

ORIGINAL PAPERS

Evolution of the incidence of inflammatory bowel disease in Southern Spain

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ABSTRACT

Background: The incidence of inflammatory bowel disease is increasing in Europe and in Spain. However, there is no recent data from Southern Spain.

Objectives: To determine the evolution of the hospital incidence of inflammatory bowel disease in Southern Spain.

Material and methods: A retrospective study was performed in two hospitals in Southern Spain. Data was collected from inflammatory bowel disease patients, divided into two periods (1995-2000 and 2001-2014) and compared. The reference population from both areas was 1,011,555 inhabitants.

Results: A total of 430 patients were registered during the first period (1995-2000); 50% (215) had Crohn's disease that resulted in a cumulative incidence rate of 7.08 cases/100,000 inhabitants per year. The overall inflammatory bowel disease incidence was 3.54 cases/100,000 inhabitants per year. During the second period (2001-2014), 2,089 patients were collected; 51.7% had ulcerative colitis (1,081). The rate of cumulative incidence of inflammatory bowel disease was 14.7 cases/100,000 inhabitants per year (7.6 cases of ulcerative colitis/100,000 inhabitants/year and 7.1 cases of Crohn's disease/100,000 inhabitants/year).

Conclusions: The incidence of inflammatory bowel disease in Southern Spain has doubled in the last decade and is similar to that of the rest of the country and Europe.

Key words: IBD. Incidence. Spain. Southern Europe.

INTRODUCTION

Inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC) are chronic relapsing disorders of an unknown etiology. It has been reported that IBD affects 1.4 million individuals in the United States, 2.5 million in Europe and several million more worldwide (1). In addition, several studies have reported that the incidence of IBD has increased markedly over the latter part of the 20th century (2,3). In a recent study from New Zealand (4), the incidence rates were 1.6-fold greater than when assessed ten years earlier. The incidence of UC and CD

has increased overall in Europe from 6.0 per 100,000 person-years for UC and 1.0 per 100,000 person-years for CD in 1962 to 9.8 per 100,000 person-years and 6.3 per 100,000 person-years in 2010, respectively (5).

A worldwide North-South gradient has long been reported for IBD. Since the 1980s, this geographic distinction has been less prominent and the highest incidence rates of IBD are reported in Southern Australia and New Zealand (6,7). In addition, the West-East gradient seems to have disappeared as some articles have reported prevalence rates in East Asia that vary from 1.2 to 21.2 for CD and 5.3 to 63.6 for UC (8). Furthermore, the incidence rate of UC reported this century is higher than that of CD, which is similar to data from other Nordic countries, where UC is more frequent than CD (9,10). Some years ago, a European study (11) concluded that rates of UC in areas of Northern Europe were 40% higher than those in the south and 80% higher for CD.

The same trend shown in epidemiologic studies from other European countries has been reported in Spain. The reported incidence was much lower than that described in Northern Europe (12,13) during the 1980s but this incidence began to rise in the 1990s. The adjusted rates were 8 and 5.5 cases per 100,000 inhabitants/year for UC and CD, respectively (14). The highest rates have been reported in Northern Spain, with 12.5-13.6 cases per 100,000 inhabitants/year (15,16). These figures are very similar to those described in countries in Northern Europe and are higher than those reported in Central and Southern Spain, which suggests a North-South gradient of the illness in Spain.

The majority of epidemiologic data originates from Northern Spain, and there are few recent data with regard to incidence, prevalence and characteristics of IBD from Southern Spain. Thus, the aims of the study were to describe the evolution of the incidence of IBD in Southern Spain during two time periods and describe the main epidemiologic characteristics of IBD in this area.

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MATERIAL AND METHODS

A retrospective territory-wide population-based registry study in the Hospital Universitario Virgen Macarena, in Sevilla, Spain, and the Hospital Universitario Reina Sofía, in Córdoba, Spain, was carried out. The population of reference in both areas was 1,111,555 inhabitants. Both hospitals are included in the National Public Health System. Results were compared between two periods of time. The first period was from 1995 to 2000 and the second was from 2001 to 2014. All the patients diagnosed with IBD during these two periods were included in the study.

Data collection

The baseline data of eligible cases were retrieved from the online database system of patients with IBD in both hospitals. Clinical data and electronic medical record of all identified patients older than 14 years of age with IBD were reviewed.

All the patients included in the study signed an informed consent. Patients met the diagnostic criteria of IBD based on clinical symptoms and endoscopic or radiologic evidence and mucosal biopsies. Only five cases of indeterminate colitis were detected, all were excluded in order to simplify the results. Both centers were university and public hospitals and, although some patients were followed up in the private sector, it was estimated that only a small proportion of patients with IBD in Southern Spain remained under the care of private physicians (less than 5%, based on the data obtained from another study) (17).

The main epidemiologic characteristics data were: age at diagnosis, localization of the illness according to the Montreal classification, gender, smoking history and family background. CD and UC were classified based on the Montreal classification. In CD, the Montreal classification is used to describe the age at diagnosis (A1: less than 16 years; A2: between 17-40 years; A3: > 40 years), extension (L1: ileal; L2: colonic; L3: ileocolonic; L4: isolated upper digestive) and behavior (B1: non-structuring, non-penetrating; B2: structuring; B3: penetrating; B4: perianal disease). In UC, the Montreal classification is used to assess the extent of the colitis (S1: proctitis; S2: left side colitis; S3: pancolitis). Disease extent was assessed by colonoscopy, small bowel studies and histology based on first-time investigations. With regard to patients diagnosed with IBD before the online database system was installed, the data were retrieved from consultation notes and information of disease diagnosis was documented during subsequent visits.

Statistical analysis

Incident cases were defined as patients with newly diagnosed IBD per 100,000 inhabitants per year during the periods included in the study and according to the attended population at both hospitals (1,011,555 inhabitants). A descriptive analysis of the main demographic variables and the extension of the illness was carried out. Demographic results and nominal results were reported as percentages and frequencies. Numerical results were reported as average and standard deviation in cases of normal distribution and as median and percentiles (P25; P75) in cases of skewed distribution. Analyses were performed using SPSS 22 (IBM Corporation). The qualitative

variables were compared using the Chi-squared test (χ^2) and the Student's t test (t) when necessary (when variables with a normal distribution were compared). A statistically significant difference was set at a p value lower than 0.05.

Ethical considerations

Ethics approval was obtained from each participating hospital and signed informed consent was obtained from all patients. All patients signed informed consent when included in the electronic database.

RESULTS

A total of 2,519 patients were included in the study, 430 in the first period and 2,089 in the second; 1,223 patients had CD and 1,296 had UC. The incidence rates of the two periods were calculated and compared.

During the first period (1995-2000), an accumulated incidence of 7.08 cases/100,000 inhabitants/year was observed. The accumulated incidence of both CD and UC was 3.54 cases/100,000 inhabitants/year. During the second period (2001-2014), the rate of accumulated incidence of IBD was 14.7 cases/100,000 inhabitants/year. The incidence of UC was 7.6 cases/100,000 inhabitants/year and 7.1 cases/100,000 inhabitants/year for CD. The differences in the incidence between the two periods of time were statistically significant, $p < 0.05$ using the Student's t test (Table 1).

During the first period of the study, 24 ± 7 cases/year were diagnosed in the Sevilla area and 25 ± 7.5 (Fig. 1 and Table 2) in the Córdoba area. A total of 430 patients were registered, 50% of whom (215) were diagnosed with UC; 53% of the patients with UC and 58% of the CD patients were male; 10.6% of the patients with UC were smokers, compared to 34% of the patients with CD; and 13.7% of the patients had a family history of IBD. Among the patients with CD, 37.6% had colonic disease (L2) and 46.3% of UC patients had left colitis (E2). The age at diagnosis in 70% of patients was between 17 and 40 years of age (A2).

During the second period (2001-2014), 74 ± 23 cases/year were diagnosed in the Sevilla area and 76 ± 9 cases/year in the Córdoba area. A total of 2,089 patients were registered; 51.7% (1,081) were diagnosed with UC;

Table 1. Incidence rate: x 100,000 person-year

Incidence rate: x 100,000 person-year	1995-2000	2001-2014	p value
CD	3.54	7.1	$p < 0.05$
UC	3.54	7.6	$p < 0.05$
IBD	7.08	14.7	$p < 0.05$

CD: Crohn's disease; UC: Ulcerative colitis. IBS: Irritable bowel syndrome.

Table 2. Incidence rate/year

Incidence rate/year	CD Incidence x 100,00 person-year	UC Incidence x 100,00 person-year
1995	2.47	3.26
1996	2.86	3.06
1997	2.57	2.37
1998	4.05	3.36
1999	3.75	4.15
2000	5.53	5.04
2001	5.53	5.63
2002	4.64	7.01
2003	6.03	7.11
2004	7.5	7.41
2005	8.4	8.00
2006	9.5	7.61
2007	10.18	7.21
2008	8.9	8.79
2009	7.3	9.39
2010	6.6	10.47
2011	7.4	10.47
2012	6.3	7.8
2013	5.6	5.43
2014	5.43	4.44

CD: Crohn's disease; UC: Ulcerative colitis.

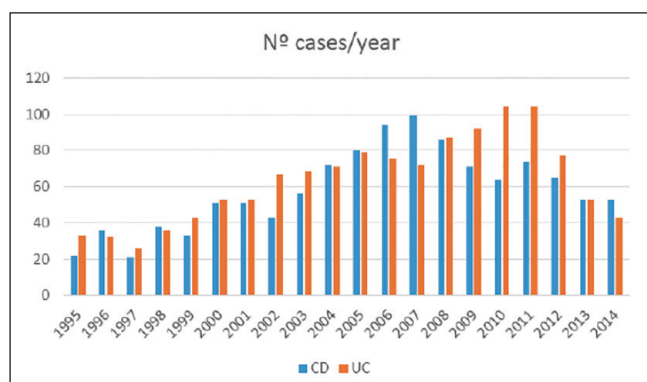


Fig. 1. No. cases/year (CD: Crohn's disease; UC: Ulcerative colitis).

57% of the CD patients were male compared to 58% of the UC patients; 12% of UC patients were smokers compared to 39.4% of the CD patients; and 22% of the total patients had a family history of the disease. Among the patients with CD, 37.7% had ileocolonic disease (L3), and among UC patients, 35% had left colon disease (E2). The age at diagnosis in 55% of the cases was between 17 and 40 years of age (A2) (Table 3).

Table 3. Epidemiological data

Epidemiological data	1995-2000	2001-2014	p value
Number of patients (n)	430	2089	
CD (n)	215	1008	
UC (n)	215	1081	
Sex (males %)			p > 0.05
CD	58%	57%	
UC	53%	58%	
Smokers (%)			p > 0.05
CD	34%	39.4%	
UC	10.6%	12%	
IBD family history (%)	13.7%	22%	p < 0.05
Disease extension (%)			
L1 (CD)	25.8%	26.6%	
L2 (CD)	37.6%	35.5%	p > 0.05
L3 (CD)	36.6%	37.7%	
E1 (UC)	31.1%	34%	
E2 (UC)	46.3%	35%	p < 0.05
E3 (UC)	22.6%	31%	
Age at diagnosis IBD (%)			
A1	10%	5%	
A2	70%	55%	p < 0.05
A3	20%	40%	

The different epidemiologic variables analyzed were compared between both periods including sex ($p > 0.05$), smoking habit ($p > 0.05$), CD extension ($p > 0.05$), UC extension ($p < 0.05$), family history of IBD ($p < 0.05$) and age at diagnosis ($p < 0.05$). Age at diagnosis, family background and extension of UC showed a statistically significant difference ($p < 0.05$). During the second period, more patients aged > 40 years were diagnosed with IBD (Table 3).

DISCUSSION

This is the first study to report incidence rates of IBD in Southern Spain using an IBD registry system. To our knowledge, this study represents one of the largest and most complete epidemiologic data set of IBD reported during this time period and several important findings have been demonstrated.

The most important observation is that the incidence of IBD in both areas has doubled in the last decade and the difference between the two periods of time was statistically significant. Overall, the current incidence of IBD is 14.7 cases/100,000 inhabitants/year, which is similar to that described in other European countries (18).

A higher average age at diagnosis of CD and UC in association with IBD was observed in this study during the second period compared with the first. However, the stratification of incidence according to age showed that IBD prominently occurs in the second to fourth decades of life, which is consistent with findings in other studies (16). The proportion of L1, L2 and L3 CD patients was similar within the two periods and was similar to that seen in other settings (18,19). A higher proportion of extensive colitis was observed in the second period analyzed in this study although the overall numbers are similar to those described in other studies (19). Of interest is the fact that among the epidemiologic variables analyzed, only age at disease diagnosis, family background and extension of UC presented differences when comparing the two periods of the study.

This study has some limitations. As it is a retrospective study, missing records are inevitable and we cannot dismiss the existence of a selection bias. In addition, the majority of the population in Spain use Public Health Care, although some patients can be followed up in private centers, and thus may not have been included. Nevertheless, we consider that the number of patients in this group is not significant (less than 5%), therefore, the results of our study should be deemed as realistic. Secondly, it is likely that cases diagnosed during the 1990s have not been counted. In addition, some patients were lost during follow-up, which would result in an underestimation of the incidence rate. Thirdly, we cannot exclude that the increase in IBD incidence during the second period is due to improved awareness of the disease and improved diagnosis due to advances in the health care infrastructure and IBD units.

Due to the lack of previous studies in these regions, a more accurate comparison of how the incidence of IBD has evolved is not possible. The design of population and prospective studies using the same methodology will aid a more exhaustive study of IBD incidence and the epidemiologic factors related to the disease. However, the findings in this study will have implications on predicted health care needs and expenditure. The progressive increase in incidence is of great interest, and these results should be considered in future economic models for the provision of optimal care and the resources offered for this chronic disease.

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CONFLICT OF INTEREST

There is no conflict to declare. The authors of the manuscript certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, seminars, membership, employment, consultancies, stock ownership or other equity interest and expert testimony or patent-licensing arrangements) or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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