio was 1,6 for CD and 0,5 for UC. The median age at the time of diagnosis was 30 years for CD and 39 years for UC. The mean time between the onset of symptoms and the diagnosis was 6,5 months for CD and only 4,8 months for UC. Family history of IBD was found in 15% of patients with CD and in 7% of UC.

Conclusions. These data show a high incidence of IBD in the area of Liège. These results confirm those reported during the first year of the prospective study which were similar to those observed in North-western France. Contrary to the other countries of Northern Europe, the incidence of UC is lower than the one of CD. Belgium appears to be a privileged country to undertake a national register and to study epidemiological aspects of IBD. (*Acta gastroenterol. belg.*, 1998, 61, 410-413).

Key words : Crohn's disease, ulcerative colitis, epidemiology, incidence.

Introduction

Inflammatory bowel diseases (IBD) are chronic diseases, of unknown aetiology. It is currently accepted that both environmental and genetic factors interact in the occurrence of these diseases. In this regard it is important to detect geographical variations in the incidence of Crohn's disease (CD) and ulcerative colitis (UC). Previous epidemiological studies have suggested a north-south gradient of IBD in Europe and North America with a higher incidence for UC than CD (2). Data published in Belgium and in France have suggested a "Belgium-French exception" with a higher incidence of Crohn's disease than ulcerative colitis (3,4). A recent multicentric European study and two French studies have shown more heterogeneous data (5,6,7). There is still no national register of patients with IBD in Belgium and epidemiological data are scarce. Our first one year prospective study as well as data from the Brussels area have shown a high incidence of IBD with results similar to those observed in the northern part of France (1,8,9). However the duration of that

study was short taking into account the small size of the population (1 million inhabitants). Therefore we have completed this prospective study for a period of three years in the Province of Liège.

Methods

Populations

The population was similar to our first one year prospective study (1). Briefly, the Province of Liège (1.014.689 inhabitants ; 1994 National Population census) was divided into four areas : the urban area of Liège (594 694 inhabitants) and the 3 other areas of Verviers, Huy, Waremme with both urban and rural population.

This prospective study included the patients who resided in the defined areas at the time of diagnosis, between the first of June 1993 and the 31th of may 1996.

Before the beginning and during the study, all gastroenterologists (47) of the Province were informed of this work by letters and by meetings of the Société Liégeoise de Gastroentérologie. Twenty-nine of private and public gastroenterologists having a clinical activity in all the major centers of the Province accepted to fill in a standard questionnaire for each patient consulting for the first time with clinical symptoms consistent with IBD.

Diagnosis criteria

Diagnosis of CD and UC (including ulcerative proctitis) was made using clinical, morphological and histological criteria of Gower-Rousseau *et al.* (1,10). Patients with a case history of chronic colitis compatible with both the diagnosis of CD or UC were defined as undetermined chronic colitis. Patients with positive stool culture or treated by antibiotics or non-steroidal anti-inflammatory drugs were excluded. The diagnosis was confirmed 6 months later.

The main data collected were : age, sex, date of diagnosis, interval between onset of symptoms and diagnosis, clinical, radiological, endoscopic and histo-

E. Louis is supported by the National Fond for Scientific Research (FNRS). Reprints : Prof. J. Belaiche, Service de Gastroentérologie, CHU Sart Tilman ; 400 Liège, Belgium.

logical features at the time of diagnosis and family history of IBD. The extent of the disease was defined in every patient by both coloscopy and or baryum enema and small bowel X-ray.

Data were checked by one of us (PL) and if necessary the gastroenterologist was contacted by phone or letter for more information.

Incidence calculation

The incidence rate was calculated by dividing the mean number of new cases year by the number of inhabitants of the Province.

Statistics

Groups and subgroups of patients were compared using Mann-Whitney test and Chi square test. Differences were considered as significant when the p value < 0.05.

Results

Table I and II show the annual incidence of IBD and the main characteristics of the diseases over the 3 years registration period.

Incidence

During the 3 years study period, 270 newly diagnosed IBD were recorded : 137 (51%) were Crohn's disease, 111 (41%) ulcerative colitis including 32 (29% of UC) proctitis and 22 (8%) undetermined chronic colitis. The mean annual incidence was 4,5 per 100 000 for Crohn's disease and 3,6 for ulcerative colitis.

The incidence rate of CD and UC for each of the three years is shown in tables I and II.

The highest age specific incidence rate for CD was between 20 and 29 years in both sexes (14 per 100 000 for women and 10.1 per 100 000 for men) (fig. 1). There were two peaks of age specific incidence rate for UC

Tableau I. — Annual incidence and main characteristics of Crohn's disease over the 3 years registration period

	first year	second year	third year	1993-1996
Number of cases IBD	104	81	85	270
Crohn's Disease	56 (54%)	35 (43%)	46 (54%)	137 (51%)
Incidence per 100.000	5.5	3.4	4.5	4.5
F/M	35/21	20/15	29/17	84/53
Age (years) (median)	33.5	30	28	30
Duration of symptoms before diagnosis (month)	6.9	7.4	5.4	6.5
Familial history	3	5	12	20
Location				
ileum	25 (45%)	13 (37%)	18 (39%)	56 (41%)
ileocolon	18 (32%)	16 (46%)	17 (37%)	51 (37%)
colon	12 (21%)	6 (17%)	11 (24%)	29 (21%)
perineal	6 (11%)	5 (14%)	3 (6.5%)	14 (10%)
pancolitis	3 (5%)	5 (14%)	14 (30%)	22 (16%)

Tableau II. — Annual incidence and main characteristics of ulcerative rectocolitis including proctitis, and annual incidence of unclassified chronic colitis

	first year	second year	third year	1993-1996
Number of cases of IBD	104	81	85	270
Ulcerative colitis	36 (35%)	43 (53%)	32 (38%)	111 (41%)
Incidence	3.5	4.2	3.1	3.6
F/M	15/21	15/28	9/23	39/72
Age (years) (mediane)	40	35	45	39
Duration of symptoms before diagnosis (months)	3.6	6.2	4.8	4.8
Familial history	1	5	2	8
Location				
rectum	7 (19%)	15 (35%)	10 (31%)	32 (29%)
rectosigmoid	12 (33%)	14 (32%)	8 (25%)	34 (30%)
left colon	9 (25%)	12 (28%)	8 (25%)	29 (26%)
pancolitis	7 (19%)	2 (5%)	6 (19%)	15 (13%)
Unclassified colitis	12 (11.5%)	3 (4%)	7 (8%)	22 (8%)

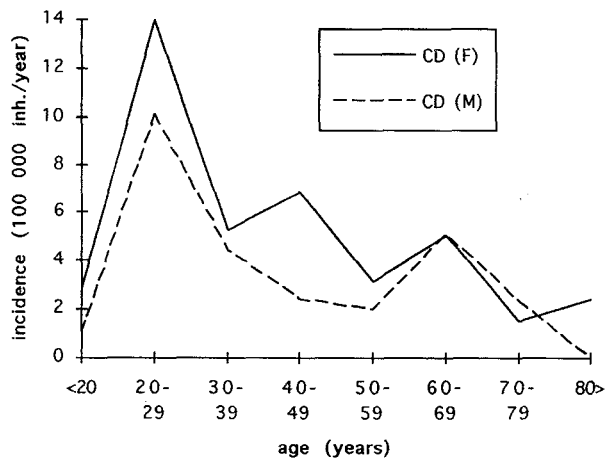


Fig. 1. — Incidence rate of Crohn's disease by sex and age.

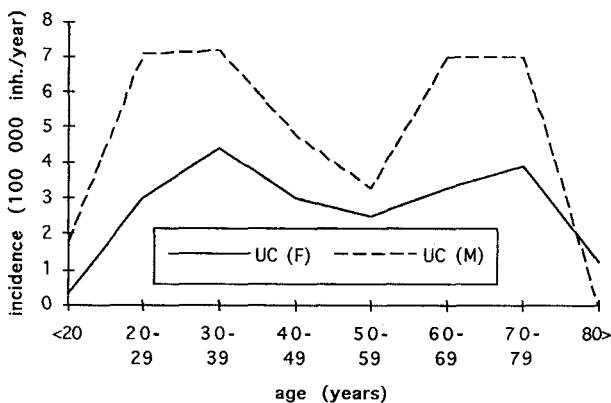


Fig. 2. — Incidence rate of ulcerative colitis by sex and age.

in both sexes: between 20 and 39 years (7.2 per 100 000) and between 60 and 79 years (7 per 100 000) for men, between 30 and 39 years (4.4 per 100 000) and between 70 and 79 years (3.9 per 100 000) for women (fig. 2).

In CD, there were significantly more women than men (sex ratio: 1,6) ($p = 0.0003$). In contrast this was the reverse in UC (sex ratio = 0,5) ($p < 0.0001$).

Manifestations of disease

At the time of diagnosis, the median age for CD (30 years) was lower than for UC (39 years); (NS).

The mean intervals from onset of symptoms to diagnosis were significantly longer in CD (6,5 months) than in UC (4,8 months) ($p = 0,017$). The diagnosis was made after four months in 52% of CD and in 68% of UC; and after one year of evolution in 18% of CD and 13% of UC respectively.

In CD, the ileum was involved in 78% of the patients; 56 (41%) had an isolated small bowel involvement and 51 (37%) combined small and large bowel. Twenty nine (21%) had an isolated large bowel involvement and ten percent of the patients had perineal lesions. This pattern of distribution was the same in

both sexes and the median age was similar in the different location groups.

In UC, 32 (29%) of the patients had an ulcerative proctitis, 63 (56%) a left sided ulcerative colitis and 15 (13%) total ulcerative colitis. The median age was similar in patients with proctitis (37) than in patients with more extensive involvement (39). The mean interval between the onset of symptoms and the diagnosis tended to be shorter in total colitis (3.4 months) than in proctitis (4.1 months) than in left colitis (5.9 months).

Family history of IBD

A family history was found in 10% of IBD patients: 15% of Crohn's disease and 7% of ulcerative colitis.

Discussion

This three years prospective study in the province of Liège has confirmed a higher annual incidence for Crohn's disease (4.5 per 100 000) than for ulcerative colitis (3.6 per 100 000). These incidence rates are comparable with those reported in northern France and in Brussels area and seem to confirm a "Belgian-French exception" (3,8,9). In contrast with other European studies the ulcerative colitis/Crohn's disease ratio was < 1 . We think that this ratio is a valid one and not secondary to an underregistration of ulcerative colitis taking into account the three years duration of the study, the frequency of proctitis and the practice of gastroenterologists in the Province of Liège.

The size of the population is small but a three years registration gave us a sufficient number of IBD cases. The duration of the study is very important because in a small population a one year registration can be misleading. This methodological problem is particularly well illustrated in our own study. As shown in table I, during the second year of the study, the total number of cases was lower, there was less undetermined colitis and the UC/CD ratio was > 1 . However during that period, the clinical pattern of IBD was similar to that described during the two other years.

The proportion of ulcerative proctitis is considered to be a good marker of the completeness of the UC collection. In our study, 29% of UC were ulcerative proctitis. This proportion is within the range (25-50%) of those published in most population based studies reporting a higher ulcerative colitis incidence (10,11). It is noteworthy that annual incidence of proctitis varied over time in our study. The increase observed in the second and third years of the study may be due either to a real increase of these form of UC during that period of time or to an increase of the recruitment by gastroenterologists. However even during these two last years the overall CD/UC ratio remained > 1 .

Only the gastroenterologists collected the new cases. We assumed, however, that all IBD patients would be seen by a gastroenterologist. This was confirmed by a validation study in the EPIDIMAD register in the

north of France (9). Most of the gastroenterologists of the province of Liège have both an hospital and a private practice like in the French Medical Care System, which is a mixture of private and public practice. Even if more than one third of the gastroenterologists did not take part in the study, it may have induced underestimation of the incidence of both diseases, but should not have influenced the CD/UC ratio. Furthermore the 29 gastroenterologists who took part in the study covered by their practice all the major gastroenterology centers of the Province.

The proportion of undetermined colitis (8%) was similar to this reported in previous studies (7,9). However the evolution of these patients, which turn eventually into UC in more than 50% of cases (12), was not followed for more than 6 months.

Main epidemiological characteristics of our IBD population are in accordance with those described in other countries, in particular in the North of France and Brussels area (8,9). These data were also similar to those published in our first one year prospective study (1).

In Crohn's disease, the age at onset, the sex ratio, the peak of incidence were similar to those in other studies (8,9,10,13,14). The ileum was the most frequent location (78%) and 41% of the patient had isolated small bowel involvement. This percentage was higher than previously published (11% to 39%) (6,7,8,13,14). The high incidence of small bowel disease may reflect a particular genetic or environmental background in the Province (15). Interestingly a high incidence of isolated small bowel disease was also been reported in Brussels area (8).

In ulcerative colitis, the age at onset, the location of the disease, the sex ratio, the two peak of incidence were also similar to those previously described (8,9,10,13).

Family history was described within the same range of those reported in previous studies (8,16,17).

In conclusion, this first prospective Belgian study over three years confirmed a high incidence of IBD in the province of Liège and a UC/CD ratio < 1 as it was observed in northern France and in the Brussels area. This seems to confirm the Belgian-French exception with a higher incidence of CD. Moreover we observed a particularly high proportion of isolated small bowel disease which may represent a particular genetic or environmental background. These results should encourage the opening of a real national register to study environmental and genetic aspects of IBD.

We thank all the gastroenterologists who had participated in this study. Bastens B., Bersoux R., Brassine A., Brixko C., Closon Th., Daenen G., Deflandre J., Defrance P., Delforge M., Demoulin J.C., Di Valen-

tin A., Etienne M., Feron P.E., Fontaine F., Frère A.M., Gast P., Gillard Ch., Kunsch J.M., Lambinet N., Lebas M., Loly J., Lu Anh H., Maisee A., Mesureur Th., Mohr E., Oger A., Thys Ch., Wain E.

References

1. LATOUR P., BELAICHE J., LOUIS E., FONTAINE F., DEFLANDRE J., LOLY J., OGER A., DEFANCE P., DI VALENTIN A., DELFORGE M., DAENEN G., LEBAS M., MOHR E., WAIN E., GILLARD C., THYS C. et la Société de gastroentérologie Liégeoise. Incidence of inflammatory bowel disease in the province of Liège (Belgium). *Acta gastroenterol. belg.*, 1996, **59** : 3-6.
2. SONNEBERG A., McCARTY D.J., JACOBSEN S.J. Geographic variation of inflammatory bowel disease within the United States. *Gastroenterology*, 1991, **100** : 143-149.
3. GOWER-ROUSSEAU C., GRANDBASTIEN B., CORTOT A., COLMBEL J.F. Epidemiology of inflammatory bowel disease : is there a "Belgian-French exception" ? *Acta gastroenterol. belg.*, 1996, **59** : 2.
4. C. GOWER-ROUSSEAU C., GRANDBASTIEN B., COLMBEL J.F., CORTOT A. Incidence des maladies inflammatoires chroniques de l'intestin, en France : le tableau s'enrichit. *Gastroenterol. Clin. Biol.*, 1997, **21** : 481-482.
5. SHIVANANDA S., LENNARD-JONES J., LOGAN R., FEAR N., PRICE A., CARPENTER L., VAN BLANKENSTEIN M. Incidence of inflammatory bowel disease across Europe : is there a difference between north and south? Results of the European collaborative study on inflammatory bowel disease (EC-IBD). *Gut*, 1996, **39** : 690-697.
6. FLAMENBAUM M., ZENUT M., AUBLET-CUVELIER B., LARPEL J.L., FABRE P., EPIMICI Gr., ABERGEL A., DAPOIGNY A., BOMMELAER G. Incidence des maladies inflammatoires du tube digestif dans le département du Puy-de-Dôme en 1993 et 1994. *Gastroenterol. Clin. Biol.*, 1997, **21** : 491-496.
7. PAGENAULT M., TRON I., ALEXANDRE J.L., CRUCHANT E., DABADIE A., CHAPERON J., ROBASZKIEWITZ M., BRETAGNE J.F. et ABERMAD. Incidence des maladies inflammatoires du tube digestif en Bretagne (1994-1995). *Gastroenterol. Clin. Biol.*, 1997, **21** : 483-490.
8. VAN GOSSUM A., ADLER M., DE REUCK M., DEVIS G., FIASSE R., VANHEURVERZWIJN R., WILLOCKX R. Epidemiology of inflammatory bowel disease in Brussels' area (1992-1993). *Acta gastroenterol. belg.*, 1996, **59** : 7-9.
9. GOWER-ROUSSEAU C., SALOMEZ J.-L., DUPAS J.-L., MARTI R., NUTTENS M.-C., VOTTE A., LEMAHIEU M., LEMAIRE B., COLMBEL L.F., CORTOT A. Incidence of inflammatory bowel disease in northern France (1988-1990). *Gut*, 1994, **35** : 1433-1438.
10. BINDER V., BOTH H., HANSEN P.K., HENDRIKSEN C., KREINER S., TORPPEDERSEN K. Incidence and prevalence of ulcerative colitis and Crohn's disease in the country of Copenhagen, 1962 to 1978. *Gastroenterology*, 1982, **83** : 563-568.
11. DELVIN H.B., DATTA D., DELLIPIANI A.W. The incidence and prevalence of inflammatory bowel disease in the North Tees health district. *World J. SURG.*, 1980, **4** : 183-193.
12. NOTTEGHEM B., SALOMEZ J.L., GOWER-ROUSSEAU C., MARTI R., LEMAHIEU M., NUTTENS M.C. et al. Que deviennent les colites aiguës inclassées : résultats d'une étude de cohorte de 104 malades dans la Région Nord Pas de Calais. *Gastroenterol. Clin. Biol.*, 1993, **17** : 811-5.
13. EKBOM A., HELMICK C., ZACK M., ADAMI H.O. The epidemiology of inflammatory bowel disease : a large population-based study in Sweden. *Gastroenterology*, 1991, **100** : 350-358.
14. LEE F.I., COSTELLO F.T. Crohn's disease in Blackpool-incidence and prevalence 1968-1980. *Gut*, 1985, **26** : 274-278.
15. LOUIS E., PIRON A., CATALDO D., FRANCHIMONT D., de GROOTE D., BELAICHE J. TNF gene polymorphism : implication in inflammatory bowel disease and functional significance. *Gastroenterology*, 1997, **112** : A 1029 (abstr.)
16. SATSANGI J., JEWELL D.P. Familial inflammatory bowel disease in relatives of patients with Crohn's disease. *Gut*, 1993, **43** : S4.9.
17. SACHAR D.B. Crohn's disease : a family affair. *Gastroenterology*, 1996, **111** : 813-815.