# Increasing Incidence of Pediatric Inflammatory Bowel Disease in Spain (1996–2009): The SPIRIT Registry

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**Background:** Although pediatric inflammatory bowel disease (IBD) diagnosis has increased in the last decades in Spain, there are no consistent epidemiologic data. Our aim was to describe the changing pattern of pediatric IBD incidence in Spain in the last 14 years.

**Methods:** A retrospective survey of patients diagnosed below 18 years of age in the period 1996–2009 was performed. Patients' data were obtained from the hospitals' databases. To avoid reduced accrual of cases diagnosed by adult physicians, adult IBD units in referral centers were invited to participate. Seventy-eight centers participated in our survey. Rates of incidence were calculated using age-stratified population-based epidemiologic data. Incidence rates were compared for the last 14 years (1996–2009).

**Results:** In total, data from 2107 patients were obtained: 1,165 Crohn's disease (CD, 55.3%), 788 ulcerative colitis (UC, 37.4%), and 154 IBD unclassified. The sex distribution was 56.4% male, with higher predominance for CD (59.3%) as compared to UC (52.8%) and IBD unclassified (53.2%) ($P = 0.012$). The median age at diagnosis was 12.3 years (p25–75 9.7–14.6) with significant differences between diseases. IBD incidence increased from 0.97 to 2.8/100,000 inhabitants <18 years/year in the study period. Although this increase is more evident for CD (from 0.53 to 1.7), UC has also risen considerably (0.39 to 0.88).

**Conclusions:** This is the first attempt to calculate the current incidence of pediatric IBD in Spain. A significant increase of incidence rates in the study period was observed. In the last 14 years pediatric IBD incidence has almost tripled, with a more important CD increase.

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**Key Words:** pediatric inflammatory bowel disease, pediatric Crohn's disease, pediatric ulcerative colitis, epidemiology, increasing incidence

A growing incidence of inflammatory bowel disease (IBD) worldwide has been recently reported.[1] Whereas it was classically referred as a disease associated with Western industrialized countries, different studies have shown rising incidence and prevalence rates in other regions, including Asia[2] and other underdeveloped countries.[3] Different environmental factors (including "westernization" of societies) have been postulated as responsible for such an increase. This changing pattern of IBD epidemiology has also been described in the Mediterranean area, with the more recent data of the Spanish adult population confirming this fact.[4,5]

A significant increase of pediatric IBD diagnosis has also been recently reported in different areas,[6–9] including some studies performed in eastern[10] and southern Europe.[11] Generally, the highest incidence figures worldwide for pediatric IBD have been reported in the northern parts of North America and in Scandinavia. Benchimol et al[12] recently published an exhaustive systematic review of the international epidemiological trends of pediatric IBD available in the literature. The authors conclude that globally rising trends of pediatric IBD have been demonstrated in both developed and developing countries, although most countries lack accurate estimates.

Very few series have previously studied specifically the epidemiology of pediatric IBD in Spain, all being limited to regional areas and most of them including patients up to 14 years of age. Some of these studies were published in the 1990s. Fernández et al[13] in 1994 published a registry of new patients diagnosed in the period 1984–1990 performed in five regions in the north of the country (Navarre, Basque Country, Aragon, La Rioja, and Cantabria). The estimated incidence for IBD, Crohn's disease (CD), and ulcerative colitis (UC) were 0.57, 0.38, and 0.19/100,000 inhabitants less than 14 years/year. The rest of the pediatric data available are mainly limited to a single region and most of them are included in general population studies.[14–16] In the most recent article, Arín et al in 2008 published a prospective, population-based study of IBD incidence in all age groups in Navarre (northern Spain) performed

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between 2001 and 2003. Globally, the authors confirmed an increase in IBD incidence as compared to previous data in the same region.[18] This study included new cases of pediatric age (including children from 0 to 14 years), showing an incidence of 2.6, 1.74, and 0.87/100,000 inhabitants/year for global IBD, CD, and UC, respectively. Therefore, this is the first attempt to calculate the nationwide current incidence of pediatric IBD in Spain.

## Objectives

Our aim was to describe the changing pattern of pediatric IBD incidence in Spain in the last 14 years.

# MATERIALS AND METHODS

This was a collaborative, multicenter study called SPIRIT (Spanish Pediatric IBD Retrospective study of Incidence Trends). The study was planned and performed inside the IBD working group of the Spanish Society for Pediatric Gastroenterology, Hepatology, and Nutrition (SEGHNP). In our society not only all the referral pediatric IBD units are represented, but also all the physicians dedicated to pediatric gastroenterology in any setting.

An initial retrospective survey of newly diagnosed IBD patients below 18 years of age in the period 1985–2009 was planned. IBD diagnosis was made according to standard clinical, endoscopic, histological, and radiological criteria.[19,20] Patients' data at diagnosis were obtained from the different hospitals' own databases. In Spain, due to regional variations, pediatric care is offered up to different ages in different settings: most of the pediatric units in general hospitals follow the pediatric patients up to 14 or 16 years of age, with older patients being controlled by the adult services, while some exclusive pediatric centers (without adult services inside the hospital) follow them up until they are 18 years old, when they are transferred to an adult unit in a general hospital.

In order to obtain the most reliable data and to avoid reduced acquisition of cases diagnosed by adult physicians, adult IBD units in referral centers were also invited to participate. With this purpose, every investigator working in a general hospital with an adult IBD unit looked for the collaboration of their adult gastroenterology colleagues. More than 400 patients were recruited from their registries. Moreover, 12 referral adult IBD units located in hospitals without pediatric assistance and that provide wide coverage throughout the country entered their data in our registry. Therefore, the possibility of pediatric IBD patients controlled in adult services being out of this registry was minimized. The Spanish Working Group in Crohn's and Colitis (GETECCU) since May 2007 promotes a large prospectively maintained Spanish database of IBD patients (ENEIDA),[21] from where it is possible to get information about the year and age at diagnosis of every patient. At the moment, 43 adult IBD units, representing more than 85% of all the referral centers, participate in ENEIDA, which includes more than 18,000 patients. As the majority of the patients diagnosed at a pediatric age will be followed up in a specialized adult unit after becoming adults, the information obtained from these adult registries can be quite useful. A specific search of these data in the centers collaborating in ENEIDA was performed.

Both for preserving confidentiality and for avoiding duplicates, every patient was identified in the registry with three letters (initial letter of the name and the two surnames used in Spain) and the date of birth indicated as ddmmyy. Patient's epidemiological and clinical data at diagnosis were obtained: sex, age, type (CD, UC, IBD type unclassified [IBDU]) and extension of the disease according to the Montreal Classification.[22] We decided not to include data from possible upper involvement or perianal involvement in CD *(L4* and *p* variants of the Montreal Classification), as we considered these could be not very reliable due to the retrospective nature of the study and the period reviewed starting before the Porto Criteria publication.[19] We assumed many of the patients diagnosed before that date would have not had an upper endoscopy performed unless there were significant upper symptoms.

Rates of incidence were calculated using population-based epidemiologic data obtained from the municipal register.[23] This source provides the official population figures of all municipalities in Spain standardized at January 1 each year. The results are available yearly from 1996 and are classified by age. It is not possible to obtain reliable pediatric age-stratified epidemiological data before that date. Moreover, as we started to analyze our data, we noticed that the results from 1985 to 1995 were quite low. At that time, concerns were raised that the accrual rate in those early years was much lower than the number of true pediatric IBD cases being diagnosed at that time and not represented due to an incomplete accrual in the pediatric IBD service model. Therefore, our final aim was to provide robust data of Spanish pediatric IBD from 1996 to 2009.

Incidence rates were calculated and compared for the last 14 years (1996–2009). From 1996 to 2009 the Spanish population age <18 years of age has remained quite stable: in 1996 the number was about 8.16 million and in 2009 the number was about 8.19 million. The population of Spain at the end of 2009 was 47.0 million. Therefore, the population age <18 years represented at the end of the study period 17% of the total Spanish population.

We also compared incidence rates in the different Spanish regions, in order to confirm the north–south gradient that has also been described not only among different countries but inside the same country.

The study was approved by the Ethic's Committee of the first author's center, as representative of the rest of the hospitals.

## Statistical Analysis

A chi-square test was applied for category data; Student's *t*-test, Mann–Whitney U-test, and one-way analysis of variance

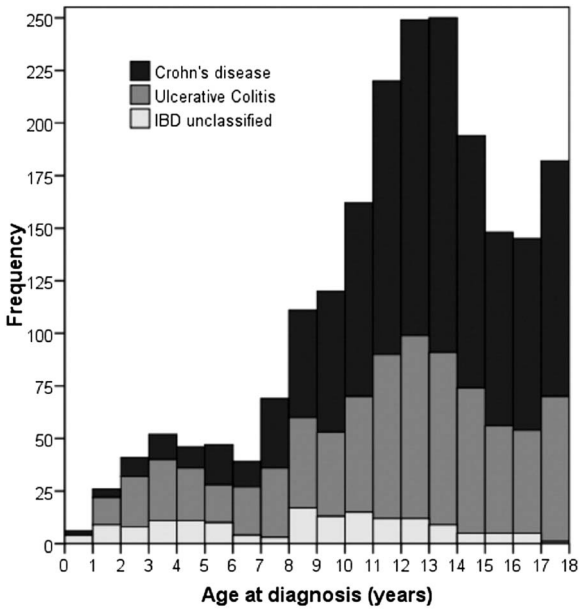


FIGURE 1. Age distribution of the diagnosed cases (1996–2009).

(ANOVA) were performed to compare continuous variables. Significance was set at $P < 0.05$. SPSS v. 19.0 (Chicago, IL) was used for statistical analysis.

## RESULTS

Seventy-eight IBD centers, both pediatric and general, participated in our survey. All the 35 referral pediatric IBD units from tertiary centers in Spain, 31 small pediatric gastroenterology units in regional hospitals representing 90% of these hospitals in which pediatric IBD patients can be followed and that usually work in a shared care network with referral IBD units, and 12 adult hospitals without pediatric assistance entered their data. From 1996 to 2009, we obtained data from 2107 patients: 1165 CD (55.3%), 788 UC (37.4%), and 154 IBDU (7.3%).

The majority of our patients were Caucasian (95.4%), 44 were of gypsy ethnicity (2.1%), and 2.5% were immigrants born abroad (mainly northern Africa, Latin-America, and Western Europe).

Regarding sex distribution, 56.4% of the patients were male and 43.6% female, with a higher male predominance for CD (59.3%) as compared to UC (52.8%) and IBDU (53.2%) ($P = 0.012$).

Global median age at diagnosis was 12.3 years (p25–75 9.7–14.6) (Fig. 1). Median age for CD was 12.9 years (p25–75 10.7–15), for UC 12.0 (p25–75 8.7–14.5), and for IBDU 9.0 (p25–75 4.4–14.5). We observed significant differences between CD and IBDU ($P < 0.001$) between CD and UC ($P < 0.001$) and between UC and IBDU ($P < 0.001$).

We divided the patients into three groups based on age of diagnosis: group 1 from 0–5 years, group 2 from 6–12, and group 3 from 13–17. The highest number of cases of IBD was observed in the second and the third age group (46% and 42.3%, respectively), with only 10% of the patients being diagnosed below 5 years of age. The infantile IBD group (<2 years at diagnosis) included 32 patients (1.5%). If we differentiate these groups, we can observe there is a predominance of UC and IBDU forms in the first 5 years of life (50% and 24.3%), whereas in groups 2 and 3, CD is the most frequent disease (55.2% and 62.5%, respectively). If we consider that 33.9% of the CD patients diagnosed under 5 years of age had isolated colonic disease, we can see that the total amount of colonic-only IBD in group 1 represents 83% of these patients. IBDU diagnosis is related to younger age at presentation and decreases in older children (24.3% in group 1, 7.8% in group 2, and 2.7% in group 3) ($P < 0.001$) (Table 1).

Disease distribution according to the Montreal Classification was: CD: L1 (isolated ileal or ileocecal involvement) 26.5%; L2 (isolated colonic involvement): 16.6%; L3 (ileocolonic disease) 56.9%. UC: E1 (proctosigmoiditis) 10.3%, E2 (left-sided colitis) 26%, E3 (extensive colitis) 63.7%.

We also tried to relate the disease distribution to age at presentation. For CD, L3 is the most frequent localization in groups 2 and 3, whereas colonic CD is predominant in younger children. We also found the highest frequency of isolated ileal or ileocecal disease in group 3 (30.3%) as compared to group 1 (25%) and group 2 (22.6%) ($P < 0.001$) (Table 2). Regarding UC, extensive colitis is the most frequent presentation in the three groups, with significant predominance in group 1 (76.1%) as compared to group 2 (67.4%) and group 3 (55.3%) ($P < 0.001$) (Table 3).

We observed an important increase of the diagnosed cases per year in the study period. In 1996, 80 new cases of IBD in

**TABLE 1.** Disease Distribution of IBD Types According Age Groups (1996-2009)

| | Age Group | | | |
|---|---|---|---|---|
| | Group 1 (0-5 years) | Group 2 (6-12 years) | Group 3 (13-17 years) | Total |
| CD (% within age group) | *n*=56 (25.7%) | *n*=535 (55.2%) | *n*=574 (62.5%) | *n*=1,165 (55.3%) |
| UC (% within age group) | *n*=109 (50.0%) | *n*=359 (37.0%) | *n*=320 (34.8%) | *n*=788 (37.4%) |
| IBDU (% within age group) | *n*=53 (24.3%) | *n*=76 (7.8%) | *n*=25 (2.7%) | *n*=154 (7.3%) |
| Total | *n*=218 (10.3%) | *n*=970 (46.0%) | *n*=919 (42.3%) | *n*=2,107 (100%) |

**TABLE 2.** Location Intestinal Involvement in Pediatric CD (Ileum and Colon Only) According to Age Group (1996-2009)

| | Age Group | | | |
|---|---|---|---|---|
| | Group 1 (0-5 years) | Group 2 (6-12 years) | Group 3 (13-17 years) | Total |
| L1 (ileal or ileocecal) (% within age group) | *n*=14 (25.0%) | *n*=121 (22.6%) | *n*=174 (30.3%) | *n*=309 (26.5%) |
| L2 (colonic) (% within age group) | *n*=19 (33.9%) | *n*=87 (16.3%) | *n*=87 (15.2%) | *n*=193 (16.6%) |
| L3 (ileocolonic) (% within age group) | *n*=23 (41.1%) | *n*=327 (61.1%) | *n*=313 (54.5%) | *n*=663 (56.9%) |
| Total | *n*=56 (4.8%) | *n*=652 (55.9%) | *n*=574 (49.2%) | *n*=1165 (100%) |

children below 18 years were recognized, whereas in 2009, 227 new cases were diagnosed. This represents a 2.8-fold increase. This increase was observed both for CD and for UC, while the IBDU cases have remained more stable. Figure 2 shows the number of new diagnoses of CD, UC, and IBDU/year in this period. A continuous increase of the total number of new diagnoses/ year can be observed.

Overall IBD incidence increased from $0.97/10^5$ inhabitants under 18 years in 1996 (95% confidence interval [CI] 0.8–1.2) to 2.8 in 2009 (95% CI 2.4–3.2) ($P < 0.001$). If we analyze the trend in incidence comparing the first half of this 14-year period (1996–2002) to the second half of it (2003–2009), we found statistically significant differences between them: 1.4 vs. $2.5/10^5$ inhabitants under 18 years ($P < 0.001$). CD incidence increased from 0.53 (95% CI 0.3–0.7) to 1.7 (95% CI 1.45–2.03) ($P < 0.001$) and UC incidence has also significantly increased: from 0.39 (95% CI 0.27–0.55) to 0.88 (95% CI 0.69–1.1) ($P < 0.001$). Both overall IBD and CD incidence at the end of the study period is 3-fold higher than the initial incidence, and UC incidence is also more than 2-fold higher in our country as compared to 14 years ago (Fig. 3).

Comparing incidence rates from the different regions in Spain, we found a higher incidence rate in the northern half of the country as compared to the south (Fig. 4). We aimed to calculate a north–south gradient statistically; to do so, we used the 2009 incidence rates of every region and divided our country in two imaginary halves by a line crossing the center of Spain (Madrid). We found significant differences between the northern half (including Galicia, Asturias, Cantabria, Basque Country, Navarre, La Rioja, Aragon, Catalonia, Castilla-León, and Madrid) and the southern one (including Castilla-La Mancha, Extremadura, Comunidad Valenciana, Murcia, Andalusia, Balearic, and Canary Islands): 3.5 vs. 2.0/100,000 inhabitants <18 years ($P < 0.001$). In the year 2009, Asturias (7.36), Navarre (5.36), and Catalonia (4.08) showed the highest incidences of all the different regions.

## DISCUSSION

Our data confirm the suspected increase of pediatric IBD incidence in Spain. Although pediatric gastroenterologists in our country have been facing a growing number of diagnosed patients in the last years,[24] until now we did not have total consistent epidemiologic data. Considering the important rise of both CD and UC in our pediatric population (3- and 2-fold increases in the period 1996–2009, respectively), our results can be compared to the ones of previous studies performed in the last century in two of the countries with the highest IBD prevalence (Wales and Scotland). Both studies have been classically referenced as paradigms of IBD increase in children. From 1983 to 1993, the incidence (per 100,000 per year) of CD in Welsh children doubled (1.3 vs. 3.11) with no corresponding increase in UC.[25] A Scottish cohort of hospitalized pediatric IBD patients noted a 3-fold increase in CD incidence from 1968 ($0.66/10^5$) to 1983 ($3.11/10^5$), with essentially no change in incidence of UC

**TABLE 3.** Extent of UC Among Different Age Groups (1985-2009)

| | Age Group | | | |
|---|---|---|---|---|
| | Group 1 (0-5 years) | Group 2 (6-12 years) | Group 3 (13-17 years) | Total |
| E1 (proctosigmoiditis) (% within age group) | *n*=7 (6.4%) | *n*=27 (7.5%) | *n*=47 (14.7%) | *n*=88 (10.3%) |
| E2 (left-sided colitis) (% within age group) | *n*=19 (17.4%) | *n*=90 (25.1%) | *n*=96 (30.0%) | *n*=205 (26.0%) |
| E3 (extensive colitis) (% within age group) | *n*=83 (76.1%) | *n*=242 (67.4%) | *n*=177 (55.3%) | *n*=502 (63.7%) |
| Total | *n*=109 (13.8%) | *n*=359 (45.5%) | *n*=320 (40.6%) | *n*=788 (100%) |

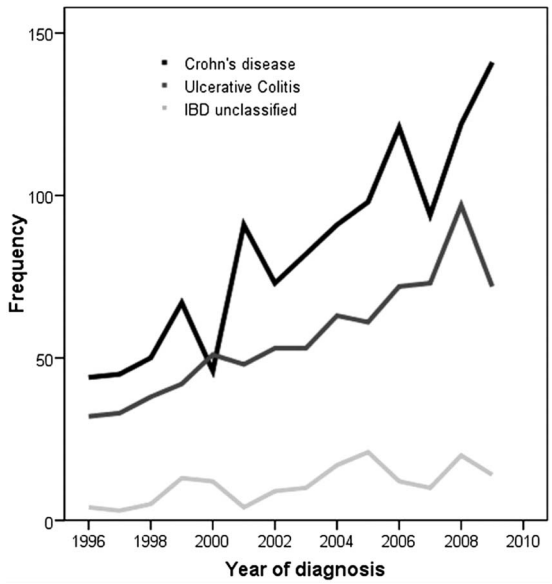


FIGURE 2. Evolution of the diagnosed cases in the study period (1996–2009).

(1.91 and 1.56, respectively).[26] A follow-up study aimed at documenting the incidence of pediatriconset IBD between 1981 and 1995 examined the temporal trends of IBD between 1965 and 1995.[27] The incidence of pediatric-onset CD kept on rising, with the prevalence increased by 30% since 1983. The authors further concluded that, unlike the previous reports, the incidence of childhood-onset UC was also increasing. These tendencies observed in Wales and in Scotland at the end of the past century seem to be reproducible in the countries of the Mediterranean area 10–15 years later.

The reported trend in Scotland has been recently confirmed in a new study that shows that IBD continues to rise, with a statistically significant 76% increase since the mid-1990s.[28] Furthermore, the authors found a significant reduction in the median age at diagnosis, from 12.7 years to 11.9 years between the two periods (1990–1995 and 2003–2008), with a continued male preponderance.

In our study the number of CD diagnoses is higher than UC (55.3% vs. 37.4%). This result is in accordance with the ones reported in the Anglo-Saxon literature, although in contrast with previous studies performed in another country of the Mediterranean area, Italy.[11] Castro et al[11] reported in their study the results of a national register of IBD incidence in the pediatric population in the period 1996–2003. They observed a UC predominance (52% vs. 40% CD), in accordance with previous Italian studies performed in the adult population.[29] Similar results have been recently reported in Finland.[30]

It is estimated that pediatric-onset IBD represents 20%–25% of the global IBD incidence. Therefore, pediatric incidence should represent one-third of the adult one. Our data confirm this trend, as the most recent reported data of adult IBD annual incidence in Spain published in 2001 was $5.7/10^5$ inhabitants.[5] The pediatric incidence in 2001 was 1.95, which is exactly 34% of the adult.

We have also shown a certain north-south gradient, with the north of Spain having an incidence >3 and the southern half of the country <3. Studies performed in adults in our country find the same trends. This gradient between the north and the south of our country was first reported in 1998; a prospective nationwide study showed important differences in IBD incidence between Catalonia (15/100,000) and Andalucia (10.8/100,000).[31] Although no later comparative nationwide data have been published, other studies have also confirmed the higher incidence trends in northern regions as compared to the south of the country.[16,32,33]

Regarding sex and age distribution, we found a similar pattern to the one described in the literature. For CD overall, the incidence among females exceeds that among males by 20%–30%.[34] In contrast, however, several studies restricted to pediatric-onset CD document a male-to-female preponderance (nearly 1.5;1).[35–37] Furthermore, no gender differences in the epidemiology is seen for UC and IBDU. A similar male preponderance in

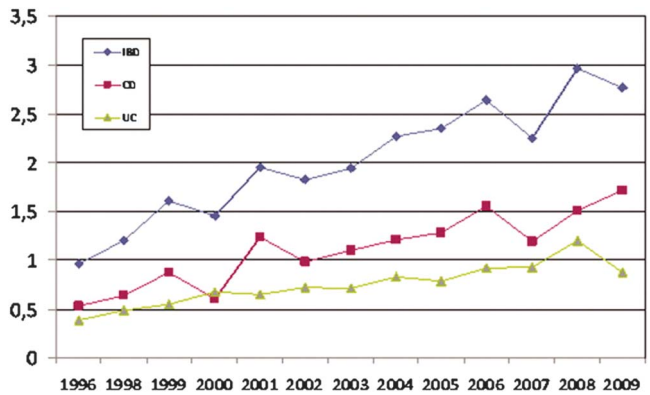


FIGURE 3. Changes in annual incidences during the study period (per 100,000 inhabitants <18 years).

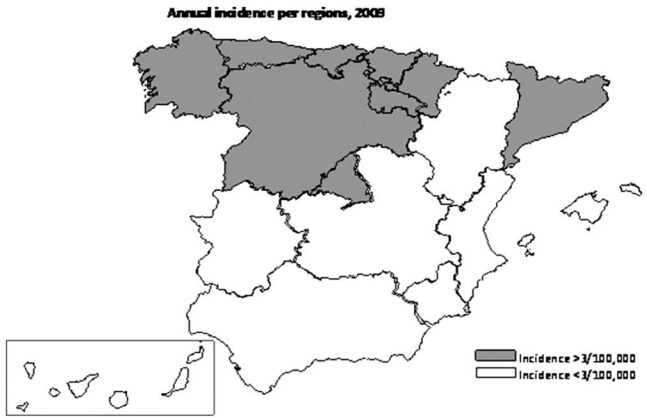


FIGURE 4. Regional differences in IBD incidence in the year 2009. A north–south gradient can be observed.

CD was found in our study (59.3% male, 40.7% female), with no differences in UC and IBDU.

Median age at diagnosis in our series was 12.3 years, which is also in accordance with the previously reported data. Sawczenko et al,[38] in a 1-year-long survey of 739 newly diagnosed pediatric IBD patients under 16 years in Great Britain and Ireland, also reported a median age of 12,6 years, with significant differences between CD (12.9) and IBDU (11.6) ($P = 0.021$) and no differences between CD and UC (12.3) ($P = 0.059$). In contrast, we observed significant differences among the three diseases, with a significant older age at diagnosis in CD than in UC and IBDU. The peak of incidence at age 12 and the declining representation of older age patients in our registry (especially in the 14–17 group, which represents 32% of the total SPIRIT group), suggest an important amount of missed late-teenage patients. One of the proposed explanations for the common age at diagnosis in young teens would be, according to some authors, that older teens could be lost to pediatric practices as they were referred to adult gastroenterologists. We tried to minimize this bias by inviting adult gastroenterology units to participate in the study. Therefore, some patients who otherwise would have been lost were recruited for the registry. But, although this potential failure of full data accrual in teenagers and young people could limit some of our findings, it is interesting to compare our data to the ones in the only nationwide registry in the Mediterranean area, in which pediatric IBD patients less than 19 years were prospectively included.[11] We observed that in our study we even have included more late teenagers; in Castro et al's study the different age groups (0–5, 6–12, and 13–17) represented 20%, 57%, and 19% of the total amount of patients, respectively, whereas in our study these same age groups represented 10%, 46%, and 43% of the total. Our own experience in the main referral center for pediatric IBD under 18 years in Catalonia, Sant Joan de Déu Hospital, Barcelona (with very few, if any, late-teenage patients being followed by adult gastroenterologists in our referral area), are also in accordance with our national results[27]; in the period 1999–2008, the median age at diagnosis was 13.1 years (p25–p75: 10.3–14.9), very similar to our nationwide results (12.3 years, p25–75 9.7–14.6). Whether this clear pattern of peak incidence in young teens is influenced not only by loss of older patients referred to adult services but also by some kind of regional specificity will need further investigation.

Finally, the distribution of disease location is in accordance with what has been previously reported, with extensive disease predominating in pediatric UC and the colon being the most affected segment in pediatric CD.[39] We have also seen a higher predominance of colonic or ileocolonic CD in younger patients, whereas exclusive ileal (or ileocecal) disease is more characteristic of adolescents. It could seem that ileal or ileocecal location in our study (26.5%) is overrepresented as compared to other pediatric series. Previous data from Great Britain and Ireland found L1 location according to Montreal Classification in 4.4%–9% of the cases.[41,42] Other studies from Italy showed contradictory results; Guariso et al[40] in 2010 reported L1 location in 6% of pediatric CD patients diagnosed in Padova (north of Italy) while the nationwide Italian registry[11] found 18% of the patients with ileal or ileocecal disease. Recent studies from the north of France have also shown similar percentages as this Italian nationwide registry: Auvin et al[7] reported 19% of the patients with ileal-only disease, and the EPIMAD registry found L1 in 13.9%.[41] Interestingly, the authors of this last study used a variation of the Montreal Classification, with the ileocecal location being diagnosed as L3 (ileocolonic). When analyzing our data, the authors tried to follow the recent recommendations of the Paris Classification[42] that insists on the correct inclusion of the ileocecal disease as L1. Considering the possibility of some kind of misclassifications in some of the previous pediatric studies, we consider it interesting to compare the global L1+L3 group in the different studies. If we do so, we observe that our results (83.4%) would be very similar to others (80.6% for Guariso et al, 73% for the Italian registry, 90% for Auvin et al, 82.9% for Vernier-Massouille, and 93% for Sawczenko et al). Only the results from Scotland (66.6% in Van Limberger et al's study) and from Sweden (43%)[43] differ from ours, with a global higher proportion of isolated colonic disease. Whether this fact could represent a difference between Mediterranean and north European countries regarding variations in NOD2/CARD15 carrier status or other factors should be elucidated. The results from previous studies show a lower frequency of NOD2 mutations in Spanish CD adult patients (between 27% and 33%)[44–48] than in other European countries (38.5% reported in Great Britain, 38.2% in Italy, 46.3% in Belgium, 38% in France, 36.5% in Germany, and 46% in Czech Republic), although in the Scandinavian countries the observed frequencies were even lower than the ones described in Spain (15.5% in Finland, 15.2% in Sweden, 21% in Denmark). There are no pediatric data on CARD 15 mutation frequency in Spain.

The main limitation of our study derives from its retrospective nature. It is obviously quite possible to have lost cases due to a poor collection of data, mainly in the earlier years of the registry. Although it is not very common for young pediatric IBD patients to be followed by pediatricians outside a gastroenterology unit or by adult gastroenterologists, some centers could have lacked reliable registries during the earlier part of the period. This could have contributed to overestimating the real increase in IBD incidence. For minimizing this bias, and also in order to collect information about old teenagers who could have been referred directly to adult units, we invited the main referral centers for adult IBD in our country to collaborate in this study.

The distribution of the participating centers was considered representative of the whole country. In the last decade pediatric gastroenterology has been developed in many centers. Therefore, IBD management has been offered not only in big centers, as in the 1980s and the beginning of the 1990s, but

also in regional or smaller centers. In this study, which included data from all the 35 referral pediatric IBD units as well as from 31 regional hospitals and from 12 adult centers, we were able to obtain data from the great majority of the hospitals (both public and private centers) that care for IBD pediatric patients.

In conclusion, this is the first attempt to calculate the total current incidence of pediatric IBD in Spain. In the last 14 years the total pediatric IBD incidence has tripled, with a more important increase in CD incidence (tripled) than in UC. A similar increase has also been reported in our country among children with other immune diseases such as diabetes mellitus and asthma.[49,50]

A north–south gradient was confirmed in our patients, with the northern regions showing higher incidence rates. However, the incidence of pediatric IBD in Spain is remarkably lower than the previous ones reported in other European countries, as well as in North America. The type of disease, location, age, and sex distribution observed in our patients were in accordance with previously reported data.

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## APPENDIX

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