

Incidence and prevalence of inflammatory bowel disease in Mexico from a nationwide cohort study in a period of 15 years (2000–2017)

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Abstract

Despite the worldwide increasing incidence and prevalence of Inflammatory Bowel Disease (IBD), our knowledge about it in Mexico is still limited. The aim of this study is to describe the incidence and prevalence of IBD as well as its clinical and socio-demographical characteristics in Mexico from a nation-wide perspective.

Multicenter nation-wide cohort study that included 42 IBD clinics from all over the country that participated with electronically register of the new cases over 17 years as well as all known existing cases together with their clinical and socio-demographical characteristics from patients with IBD (ulcerative colitis [UC], Crohn disease [CD], and inflammatory bowel disease unclassified [IBDU]). The data collection was conducted between January and October 2017. Incidence, prevalence, and mean incidence over 2 decades were then calculated. Data base was analyzed using SPSS v24 program SPSS (version 24, IBM Corp., Armonk, NY, USA).

A total of 2645 patients with IBD were registered. The crude incidence rates of IBD, UC, and CD, respectively, were 0.21, 0.16, and 0.04 cases per 100,000-person year. The highest incidence was registered in the year 2015, compared with to the previous years. The mean incidence of IBD has increased steadily from 0.05 to 0.21 per 100,000 person-years over the past 15 years ($P = .06$). The incidence of IBD new cases have increased significantly throughout the last 16 years, 5.9-fold for IBD, 5.3-fold for UC, and 9.5-fold for CD. The prevalence rates of IBD, UC, and CD, respectively, were 1.83, 1.45, and 0.34 cases per 100,000-person-year.

This is the first study from a nation-wide perspective that demonstrated a significant increase of prevalence and incidence of IBD in Mexico in the last 15 years.

Abbreviations: CD = Crohn disease, IBD = inflammatory bowel disease, UC = ulcerative colitis.

Keywords: Crohn disease, incidence, Mexico, prevalence, ulcerative colitis

1. Introduction

Ulcerative colitis (UC), Crohn disease (CD), and inflammatory bowel disease unclassified (IBDU), together known as inflammatory bowel disease (IBD), are multifactorial chronic entities

influenced by genetic, environmental, and immunologic factors.^[1] They present as chronic diarrhea with blood and mucus characterized, in the case of UC, by inflammation of the colonic mucosa and submucosa, and in the case of CD, by transmural

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inflammation that may appear in any part of the gastrointestinal tract.^[2] In almost 20% of the cases, IBD can have a continuous clinical course with severe consequences,^[3] among which we can highlight progression of disease extension, relapses, acute severe colitis, the need of surgical treatment, or cancer development.^[4]

As a general overview, published IBD descriptive epidemiology has given us important information about the characteristics and behavior of the disease around the world. Interestingly, due to an increase in CD incidence in the last few decades, recent prevalence data show that CD and UC may be now equally prevalent in North America.^[5,6] The peak age of onset for CD is between 20 and 30 years of age and for UC, between 30 and 40 years.^[6,7] Besides, between 5% and 15% of patients are diagnosed when aged >60 years old^[8–10] and 25% are diagnosed before the age of 18,^[8] which is particularly important as the phenotype and natural history of disease may be different according to age of onset.^[9] For instance, pediatric-onset UC is characterized by a high rate of disease extension and need of surgical treatment, which presents in about 20% of children in the first 10-years of follow-up after diagnosis.^[10] On the other hand, although older IBD patients appear to have a milder clinical course with a minimal disease progression over time,^[11] they are also more susceptible and have higher rates of many disease and treatment-related adverse effects, as well as an increased risk for infection, malignancy, bone disease, eye disease, malnutrition, and thrombotic complication.^[12]

Today, the increasing incidence IBD has had throughout the last years has led experts to consider it an expanding global health problem of industrial-urbanized societies.^[5] Epidemiological data in this regard may vary widely depending on the region studied; nevertheless, the notion that prevalence and incidence are beginning to stabilize in high-incidence areas such as northern Europe and North America has been challenged by data from new cohorts and follow-up data from historical incidence cohorts^[13–15] while they continue to rise in low-incidence areas such as southern Europe, Asia, and much of the developing world,^[16] which can be probably attributed to a westernized lifestyle and other associated environmental factors.^[5]

Even with the great advances in our knowledge about pathophysiology and treatment of IBD, a big knowledge gap remains in the global epidemiology of IBD, coming precisely from developing countries, where IBD was a rare occurrence; however, as these nations have become more industrialized, the incidence of IBD has increased.^[7] The majority of epidemiological studies were conducted in European countries, whereas population-based data on the incidence and prevalence of IBD in developing countries were lacking. Among the most important epidemiological studies that have been carried out around the world, the highest prevalence of IBD worldwide was reported in Canada and Europe, whereas Asia had a lower prevalence of IBD. Studies that explored temporal trends showed that the incidence of IBD continues to increase in many regions of the world. Consequently, IBD appears to be emerging as a global disease.

There are several countries with high incidence rates of IBD such as Canada,^[17] Iceland,^[18] United Kingdom,^[19] and Australia.^[20] Similarly, prevalence was highest in Europe (505 per 100,000 for UC in Norway^[21] and 322 per 100,000 for CD in Italy)^[22] and Canada (248 per 100,000 for UC and 319 per 100,000 for CD).^[17]

This geographic distribution of IBD provides clues for researchers to investigate possible environmental determinants of IBD. For example, the abuse of antibiotics in infants, mode of

birth delivery, western diet, excessive sanitation, oral contraceptives, non-steroidal anti-inflammatory drugs, and several unknown pollution exposures might be environmental factors implicated as triggers in the development of IBD.^[23]

In Mexico, it was reported that about 18 new cases were annually diagnosed in a tertiary care center until 2004,^[24] and from this year on, it was estimated that this number had increased approximately 50% until 2007.^[25] After that, there is other study that concludes that the incidence of new cases increased 2.6-fold comparing 2 periods of time before 2007,^[26] but from then on, there is no more data available from recent years, besides the fact the previously mentioned studies come from a limited number of patients that hardly represent the whole Mexican population.

Prompted by the need of recent national data about the epidemiology and behavior of IBD in Mexico, the aim of this study was to describe the incidence, the prevalence as well as clinical and socio-demographical characteristics of Mexican IBD patients from a nation-wide perspective, as contributing to the global knowledge of IBD epidemiology constitutes a landmark for the international understanding of this disease.

2. Materials and methods

This is a cohort and multicenter nation-wide study that included a total of 42 IBD clinics from all over the country, which included at least one clinic of IBD by each state of the country, thus covering the 32 states that integrate the Mexican Republic. Each center participated as a member of EPIMEX-IBD Study Group between January and October of the year 2017. According to the 2015 national census, the total population of Mexico was 119.5 million habitants in the 32 states of the Republic.

2.1. Collection of data

The centers that accepted to participate were requested to fill-in an electronic data-collection sheet with clinical and socio-demographical characteristics for each one of their patients with definitive diagnosis of IBD including (UC, CD, or Inflammatory Bowel Disease unclassified [IBDU]). The collection of data was meticulously reviewed by a full-time research assistant who was responsible for verifying and filling the databases throughout the duration of the study. Prior to the commencement of the study, all investigators met for a half-day detailed discussion on the operations of the study, and the full-time research assistant periodically (once every week) contacted all the participant gastroenterologists, physicians, and surgeons in charge of the study to ensure all cases were collected.

The data of each patient that was included in the study was initially captured using the standard electronic data collection sheet and subsequently transferred to an electronic database developed specially for the study. Each case was then carefully assessed to ensure that the criteria for the diagnosis of IBD were met based on clinical, endoscopic, histological, and radiological features according to European Crohn and Colitis Organization (ECCO) guidelines.^[27,28]

The following variables were registered in the electronic data-collection sheet: initials of the full name and date of birth in order to avoid duplicated patients, sex, age, and date of birth, place of birth and residency, smoking habits and smoking rate (calculated as number of daily cigarettes times the number of years divided into 20), history of appendectomy or tonsillectomy, history of atopic dermatitis, allergic rhinitis or asthma; family history of

autoimmune diseases and of IBD; personal comorbidities, UC distribution (E1: proctitis, E2: left sided, and E3: extensive or pancolitis) or CD location (L1: terminal ileum, L2: colon, L3: ileocolonic, and L4: upper gastrointestinal location), both classifications according to the recommendations of the third ECCO consensus guidelines,^[27,29] age and year of diagnosis of IBD, age and year at initial IBD symptoms, pharmacological treatment for IBD (aminosalicylates, steroids, immunomodulators, or biologic treatment), response to pharmacological treatment according to ECCO guidelines^[27,29] (aminosalicylate intolerant, steroid dependent, steroid refractory, thiopurine refractory or intolerant, and whether they had a primary response to biologic treatment or they lost response), number of IBD-related hospitalizations, total number of relapses, extraintestinal manifestations (arthralgia, arthritis, sacroiliitis, primary sclerosing cholangitis, pyoderma gangrenosum, erythema nodosum, uveitis, ankylosing spondylitis), personal history of osteopenia or osteoporosis, IBD complications such as fistulae, perforation, toxic megacolon, or pouchitis as well as history of surgical treatment and type of procedure.

2.2. Statistical analysis

For the statistical analysis, the total population was divided into 3 different groups, each one of them further divided by UC, CD, or IBDU groups: pediatric population (age ≤ 18 years), adult population (age between 19 and 59 years), and elderly

population (age ≥ 60 years). A second sub-analysis was made dividing the population by pediatric, adult, or elderly age of IBD onset.

Descriptive statistics were used to initially explore and describe data, using frequency and percentage for categorical variables and mean (standard deviation) or median (range) for numeric variables according to distribution. The Kruskal Wallis test was used to assess differences in quantitative clinical variables among pediatric, adult and elderly IBD onset, using Bonferroni multiple comparison as post hoc tests. Multivariate logistic regression was used to study the differences in clinical course among these groups. Simple regression was used to describe incidence trends.

2.3. Incident cases

The new cases confirmed by the gastroenterologists of each center from the entire republic were meticulously captured over 15 years. Each case was then carefully assessed to ensure that the criteria for the diagnosis of IBD were met based on clinical, endoscopic, histological, and radiological features. The crude incidence rates of IBD, UC, and CD were calculated based on the whole population of Mexico in the year 2015 as the denominator. The incidence rates according to year of diagnosis along with 95% confidence interval were then calculated using the total number of population obtained for each age group. The age-standardized incidence rates were derived using available data from INEGI.^[30]



Figure 1. Map of the Mexican Republic which is formed by 32 states.

2.4. Prevalent cases

For calculation of prevalence, all available case notes from each center were included, whether active or inactive, with the diagnosis of IBD in each of the participating centers from 2000 to 2017. Each case was carefully reviewed to confirm the diagnosis of IBD. The prevalence was calculated based on the whole population and the population of each age group with 95% confidence interval.

2.5. Calculation of incidence trend

The incidence trend was calculated using retrospective data. For the numerator, we documented the years of diagnosis for all confirmed cases of IBD obtained from all the available case notes in each of the centers, and for the denominator, we estimated the total population of Mexico for each year from 1990 till 2017. Population data were obtained from INEGI.^[30] Subsequently, we grouped the cases diagnosed in the years (2000, 2005, 2010, and 2015) as numerator. Mean crude incidence was then calculated and expressed as number of cases per 100,000 person-years along with the corresponding 95% confidence interval for each case (Fig. 1).

2.6. Ethical considerations

This study was performed according to the principles expressed in the Declaration of Helsinki. The study was approved by the Ethical and Medical Committee from the National Institute of Medical Science and Nutrition Salvador Zubirán, and a written informed consent was obtained from all subjects.

3. Results

A total of 2645 IBD patients from whole country were registered, 2073 (78.3%) with UC, 501 (18.9%) with CD, and 72 (2.7%) with IBDU; 1253 (47.4%) were men and 1393 (52.6%) women. Specific clinical and socio-demographical descriptions of pediatric, adult, and elderly IBD in the Mexican population are represented in Table 1. No statistically significant differences were found between sexes within each age group.

3.1. Incidence of IBD in Mexico

Incidence calculated for the year 2015 is shown in Fig. 2. Incidence by age group is described in Table 1. The crude incidence rates of IBD, UC, and CD, respectively, were 0.21 (95% CI: 0.18–0.23), 0.16 (95% CI: 0.14–0.18), and 0.04 (95% CI: 0.03–0.05) per 100,000 persons. By the age groups, the incidence in 2015 of IBD was 0.04 (95% CI: 0.02–0.06) for pediatric, 0.28 (95% CI: 0.24–0.45) of adults, and 0.34 (95% CI: 0.24–0.45) for elderly adults per 100,000 persons.

3.2. Incidence trend

Incidence calculated for the years 2000, 2005, 2010, and 2015 appears in Fig. 3. A clear rise in the incidence through the past 15 years was found for both UC and CD; from 0.05 per 100,000 population-year in 2000 to 0.21 per 100,000 population-year in 2015. In average, the number of UC diagnoses increased annually 10.8 ± 6.3%, the number of CD diagnoses increased annually 31.06 ± 22.01%. The number of IBDU diagnoses increased 28.4% ± 21.3%. A significant increased incidence of 5.9-fold of

Table 1

Incidence for ulcerative colitis (UC), Crohn disease (CD), and inflammatory bowel disease (IBD) by age group.

	2000			2005			2010			2015			Simple regression statistics	
	Cases	Total population	Incidence per 100,000 person-year	Cases	Total population	Incidence per 100,000 person-year	Cases	Total population	Incidence per 100,000 person-year	Cases	Total population	Incidence per 100,000 hab year		
Pediatric	UC	0	40,799,002	0.00	1	39,969,189	0.00	5	41,542,388	0.01	13	41,495,227	0.03	R ² = 0.88 P = .06
	CD	0		0.00	1		0.00	0		0.00	2		0.00	R ² = 0.44 P = .33
	IBD	0		0.00	2		0.01	5		0.01	17		0.04	R ² = 0.83 P = .08
Adults	UC	27	47,682,152	0.06	54	52,144,644	0.10	79	59,341,365	0.13	144	65,512,436	0.21	R ² = 0.95 P = .02
	CD	4		0.01	6		0.01	14		0.02	36		0.05	R ² = 0.85 P = .08
	IBD	32		0.07	60		0.12	97		0.16	183		0.27	R ² = 0.94 P = .02
Elderly adults	UC	11	6,948,457	0.16	22	8,338,835	0.26	18	10,055,379	0.18	31	12,436,321	0.24	R ² = 0.21 P = .53
	CD	2		0.03	5		0.06	6		0.06	10		0.08	R ² = 0.88 P = .06
	IBD	13		0.19	29		0.35	26		0.26	43		0.34	R ² = 0.41 P = .35

Pediatric <18 years old, adults 18–59 years old, and elderly adults >60 years old. Simple regression was used for determination of statistical significance in the increase of diagnosed cases. (28) Instituto Nacional de Estadística y Geografía. www.beta.inegi.org.mx/temas/estructura, 2000–2015.

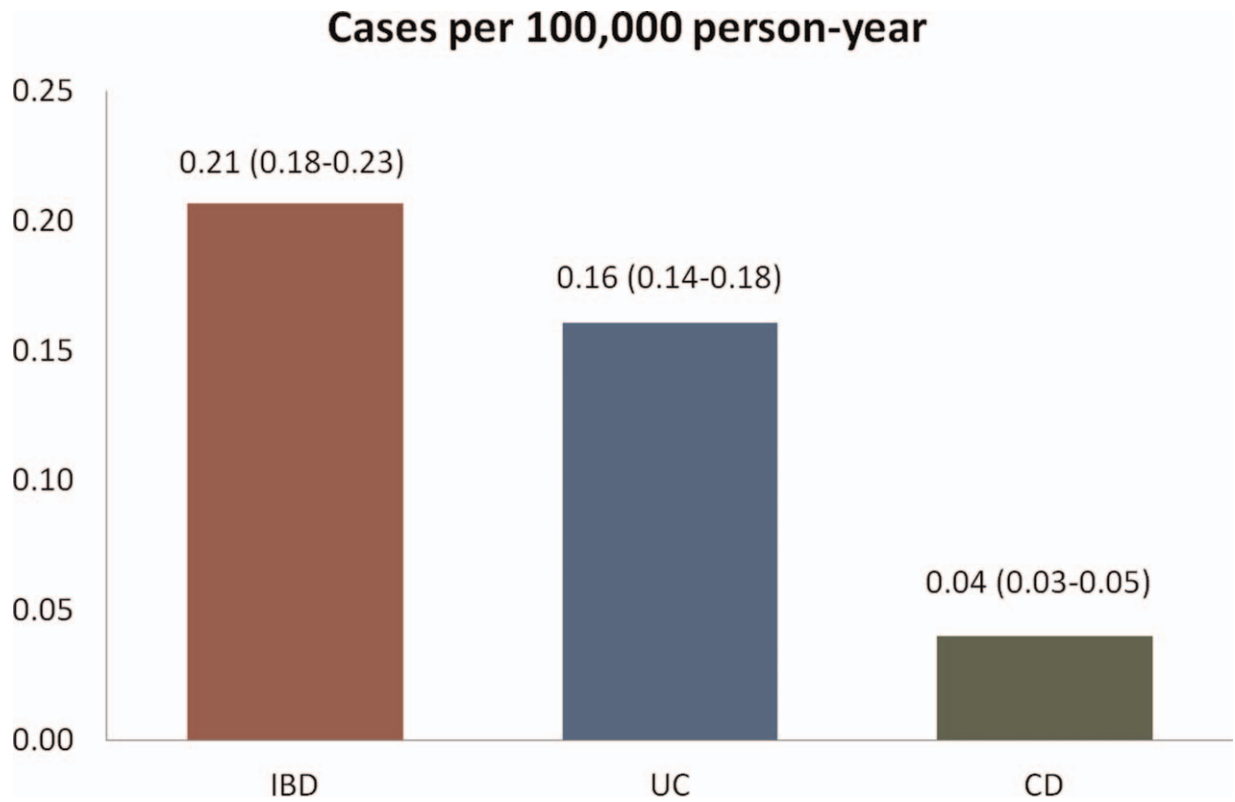


Figure 2. Incidence of inflammatory bowel disease (IBD), ulcerative colitis (UC) and Crohn disease [CD] in Mexico [year 2015].

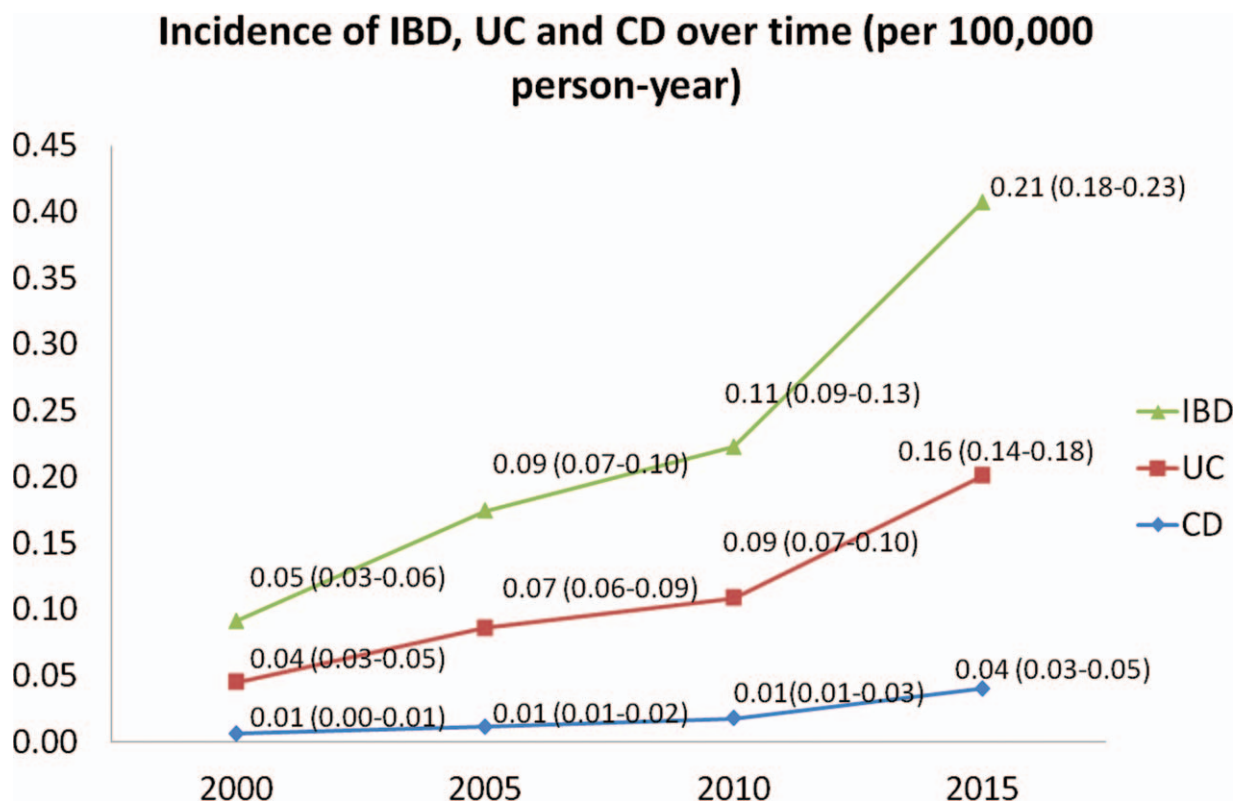


Figure 3. Incidence trend through years 2000, 2005, 2010, and 2015 of inflammatory bowel disease (IBD), ulcerative colitis (UC) and Crohn disease (CD) in Mexico (year 2015). Simple regression was made in order to determine R^2 and P for each series. CD $R^2=0.93$, UC $R^2=0.93$, and IBD $R^2=0.88$.

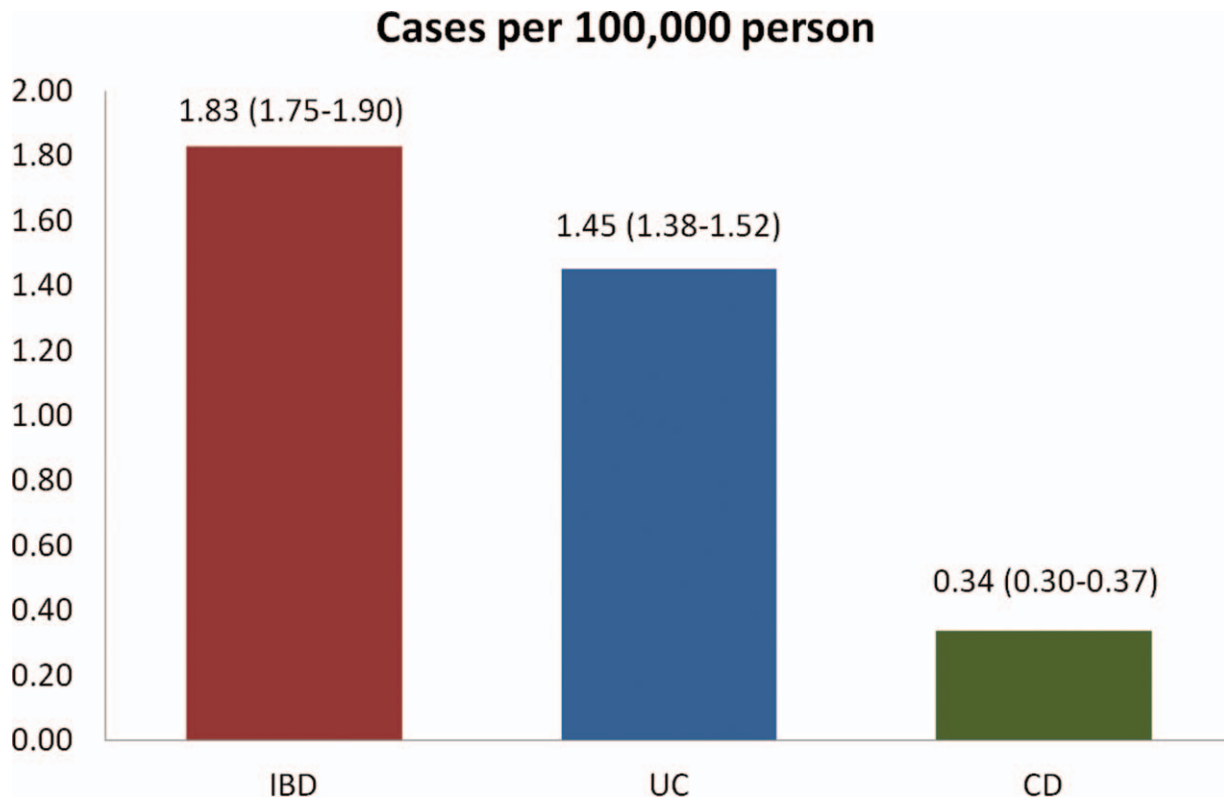


Figure 4. Prevalence of inflammatory bowel disease (IBD), ulcerative colitis (UC), and Crohn disease (CD) in Mexico (year 2015).

IBD was found between the year 2000 and 2016 ($P < .0001$), regarding to UC an increase of 5.3-fold ($P < .0001$) and for CD was 9.5-fold ($P < .0000001$) in the same period of time. Comparing the proportion of new IBD diagnoses in the year 2000 to the proportion in the year 2008, and the difference between the year 2009 and 2016, the increased in the incidence of new cases was statistically significant ($P = .0001$ in both cases).

3.3. Prevalence

The prevalence rates of IBD, UC, and CD are shown in Fig. 4 per 100,000 persons. Prevalence by age group is described in Table 2. Prevalence rise through the years 2000, 2005, 2010, and 2015 are shown in Fig. 5. Prevalent cases had an important increase through the years.

3.4. Ulcerative colitis extension and Crohn disease location

Pancolitis was the most frequent extension of UC in children, adults, and elderly patients, being present in 64.4%, 62.2%, and 57.7% patients respectively; the second most frequent extension was distal or proctosigmoiditis in 22.2%, 24.8%, and 26.8% patients respectively and the least frequent was left sided colitis, which was found in 13.3%, 13%, and 15.6% for each of the age-group evaluated. In the case of CD, the most frequent location in children and adults was ileocolonic, being present in 9 (47.4%) and 159 (50.2%) patients, respectively. For these 2 age groups, the second most frequent location was colonic, present in 26.3% and 23.7% patients, respectively. In the case of pediatric patients,

15.8% had an upper digestive tract location of CD and 10.5% had ileal location. In the case of adults, the third more frequent location was ileal (23%) while the least frequent was upper digestive tract that was present in 3.2% of the patients. On the other hand, in elderly patients colonic location of CD was the most frequent, present in 73.9% patients, the second most frequent location was ileocolonic (16.4%), and 7.3% presented ileal CD location and finally, none of them had an upper digestive tract involvement.

3.5. Groups of age affected by IBD and anti-TNF therapy

According to the group of age, most frequently affected by UC onset is between 21 and 40 years, while in CD 2 similar peaks of frequency were observed between 21 and 40 years and between 41 and 60 years. It is important to note that 18.9% of the children with UC, 52.6% of the children with CD, 15.3% of adults with UC, 38.5% of adults with CD, 17.6% and 24.8% of the UC and CD elderly patients have been treated with anti-TNF therapy.

3.6. Extra-intestinal manifestations

Twenty five percent of the children with UC, 47.4% of the children with CD, 26% of the adults with UC, 27.4% of the adults with CD, 24.7% of the elderly patients with UC, and 25.5% of the elderly patients with CD had at least one extra-intestinal manifestation (EIM). Arthropathy was the most frequent EIM in all of the groups studied, but the greatest frequency was found in children with CD, 8 (42.1%) of the patients. On the other hand, the greatest frequency of primary

Table 2 Prevalence for ulcerative colitis (UC), Crohn disease (CD), and inflammatory bowel disease (IBD) by age group.

	2000			2005			2010			2015			
	Cases	Total population	Prevalence per 100,000 person	Cases	Total population	Prevalence per 100,000 person	Cases	Total population	Prevalence per 100,000 person	Cases	Total population	Prevalence per 100,000 person	Simple regression statistics
Pediatric													
UC	2	40,799,002	0.00	7	39,969,189	0.01	23	41,542,388	0.05	63	41,495,227	0.15	$R^2=0.86$ $P=.07$
CD	0		0	2		0.00	3		0.00	10		0.02	$R^2=0.84$ $P=.08$
IBD	2		0.00	9		0.02	26		0.06	75		0.18	$R^2=0.85$ $P=.07$
Adults													
UC	160	47,682,152	0.33	353	52,144,644	1.17	699	59,341,365	1.17	1335	65,512,436	2.03	$R^2=0.96$ $P=.02$
CD	41		0.08	67		0.12	110		0.18	257		0.39	$R^2=0.86$ $P=.07$
IBD	201		0.42	421		0.80	814		1.37	1607		2.45	$R^2=0.94$ $P=.03$
Elder adults													
UC	62	6,948,457	0.89	126	8,338,835	2.13	215	10,055,379	2.13	337	12,436,321	2.7	$R^2=0.99$ $P=.00$
CD	34		0.48	47		0.84	85		0.84	146		1.17	$R^2=0.94$ $P=.03$
IBD	96		1.38	176		2.11	308		3.06	502		4.03	$R^2=0.99$ $P=.00$

Pediatric <18 years old, adults 18–59 years old, and elder adults >59 years old. Simple regression was used for determination of statistical significance in the increase of diagnosed cases. (28) Instituto Nacional de Estadística y Geografía. www.beta.inegi.org.mx/temas/estructura, 2000–2015.

schlerosing cholangitis (PSC) was found in adult patients with UC, 41 (4.6%) of the cases.

The frequency of each EIM according to the time across the years of evolution of IBD at which they appeared for the first time. As it is shown, musculoskeletal manifestation was the most frequent during the first year of diagnosis. Regarding the time of evolution of disease and the diagnosis of each EIM, arthropathy was the EIM that appeared earlier after IBD diagnosis, 70.3%, 46.5%, and 45.5% of the patients who developed EIM in each of the age groups studied were diagnosed with this type EIM within the first year of IBD diagnosis. In the case of children, the CD patient that developed sacroiliitis after 5 years of IBD diagnosis and the 2 patients who developed PSC did it within the first year of UC diagnosis. In the case of adults, sacroiliitis was diagnosed mostly within the first year of IBD diagnosis in 50%. In the case of PSC, 34.4% debuted within the first year of diagnosis and 34.4% within the first 5 years after the diagnosis of IBD. In this same age group, all of the other EIM were most frequently diagnosed within the first year of diagnosis, 58.3% of the patients with PG, 70% of the EN cases, 40% of the uveitis, and 45.5% of the AS cases. In the elderly group of patients, all of the other EIM manifestations debuted within the first 5 years of diagnosis.

3.7. Risk and protective factors in IBD patients

The total sample of IND Mexican patients were divided in 3 groups: 266 (10.1%) with pediatric onset, 2099 (79.4%) with adult onset, and 280 (10.6%) with elderly onset.

Multivariate regression models, considering appendectomy, tonsillectomy, autoimmune family history, and current smoking habit as possible predictors of IBD age of onset, determined in the case of UC, that current smoking habit is as a protective factor for adult onset UC (OR = 0.623, 95% CI: 0.449–0.863, P = .004). In the case of CD, the model determined was the presence of autoimmune family history which increased 4.5 times the risk of adult CD onset (OR = 4.498, 95% CI: 3.494–5.790, P = .0001) and personal history of tonsillectomy was a protective factor for adult CD onset (OR = 0.370, 95% CI: 0.163–0.841, P = .018). No significant associations were found regarding the pediatric UC or CD group.

3.8. Inflammatory bowel disease unclassified (IBDU) in Mexico

This study recruited 72 (2.7%) patients with IBDU and were distributed as follows: 6 (8.3%) in pediatric population, 50 (69.4%) in adults, and 16 (22.2%) in elderly patients. Regarding pediatric population, 4 (66.6%) were women and 2 (33.3%) men with a median age at diagnosis of 12 years (range: 2–18 years) and median disease of evolution of 2 years (range: 0–16 years). From all adult patients, 31 (62%) were women and 19 (38%) were men with a median age at diagnosis of 46 years (range: 24–59 years) and a median of disease evolution of 4 years (range: 0–21 years). From elderly group, 7 (43.8%) were women and 9 (56.3%) were men with a median age at diagnosis of 66 years (range: 60–84 years) and median disease evolution of 2 years (range: 0–11 years).

4. Discussion

This is the first epidemiological study that evaluates the incidence and prevalence of IBD in Mexico. We are confident that we have

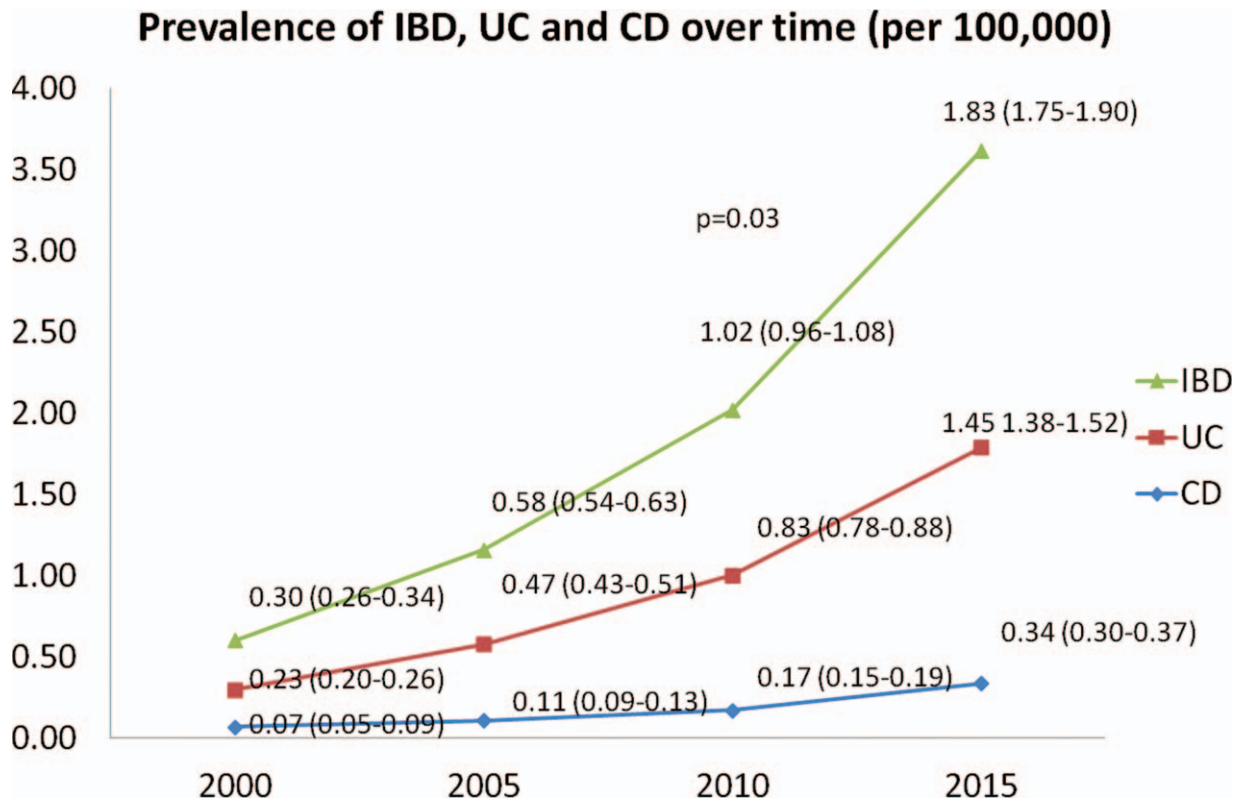


Figure 5. Prevalence in years 2000, 2005, 2010, and 2015 of inflammatory bowel disease (IBD), ulcerative colitis (UC), and Crohn disease (CD) in Mexico (year 2015). Simple regression was made in order to determine R^2 and P for each series. CD $R^2=0.95$, UC $R^2=0.86$, and IBD $R^2=0.84$.

captured the majority of the patients during the study. This study confirms that there is a wide increased in the prevalence of IBD in Mexico in recent years, regarding from 0.30 cases per 100,000 person-year in 2000 to 1.83 cases per 100,000 person-years in 2015 ($P=.05$). The same phenomenon has been observed worldwide, which IBD is now considered an expanding global health problem due to its constant increase in terms of incidence and prevalence through the last 20 years in adults^[5] and children.^[31] Interestingly, this ascending tendency of IBD incidence continues, the prevalence of this disease is expected to increase from 660 to 790 per 100,000 inhabitants between 2015 and 2025 in United States.^[32] Malik et al^[33] proposed that Mexico a developing country near the equator, would have a rising incidence of IBD.

As we observed in the present study the crude incidence rates of IBD, UC, and CD, respectively, were 0.21 (95% CI: 0.18–0.23), 0.16 (95% CI: 0.14–0.18), and 0.04 (95% CI: 0.03–0.05) cases per 100,000-person year, and the highest incidence was registered in the year 2015, compared with to the previous years. The mean incidence of IBD has increased steadily from 0.05 to 0.21 per 100,000 person-years over the past 15 years ($P=.06$). This increased in the incidence and prevalence of IBD in Mexico could be explained by changes in the lifestyle, occidental diet, and admixture with Caucasian population.^[28,34,35] Previous studies in Mexico from tertiary care referral centers have shown an increased in the frequency of UC new cases in Mexico City in a 10-year-period^[26] and in the north-eastern region of Mexico.^[36] Although, epidemiological data from whole country was lacking as same as from other countries of Latin America, the same has

been reported in Brazil from a specific region^[37] and raising cases of IBD during the next 20 years in this region of the world has been predicted taking into account the industrialization of Latin American countries.^[38] Regarding the faster increase incidence in CD cases compared with UC that was observed in this study, this finding is consistent with what has been recently reported in North America, where both diagnoses have similar prevalence.^[39] From this study, it can be noted that cases of CD are increased importantly during the last 15 years in the Mexican population which it is similar to reported in other regions.^[26,34,35]

The results of the clinical description reported in this study, for instance no sex predominance of IBD, pancolitis as the most frequent extension of UC in all age groups, most frequent ileocolic CD location in children and adults, as well as colonic CD in elderly Mexican patients, are entirely consistent with what has been reported in international literature about the behavior of IBD across the age spectrum.^[40] Nevertheless, a high frequency of pancolitis found in our population differs from previous studies in which pancolitis is no more than one-third of all UC cases. This finding might be explained by reference bias due to most of the UC patients in the present study were treated by gastroenterologists in IBD clinics compared with other studies that included patients from community centers followed by primary care physicians where they have lower rate of pancolitis. However, another explanation can be by the fact that previously noted racial and ethnic differences seem to be narrowing.^[41]

The findings of the present study revealed that UC is 4 times more frequent than CD in the Mexican population. In spite of

that, according to the rate of annual IBD new diagnoses that has been observed across the years included in this study, from the year 2000 to 2016, the average of UC diagnoses increased annually $10.8 \pm 6.3\%$ while the number of CD diagnoses increased annually $31.06 \pm 22.01\%$. It seems that incidence of UC is stabilizing while the incidence of CD increases at a greater rate, which will finally lead to equal the frequency of both diseases.^[33]

Regarding risk factors for UC, in this study, current smoking habit is as a protective factor for adult onset UC, which is consistent with what has been generally accepted in previous literature. Smoking, besides being a protective factor for UC, is associated with less frequent exacerbations of UC^[1,40] and even a reduced risk of colectomy.^[42] On the other hand, in this study, the presence of autoimmune family history increased the risk of CD diagnosis. We know that a positive family history remains the strongest recognizable risk factor for the development of IBD,^[43] but there is not enough published information about a relationship between family history of any autoimmune disease and the specific development of CD. Besides, personal history of tonsillectomy, in this study, appeared as a protective factor for adult CD onset. The association between tonsillectomy and IBD has been controversial throughout the different studies published until today. For instance, different meta-analysis have concluded that there is no association between these 2 factors,^[44] and even that tonsillectomy is a risk factor for developing CD,^[45] contrary to what has been found in this study.

In this first national multicentric study from a Latin American country, it is clear to note the important increase in the incidence of IBD cases in the whole country characterized by significantly increased of 5.9-fold for IBD, specifically 5.3-fold for UC and 9.5 fold for CD. These results are according to studies from other regions about the increased of the incidence of IBD incidence, for instance The Netherlands,^[46] Iran,^[47] China,^[48] or Denmark.^[49] Regarding Latin America, data are scarce and recent studies about IBD epidemiology are lacking. Even though, we do count with some single-center studies from Chile,^[50] Brazil,^[51] Puerto Rico,^[52] Argentina and Panama,^[53] that account for an increasing interest and research from previously thought low-incidence regions.^[30]

This increase in IBD incidence might be multifactorial. The possible explanations of this increased incidence and prevalence in Mexico may be a Westernized lifestyle, in terms of dietary habits, abuse of the antibiotics use as well as improving the diagnostic modalities specially for CD and a lower prevalence of infectious diseases by worm parasites, where helminth carriage has steadily declined.^[54] We have noted this important increase in incidence in states located close the United States of America border and central part of Mexico where a high consumption of saturated fat and complex carbohydrates have been increased.^[55]

The strength of the present study is the first one in Latin American region that reports an estimated incidence and prevalence from whole country (covering the 32 states that integrate the Mexican Republic or Mexico), however, data are from hospitals in most of the cases and it is a limitation of the study where incidence and prevalence could be underestimated.

In conclusion, this is the first study from a nation-wide perspective from Latin America region that demonstrated a significant increase the incidence and prevalence of IBD in Mexico in the last 15 years predominantly CD over UC. Clinical and sociodemographical characteristics of Mexican patients are similar to other geographical regions.

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