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Epidemiologic study on the current incidence of inflammatory bowel disease in Madrid

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ABSTRACT

Introduction: the incidence of inflammatory bowel disease (IBD) varies widely according to geographical area and has been reported to have increased in the last few years. No data are available on the current incidence of this disease in Madrid (Spain).

Aim: to determine the incidence of inflammatory bowel disease in the area of influence of University Hospital Fundación Alcorcón (Madrid), and to compare our results with those from other Spanish and European series.

Patients and methods: a prospective, population-based study was performed to determine the incidence of IBD in the area of University Hospital Fundación Alcorcón in Madrid between 2003 and 2005. Total population: 213,587 inhabitants (177,490 older than 14 years). Crude rates and age- and sex-specific rates adjusted to the European standard population were calculated. A retrospective study (1998-2003) was also performed.

Results: a total of 69 cases were diagnosed –Crohn´s disease (CD): 35, ulcerative colitis (UC): 33, indeterminate colitis: 1– in the prospective period. Crude rates of CD and UC were 7.92 and 7.47 cases/100,000 inhabitants/year, respectively (the population aged 0-14 years). Specific rates were 8.0 (95% CI, 7.03-8.97) and 7.47 (95% CI, 6.5-8.4), respectively. Mean age at diagnosis was 31.02± 10.76 and 39.91±16.19 years for CD and UC, respectively. Incidence in the retrospective study was 7.13 and 6.22 cases/100,000 inhabitants/year, respectively for CD and UC.

Conclusions: the incidence of CD and UC in Madrid has increased in the last decades, with rates close to those in northern European countries for CD, higher than those recently published in Spanish prospective studies and similar to those previously described in Spain and southern countries for UC. Rates were higher in the prospective period than in the retrospective one

Key words: Inflammatory bowel disease. Ulcerative colitis. Crohn's disease. Epidemiology. Incidence. Madrid.

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INTRODUCTION

In the second half of the twentieth century the incidence of Crohn's disease and ulcerative colitis increased rapidly in northern European countries, and then leveled out at 10-15 cases per 100,000 inhabitants and year (1); it is still rising in developing countries. Epidemiological data published years ago showed a north-south gradient, with an incidence 3-5 times higher in the northern countries of Europe (2) and America (3) than in most southern countries, including Spain (4) (Table I).

This north-south gradient has suggested that environmental factors, and therefore different lifestyles, could play an important role in the etiology of these diseases. However, a geographical gradient can also be influenced by other factors such as differences in study design (population *versus* hospital or prospective versus retrospective), methodology used for the detection of cases, and criteria for case definition.

At present, in southern Europe, and particularly in our country, where recent epidemiological studies have been carried out (5), these differences are becoming milder. We can presume that in the future rates seen in developing countries will be similar. However, epidemiological data about the incidence in the center area of Spain are out of date (6), and show much lower rates than those reported by recent studies in Europe and other areas of Spain.

Table I. Incidence of IBD in the Spanish studies selected (4)

Author	*Region*	*Period*	*Type study*	*UC*	*CD*	*CI*	*UC/ CD*
Rodrigo et al.	Oviedo	2000-2002	P, po	9,1	7,5		1,21
Garrido et al.	Huelva	1996-2003	R+P, po	5,2	6,6		0,78
Brullet et al.	4 áreas españolas	1991-1993	P, po	8	5,5		1,45
Saro	Gijón	1994-1997	P, po	9,63	6,08	0,77	1,58
EIICEA	Asturias	1994-1997	P, po	9,52	5,95	1,08	1,6
Herráez	Extremadura	1994-1998	R, po	8,1	4,5		1,8
Monferrer	Castellón	1992-1996	R, po	6,8	1,9	0,8	3,57
Gomollón	Zaragoza	1992-1993	P, po	5,1	3		1,7
Hinojosa	Sagunto	1983-1989	R, H	4	3		1,3
Maté et al.	Madrid	1981-1988	P, po	3,16	1,87		1,68
Salmerón	Granada	1979-1988	R, po	2	0,9		2,2
Ruiz Ochoa	Galicia	1976-1983	R, po		0,8		

P: prospective; R: retrospective; Po: poblational; H: hospital (adapted from Saro C, Ochoa Ruiz V. Conceptual definitions of inflammatory bowel disease. In: Gassull MA, Gomollón F, Obrador A, Hinojosa J, editors. Inflammatory Bowel Disease. II edition. Madrid; 2002. p. 7-19).

Due to the lack of recent studies in our region, a description of the current situation regarding this disease would be very valuable in order to improve the organization of Gastroenterology and Inflammatory Bowel Disease Units, and as reference to calculate costs of care for these patients. The objective of this study was to evaluate the current incidence of IBD in Madrid, focusing on the area of influence of our hospital, located in the southwestern stretches of the Community.

PATIENTS AND METHODS

To determine the incidence of IBD in the reference area of our hospital, University Hospital Fundación Alcorcón in Healthcare Area 8 of Madrid, we conducted a population-based prospective study by collecting all patients diagnosed with ulcerative colitis, Crohn's disease and otherwise nonspecified IBD (indeterminate colitis) during the inclusion period, which covered from July 1, 2003 to December 31, 2005.

We also carried out a retrospective study including all IBD patients diagnosed from January 1998 to July 2003, and we compared incidence rates between these two study periods.

Population area

University Hospital Fundación Alcorcón provides care for 19 municipalities in the southwestern region of Madrid, with a total of 213,587 inhabitants (according to the 2004 census). Fifty percent are males, and 177,750 inhabitants are adults over 14 years. This area meets the conditions prescribed by the European study (European Collaborative Study on the Epidemiology of Inflammatory Bowel Disease) – it is a geographical area with a defined population and broad coverage, and has the appropriate medical facilities and diagnostic tools. It also permits good coordination between the various levels of care.

Health care in this area is mostly public. Private health care is mainly represented by Hospital del Sur in Alcorcón. Outside this facility the presence of private medicine directly related to IBD was negligible during the study period. To minimize lost cases we contacted primary care physicians to refer to our department all patients with suspected IBD or diagnosed with IBD in any other center.

We included as incident cases all new patients diagnosed with IBD during the study period who resided in the area at least during the previous year. To include diagnosed patients we carried out a systematic review of the records of all hospital units involved.

Prior to inclusion, the clinical history of cases was reviewed, and we excluded those that did not meet the diagnostic criteria by Lennard-Jones (7), or if there were reasonable doubts about the diagnosis. Indeterminate colitis (IC) was considered when there were clear signs of IBD but insufficient evidence to establish a definitive diagnosis with UC or CD.

Once the validated information was entered into the database designed for this purpose (Microsoft Access) unique identifiers replaced personal identification data, and this data set was used for all analyses to ensure patient confidentiality. For the statistical evaluation of results the SPSS (version 13.0) program was used.

The crude incidence of UC, CD and CI were calculated as the number of new cases per 100,000 inhabitants

per year. We used the direct method for standardization (European standard population: EU 25 in 2000) to adjust incidence rates for different ages (ten-year intervals from an initial range between 15 and 25 years) and genders. Most studies excluded pediatric populations (< 15 years), so calculations excluded this group. Truncated (15-64 yr) age-standardized incidence rates were used to compare our results with those in the European standard population. Confidence intervals (CI) for incidence rates were assessed with a 95% level of probability by using a Poisson distribution or normal distribution. Differences between groups were examined using a two-sided approach, with $p < 0.05$ considered significant.

RESULTS

A total of 69 new patients were diagnosed as having IBD during the 2-year prospective enrollment period (July 1, 2003 to December 31, 2005), of which 35 had CD, 33 UC, and one undetermined colitis. The UC/CD ratio was 0.94. The mean annual incidence rate of CD was 7.92 (8.144 and 7.7 in females and males, respectively). The annual incidence of UC was 7.47 per 100,000 inhabitants (7.7 and 7.14 for females and males, respectively). Figure 1 shows overall age and gender-specific incidence rates for both diseases.

Adjusted incidence rates for CD and UC after standardization were 8.00 (95% confidence interval (CI): 7.03-8.97) and 7.47 (95% CI 6.5-8.4), respectively. Truncated rates for the population aged 15-64 years were 9.12 per 100,000 inhabitants and year (95% CI, 8.15-10.09) in CD patients, and 7.53 (95% CI, 6.59-8.47) in UC patients (Table II).

Crude annual rates per 100,000 inhabitants in the retrospective period (1998-2003) were 7.13 for CD (6.32 and 7.94 in women and men, respectively), and 6.22 for UC (7.46 and 4.98, respectively). These are no significant differences ($p > 0.05$), but there is a trend towards an increased incidence over the study interval 1998-2003. Crude incidence of IC was 0.22 cases per 100,000 inhabitants per year, which will be excluded from the following tests performed.

Mean age in CD patients was 31.02 ± (SD = 10.76) years (range 17-73), significantly lower than patients with UC: 39.91 (SD = 16.54) years (range 26-77), $p < 0.01$ (Figs. 1, 2 and 3). Mean age in patients diagnosed in the retrospective period (1998-2003) was higher for both diseases, but without significant differences: 36.10 (SD = 16.19) years ($p = 0.12$) in CD patients, and 43.35 (SD = 17.64) years ($p = 0.14$) in UC.

Table II. Adjusted incidence rate for UC and CD per 100,000 inhabitants at 15-64 years, reported by the European Collaborative Study on Inflammatory Bowel Disease, several Spanish prospective, population-based studies, and the present study

EC	*Men*	*Women*	*Total*
Europe			
North	6.2 (4.2-8.1)	7.9 (5.9-9.8)	7.0 (4.2-9.8)
South	3.8 (1.9-5.8)	4.0 (2.0-6.0)	3.9 (2.1-6.7)
Spain			
Brullet et al.	6.0 (3.9-8.0)	5.0 (3.1-6.9)	5.5 (4.1-6.9)
Rodrigo et al.	6.2 (1.4-11)	8.8 (3.2-14.4)	7.5 (3.8-11.2)
Arin Letamedia et al.			7.79 (6.25- 9.94)
Our study	9.34 (8.37-10.31)	8.99 (8.02-9.96)	9.12 (8.15-10.09)
UC	*Men*	*Women*	*Total*
Europe			
North	12.5 (10.5-14.5)	11.1 (9.2-13.1)	11.8 (9.0-14.6)
South	10.3 (8.4-12.3)	6.9 (5.0-8.9)	8.7 (5.9-11.5)
Spain			
Brullet et al.	9.5 (6.8-12.2)	4.6 (4.3-8.6)	8.0 (6.3-9.7)
Rodrigo et al.	9.7 (3.7-15.7)	8.5 (3.1- 14)	9.1 (5-13.1)
Arin Letamedia et al.			13.19 (11.15- 15.39)
Our study	6.34 (5.4-7.28)	8.06 (7.12-9.03)	7.57 (6.63-8.1)

Adapted from Rodrigo L, et al. Incidence of inflammatory bowel disease in general population in the area of Oviedo. Rev Esp Enferm Dig 2004; 96: 296-305.

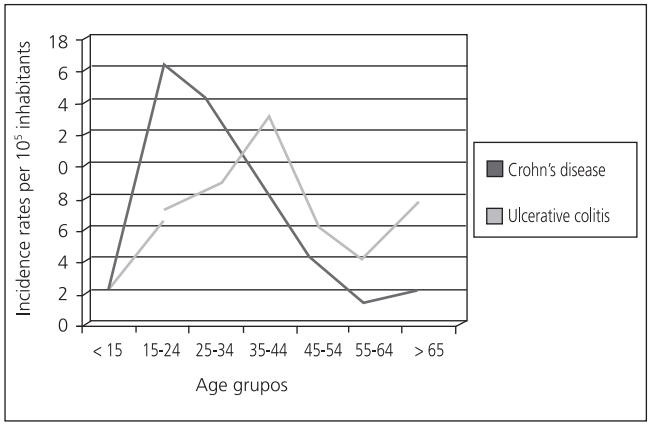

Fig. 1. Age-specific incidence rates per 100,000 inhabitants per year for Crohn´s disease and ulcerative colitis.

DISCUSSION

The main finding of this study is the significant increase in the incidence of IBD in Madrid over previous studies, updating the information on incidence in this Spanish region with a population of approximately 6 million people and expanding. The incidence of IBD has changed substantially in recent decades in Spain alongside the socio-economic development of the last twenty years, resembling rates seen in other European areas. In our region, Maté et al. (6) reported annual rates per 100,000 inhabitants of 3.15 to 3.25 for UC and 0.86 to 1.87 for CD two decades ago, much lower than those described more recently in other areas of our country. As

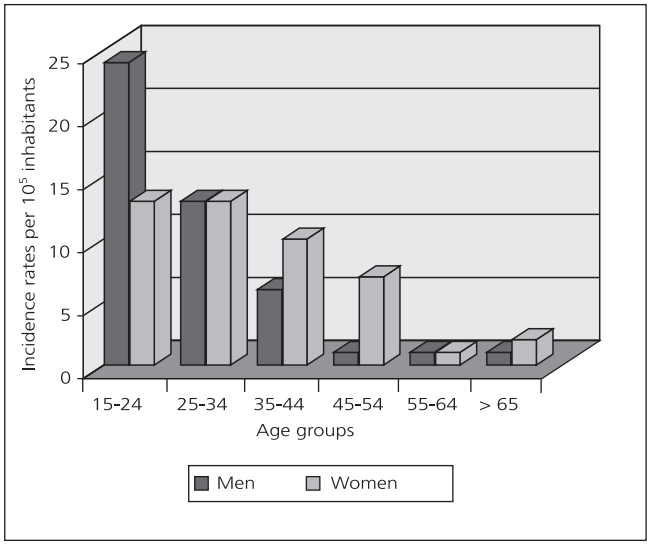

Fig. 2. Specific incidence rates adjusted for age and sex, expressed in number of inhabitants cases/100,000/year for Crohn's disease.

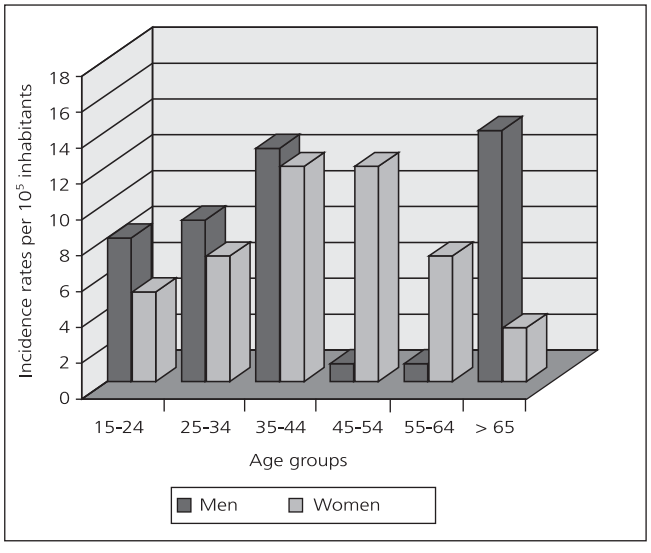

Fig. 3. Specific incidence rates adjusted for age and sex, expressed in number of inhabitants cases/100,000/year for ulcerative colitis.

we expected when we designed our study, the incidence of IBD has increased significantly: it has tripled for CD and doubled for UC.

The increase in prevalence may be due to several factors (5): universal high-quality medical services, widespread use of endoscopic techniques, and the creation of specific IBD units (8). Moreover, prospective and population-based epidemiological studies involve a significantly lower loss of cases than retrospective or hospital-based ones, which exhibit a clear selection bias and prevent data from being extrapolated to the general population. The sharp increase in incidence detected in our study cannot be solely attributed to these reasons, and reflects a real increase in the frequency of these diseases. Also, we have detected an increased, but not significant, incidence in the period 2003-2005 over the previous 1998-2003. In this case the difference can be justified by the retrospective design of the study in this period.

Several studies (9-12) describe a relationship between the increased incidence of IBD in recent decades and socio-economic status growth in a country, and suggests that some environmental factors (diet, industrialization and development) may be linked to the pathogenesis of the disease.

To compare our results with those from the European Cooperative Study (2), we used the truncated rates for the population aged 15-64, adjusted by age and sex. Regarding UC, we found an incidence rate of 7.53/100,000 inhabitants, which is similar to that reported in southern Europe, and lower than in northern areas (13-17). The truncate rate of CD was 9.12, higher than the incidence of those Spanish areas which participated in that study. It is also higher than the average incidence in countries of northern and southern Europe (Table II). However, we cannot ignore the fact that there ten years separate our study from the European one, and incidence in those participating countries may have increased as well (18).

We have also compared our results with other epidemiological data from Spain (19-28) (Table I). The incidence of CD is lower in all of them, while recent publications show higher rates than those in our study for UC. Specifically, we have analyzed the latest studies published by Rodrigo et al. (25) in Oviedo between 2000 and 2002, and by Arin Letamendia in Navarre between 2001 and 2003 (Table II). The incidence of CD in our study is clearly superior, but not in the case of UC. This could be due to a lost of cases with mild disease (mainly ulcerative proctitis); however, the proportion of distal colitis among our patients, published previously (29), is similar to that observed in most studies (19,20,30,31), about 30%.

This relative decrease in the frequency of UC – in our work the ratio CU/CD is 0.94, while in other Spanish populations ranges from 1.5 to 2 (14-18) – is observed also by other authors, like Loftus et al. (32) in the U.S., and may suggest that while the incidence of CD continues to increase, that of UC is stable or decreasing.

Regarding gender distribution, including all patients diagnosed since 1998, the male/female (M/F) ratio is 1.28 in CD, similar to Arin et al. (5), and 0.7 in UC. These results are opposed to most previous series, in which CD was more common in women, and UC more frequent in men, and may be due to environmental factors, hormonal factors or changes in the pattern of current smoking according to sex (33).

Mean age at diagnosis in patients with CD is 31 years, significantly lower than that of UC, which coincides with the behavior previously suggested (1,4). Focusing our attention on mean age at debut, during 2003-2005 it was lower, although without statistical significance, than in

1998-2003. This can be interpreted as an effect of anticipation in the onset of disease, consistent with an increased incidence in the pediatric age (4). Regarding specific incidence rates by age, CD in our study shows a similar pattern to that described so far, with a peak incidence for both genders in the age group of 15 to 24 years, and a progressive decrease later. In the case of UC, the highest peak of incidence occurs in the group between 35 and 45 years; however, in the European Cooperative Study it was in the group between 25 and 34 years. A bimodal distribution has been described for this disease, but has not been confirmed by all studies. We found only this second peak of incidence in male patients older than 65 years, but not in women, where incidence decreases gradually.

In conclusion, our study reveals a significant increase in the incidence of both UC and CD to the south of Madrid when compared to previous years, thus confirming the trend observed in other Spanish areas. In this study the incidence of CD is the highest described so far in our country, and one of the highest in Europe, reflecting a relative increase in frequency with respect to UC.

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