Observational Study

Epidemiology of inflammatory bowel diseases in the state of Rio Grande do Sul, Brazil

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Abstract

BACKGROUND

This is the first study on the epidemiology of inflammatory bowel diseases (IBDs) in Rio Grande do Sul (RS), the southernmost state of Brazil with the country's fifth largest population. Crohn's disease (CD) and ulcerative colitis (UC) are collectively termed IBDs. They have high incidence and prevalence rates in high-income countries, although in recent years there has been a change in the classic geographical distribution of IBDs, with growing rates in traditionally low-incidence regions.

AIM

To estimate the incidence and prevalence of IBDs in the RS state, Brazil, between 2014 and 2019.

METHODS

This is a cross-sectional descriptive observational study. Patients with IBD who had initiated treatment and met the inclusion criteria of the RS state free drug distribution program were included. Data were obtained from registration or renewal records of the RS state specialty pharmacy. The male, female, and total

populations were estimated according to mid-year data from the Brazilian Institute of Geography and Statistics, which served as a reference for calculating the incidence and prevalence rates of IBDs during the study period. Results were described using mean, standard deviation, and range.

RESULTS
We included 1082 patients with IBD, of whom 57.5% were female and 42.5% were male. Patients with CD accounted for 72.45% of the sample, and those with UC accounted for 27.54%. IBD prevalence during the study period was 9.51 per 100000 population, of which 6.89 corresponded to people with CD and 2.62, to people with UC. Incidence rates per 100000 population/year were 2.54 in 2014, 2.61 in 2015, 1.91 in 2016, 0.80 in 2017, 0.83 in 2018, and 0.96 in 2019. The mean IBD incidence rate per 100000 population was 1.61, of which 1.17 corresponded to CD and 0.44, to UC. The mean age was 41 years, and patients were mostly aged 30-40 years. Prevalence by region was higher in the state capital metropolitan area: 12.69 per 100000 population.

CONCLUSION
Our results demonstrated an IBD prevalence of 9.51% and incidence of 1.61 per 100000 population. The patients were predominantly female, and CD was more prevalent than UC.

Core Tip: This is the first study in the state of Rio Grande do Sul to address the epidemiology of inflammatory bowel diseases (IBDs). We assessed the incidence and prevalence of IBDs between 2014 and 2019, including 1082 patients (57.5% female and 42.5% male). Crohn's disease corresponded to 72.45% of the analyzed cases and ulcerative colitis, to 27.54%. Prevalence was 9.51% and the mean incidence rate was 1.61 per 100000 population. The mean age was 41 years, and the capital metropolitan area had the highest prevalence. This study showed a similar prevalence to other studies and a decrease in annual incidence rates.

INTRODUCTION

Inflammatory bowel diseases (IBDs) are characterized by a chronic inflammatory process that compromises the digestive tract. The main presentations are Crohn's disease (CD) and ulcerative colitis (UC), which are chronic idiopathic diseases causing inflammation of the gastrointestinal tract, with individual clinical and pathophysiological characteristics[1-3]. Children and young adults are more commonly affected[4]. Although uncommon, the chronicity, severity, progression, and morbidity of IBDs can significantly affect the patient's quality of life and are associated with an increased risk of hospitalizations and surgery[3,4].

IBDs are contemporary health conditions of industrialized societies. The prevalence of IBDs continues to increase steadily in Western countries, and their incidence is growing in newly industrialized countries. The global spread of IBDs seems to be associated with the Westernization of human diets and environments, affecting the gut microbiota and increasing the risk of IBDs in genetically susceptible individuals. It is therefore important to deepen our understanding of these events to delay the progression of IBDs[5].

Despite the paucity of population-based studies from low- and middle-income countries, epidemiological studies of IBDs have shown increased incidence and prevalence of CD and UC in different parts of the world. The increasing epidemiology of IBDs in newly industrialized countries in Latin America resembles that of high-income countries. Although a stabilization of incidence rates has been observed in many Western countries, the global burden of IBDs is still high, with an estimated prevalence exceeding 0.3% of the population in North America and Europe and 0.7% in Canada in 2018[6].

In newly industrialized countries, obstacles to conducting epidemiological studies of IBDs include the lack of disease surveillance systems and reliable unified health care databases, which are available in high-income countries. In countries of continental dimensions with economic problems such as Brazil,

an additional challenge is the country's generally disorganized health care system, which can result in inadequate records and, consequently, few population-based studies[6]. In this respect, Rio Grande do Sul (RS), the southernmost state of Brazil with the country's fifth largest population, still does not have a specific study on the epidemiology of IBDs. Therefore, the purpose of this study was to estimate the incidence and prevalence of IBDs in the state of RS.

MATERIALS AND METHODS

Study design

This is a cross-sectional descriptive observational study. All patients who had initiated treatment for IBD and met the inclusion criteria for the free drug distribution program of the state of RS between 2014 and 2019 were included. Drugs for the treatment of CD and UC are dispensed by the specialty pharmacy [*Farmácia de Medicamentos Especializados* (FME), or FME for short, in Portuguese] according to clinical protocols and therapeutic guidelines published by the Brazilian Ministry of Health. In Brazil, access to care is provided through private health insurance or the Unified Health System, which is a universal health care system funded by federal taxes and operated by state or municipal governments that includes the public provision of core physician and hospital services without copayments or patient charges. Approximately 22% of the population in the state of RS have private health insurance and only occasionally use the public health system. Therefore, because the FME is a government program within the Brazilian Unified Health System, it is responsible for supplying specialty medications to approximately 78% of the state population, all of them users of the public health system. Data from private health insurance companies are not included in this study.

Demographic characteristics and incidence and prevalence data were obtained from registration or renewal records of the FME. We requested from the State Health Department and its affiliated School of Public Health the data of patients included in the specialty medication distribution programs of the FME, which were provided through administrative and judicial means[7].

As variables to be analyzed, we included CD or UC diagnosis using International Classification of Diseases codes K50 and K51, date of treatment initiation, sex, and age.

Data analysis

Quantitative variables, such as age, were described using mean, standard deviation, and range. Categorical variables were expressed as counts and percentages. Disease prevalence and incidence were estimated by dividing the annual case notifications by the total estimated population of that year and presented as cases per 100000 population. Binomial distribution was used for obtaining 95% confidence intervals. All comparisons between rates assumed the binomial distribution and were based on the chi-square test. Findings with $P \leq 0.05$ were deemed statistically significant. All estimates of incidence and prevalence were calculated considering the population of the state of RS between 2014 and 2019[8]. Data analysis was conducted using IBM-SPSS, version 25.0.

Ethical considerations

This study did not involve the collection of biological material from participants. Data obtained with the data collection instrument were coded to preserve the participants' privacy and anonymity. All investigators signed a data use agreement.

The study was conducted after approval by the Research Ethics Committees of Pontifícia Universidade Católica do Rio Grande do Sul, Certificate of Presentation for Ethical Appreciation No. 25551019 9 0000 5336, and of the State Health Department and its affiliated School of Public Health, Certificate of Presentation for Ethical Appreciation No. 25551019 9 3001 5312. The study followed the guidelines of Resolution No. 466/12 of the Brazilian National Health Council and the Brazilian General Data Protection Law No. 13709.

RESULTS

This study involved 1082 patients with IBD of a total population of 11377239 people. Of these, 784 (72.45%) had CD and 298 (27.54%) had UC.

Age

Patient age ranged from 1 to 91 years, with a mean of 41 years and standard deviation of 15 years. The highest IBD incidence was between 20 and 60 years of age, and patients were mostly aged 30-40 years (Figure 1A). The highest incidence occurred between the ages of 30 and 40 years for CD, and between the ages of 50 and 60 years for UC. UC affected a higher percentage of people aged 40 years or more ($P <$ 0.01), whereas CD affected a higher percentage of people under 40 years of age ($P <$ 0.01) (Figure 1B).
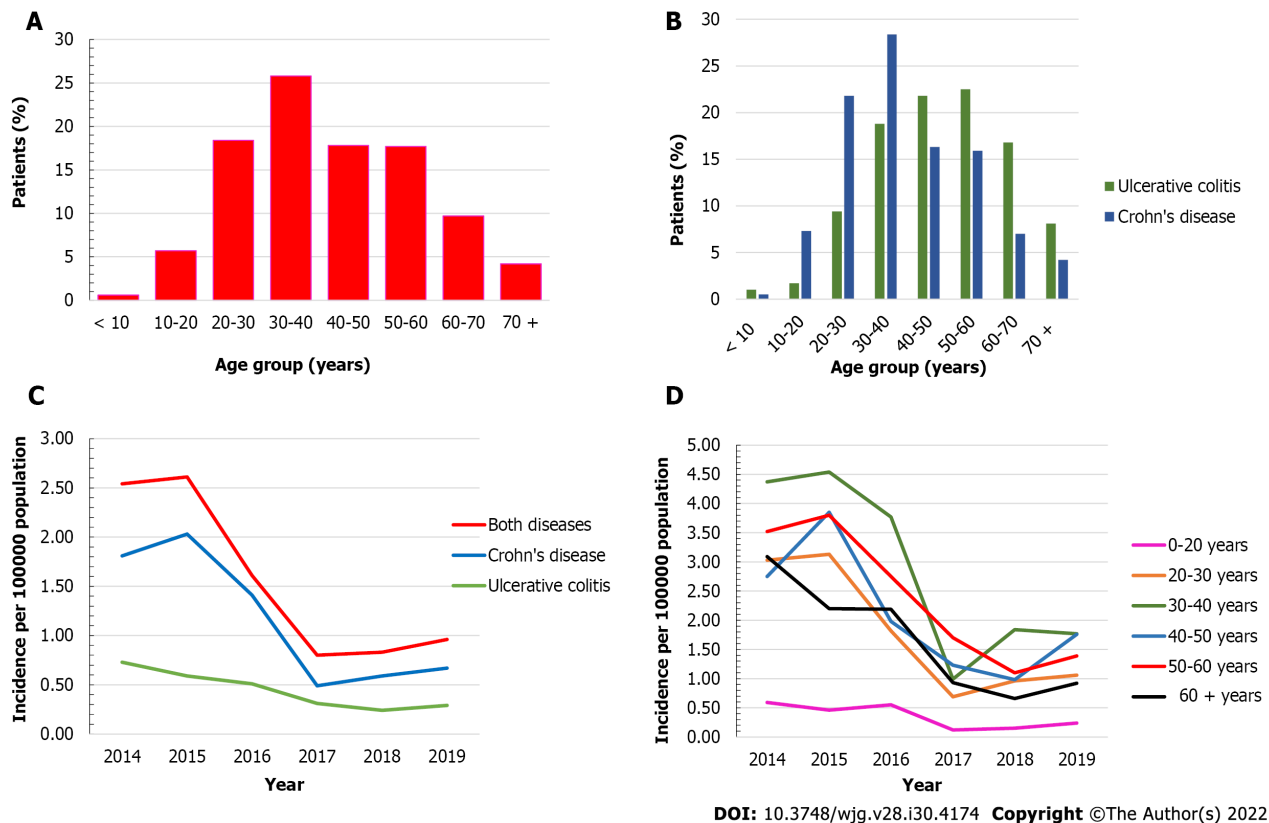
Figure 1 Age distribution and incidence rates of patients with inflammatory bowel diseases. A: Age distribution of patients with inflammatory bowel diseases (IBD) (*n* = 1082), state of Rio Grande do Sul, Brazil, 2014-2019; B: Age distribution of patients with Crohn's disease (*n* = 784) and ulcerative colitis (*n* = 298), state of Rio Grande do Sul, Brazil, 2014-2019; C: Annual IBD incidence rates, new cases per 100000 population/year in the state of Rio Grande do Sul (Brazil), 2014-2019; D: Annual IBD incidence rates by age group, new cases per 100000 population/year in the state of Rio Grande do Sul (Brazil), 2014-2019.

Sex

Of all patients with IBD, 622 (57.5%) were female and 460 (42.5%) were male (female-to-male ratio of 1.35:1.00; $P < 0.001$).

Considering CD only, 432 (55.10%) patients were female and 352 (44.89%) were male (female-to-male ratio of 1.23:1.00; $P < 0.001$). For UC, 190 (63.75%) were female and 108 (36.25%) were male (female-to-male ratio of 1.76:1.00; $P < 0.001$).

Incidence and prevalence

Overall, IBD prevalence was 9.51 per 100000 population during the study period (2014-2019), of which 6.89 corresponded to CD and 2.62, to UC. Table 1 shows the sex distribution of prevalence for each disease.

Figure 1C shows the annual incidence rates of IBD in the state of RS. The mean incidence rate was 1.61, of which 1.17 corresponded to CD and 0.44, to UC.

Table 2 shows annual incidence percentages. There was a 62% reduction in the accumulated incidence between 2014 and 2017 ($P < 0.015$). A statistically significant reduction in incidence was observed when comparing 2014 and 2019 ($P < 0.001$).

Figure 1D shows that, when listing annual incidence rates by age group, all groups showed reductions in 2017, with increases in the following years.

DISCUSSION

Historical data on the geographical distribution of IBDs worldwide have shown higher incidence and prevalence rates in high-income countries with predominantly White populations. More recently, IBDs have shown an increasing frequency in all continents, including low- and middle-income countries[2].

In Brazil, IBDs are not notifiable diseases. Therefore, data on the incidence and prevalence of CD and UC are scarce, and health systems lack adequate records. These data would be useful for better organization and political and economic planning of the public health system[9,6].

Table 1 Prevalence of inflammatory bowel diseases in the state of Rio Grande do Sul between 2014 and 2019 (per 100000 habitants)

Item	CD	UC	IBD
Female	7.40	3.26	10.66
Male	6.35	1.95	8.30
Total	6.89	2.62	9.51

CD: Crohn's disease; UC: Ulcerative colitis; IBD: Inflammatory bowel disease.

Table 2 Annual percentages of incidence rates

Year	Percentage
2014-2015	↑ 3%
2014-2015	↓ 26%
2014-2015	↓ 58%
2014-2015	↑ 3%
2014-2015	↑ 15%

In North America, 6.30 to 23.82 new cases per 100000 population are estimated per year for CD, and 8.8 to 23.14 new cases per 100000 population for UC. Prevalence rates are far higher than those in Brazil, with 96.3 to 318.5 cases/100000 population for CD and 139.8 to 286.3 cases/100000 population for UC[1, 10].

A cohort study published in the United Kingdom reported incidence and prevalence rates much higher than those in Brazil between 2000 and 2018. The study estimated incidence rates of 28.6, 10.2, and 15.7/100000 population for IBD, CD, and UC, respectively, and prevalence rates of 725, 276, and 397/100000 population[11].

In the state of RS, we observed a predominance of CD during the study period (CD 72.54% and UC 27.54%), which differs from previous studies published in Brazil reporting a predominance of UC[2,3,12, 13]. This is consistent with a study conducted in the Southeast region of Brazil by Souza *et al*[14], who reported an increase in CD cases in comparison with UC. These differences between countries and regions may reflect differences in environmental risk factors and genetic predispositions, such as those observed in Europe, where the incidence of NOD2 mutations appears to be higher in the central part of the continent, corresponding to areas with a higher proportion of CD cases[15].

According to the present study, the state of RS had a mean annual IBD incidence rate of 1.61 new cases per 100000 population/year (CD = 1.17 and UC = 0.44 new cases per 100000 population/year) between 2014 and 2019, which is consistent with the results reported by Kaplan *et al*[5] in a systematic review considering 147 studies on IBD worldwide. This comprehensive review demonstrated a CD incidence of 0-3.5 new cases per 100000 population/year, and an UC incidence of 0.19-6.76 new cases per 100000 population/year in Brazil[1]. In comparison, the systematic review by Selvaratnam *et al*[16] on the epidemiology of IBD in South America showed higher incidence rates, ranging from 4.3 to 5.3 per 100000 population/year for UC and from 0.74 to 3.5 per 100000 population/year for CD between 1990 and 2018. Similarly, a Brazilian study conducted in the state of Sao Paulo reported higher incidence rates than those found in the state of RS, with rates of 6.14 for CD and 7.16 for UC (per 100000 population/year)[3].

Regarding IBD prevalence, the mean rate observed during the study period (2014-2019) was 9.51 cases per 100000 population, of which 6.89 corresponded to CD and 2.62, to UC. Prevalence in the state of RS was higher than that reported for Brazil in a systematic review by Ng *et al*[1], with rates ranging from 0.9 to 6.75 cases/100000 population for CD and from 2.42 to 21 cases/100000 population for UC. Prevalence was also higher in a systematic review on IBD epidemiology conducted in South America, reaching 15-24.1/100000 population for UC and 2.4-14.1/100000 population for CD[16]. Similarly, in the Brazilian study by Gasparini *et al*[3], overall prevalence rates were 24.3 for CD and 28.3 for UC per 100000 population.

If we were to analyze the state of RS according to the epidemiological transition theory proposed by Gilaad G Kaplan and Joseph W Windsor in 2021, where each region of the world is at an epidemiological stage (Emergence, Acceleration in Incidence, Compounding Prevalence, and Prevalence Equilibrium), RS would be in the Compounding Prevalence stage, where a steady increase in the population living with IBD is observed despite stabilization or even a decrease in incidence[17].

Regarding patient age, studies show a clear predominance of IBD in individuals aged 20 to 50 years. In our study, the mean age was 41 years. The highest IBD incidence was between 20 and 60 years of age, and patients were mostly aged 30-40 years. The highest incidence was at 30-40 years of age for CD, and at 50-60 years of age for UC. UC showed a trend toward an increased incidence among patients aged 50 to 60 years, and these results are consistent with those of national and international studies[3,11]. A limitation of this variable is that patients were selected through the FME, which provides the age that the patients begin to receive the free specialty medications rather than their age at diagnosis.

Regarding the sex distribution of patients with IBD, we observed a predominance of female patients for both CD and UC, which is consistent with the Brazilian studies conducted by Victoria *et al*[12] in the state of Sao Paulo and Lima Martins *et al*[13] in the state of Espírito Santo. However, our findings differ from those reported in the state of Piauí by Parente *et al*[2], who found a male-to-female ratio of 1.2:1.0 for patients with CD, but with no significant association when considering sex in statistical analyses. Patients with UC, on the other hand, were mostly female (male-to-female ratio of 1.8:1.0, statistically significant)[2].

CONCLUSION

Based on the methodology used in this study, our results demonstrated an IBD prevalence of 9.51% and incidence of 1.61 per 100000 population in the state of RS between 2014 and 2019. The patients were predominantly female, and CD was more prevalent than UC. Our prevalence rate was similar to that reported in previous Brazilian studies. Mean CD and UC incidence rates were, respectively, 1.17 and 0.44 new cases per 100000 population, decreasing until 2017 and increasing afterwards. Women were more affected than men by both CD and UC. IBD occurred more frequently in major urban centers, where the referral centers that care for patients with IBD are often located. The highest IBD incidence was observed in patients aged 20 to 60 years, predominantly between the ages of 30 and 40 years; this was slightly higher than the mean values reported in previous studies.

This is the first study to estimate IBD incidence and prevalence in the state of RS. Our findings suggest that detailed studies in this field are needed to properly understand in which epidemiological stage the state of RS currently is. We believe that the difficulty in keeping accurate epidemiological records and the consequent underestimation of disease burden result from a disorganized health care system, associated with economic problems, inadequate records, lack of population-based studies, and the inaccurate diagnosis of IBD as an infectious disease before the proper knowledge of CD and UC.

ARTICLE HIGHLIGHTS

Research background

First study on the epidemiology of inflammatory bowel diseases (IBDs) in Rio Grande do Sul (RS), the southernmost state of Brazil. IBDs have high incidence and prevalence rates in high-income countries, although in recent years there has been a change in the classic geographical distribution of IBDs, with growing rates in traditionally low-incidence regions.

Research motivation

The importance of this study lies in the lack of research on the incidence and prevalence of IBDs in the state of RS. A challenge for future studies is related to access to data of all patients with IBDs, as these are not notifiable diseases in Brazil.

Research objectives

To determine the incidence and prevalence of IBD in the state of RS. The relevance of the results lies in the lack of knowledge of such data until the present study.

Research methods

This is an observational study of IBDs from the state of RS between 2014 and 2019. Drugs for the treatment of Crohn's disease (CD) and ulcerative colitis (UC) are dispensed by the specialty pharmacy. The variables analyzed were incidence, prevalence, age, sex, and CD or UC.

Research results

These are the first data on the incidence and prevalence of IBDs in the state of RS. However, these are not comprehensive data, as only patients from the public health system were included. Studies also including patients from the private health insurance sector are needed.

Research conclusions

The most relevant of the following questions should be briefly answered: What are the new theories that this study proposes? This study showed a similar IBD prevalence to other Brazilian studies and a decreasing incidence. What are the new methods that this study proposed? We propose that studies covering patients from both public and private health sectors should be conducted.

Research perspectives

Future studies should include a larger sample to provide a more reliable understanding of the real epidemiology of IBDs in the state of RS.

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