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INCIDENCE AND PREVALENCE RATES OF INFLAMMATORY BOWEL DISEASES, IN MIDWESTERN OF SÃO PAULO STATE, BRAZIL

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ABSTRACT - ***Context*** - The incidence and populational prevalence of inflammatory bowel diseases, hitherto unknown in Brazil, were estimated for a region in the Midwest of São Paulo State, Brazil. ***Methods*** - Using a sequential registry of 115 adult patients (>15 years old) with inflammatory bowel diseases – exclusively residing in the studied region with 533,508 inhabitants (2005) and attended at the reference hospital during a 20 year interval (1986-2005) – were estimated, in four consecutives periods of 5 years each, the incidences according to gender, type of the disease and the prevalence of these diseases, and its inner-relations evaluated by the Poisson regression model. ***Results*** - The inflammatory bowel diseases in the studied region predominated among young, white race and people living in urban area, and the incidence on the female population rose during this period. The incidence of ulcerative colitis were higher than Crohn's disease and non-classified colitis, and showed a progressive increase in the first three periods with a decrease in the last one (2001-2005), where the observed rates of ulcerative colitis, Crohn's disease and non-classified colitis were 4.48, 3.50 and 1.75 cases/100,000 inhabitants, with prevalence of 22.61, 14.81, 5.65, 2.14 cases/100,000 inhabitants for total inflammatory bowel diseases. ***Conclusion*** - The inflammatory bowel diseases incidence in the studied area was as low as in other countries of Latin America and smaller than that found in countries of South Europe. The crescent prevalence justifies the policies to adequate medical cares for inflammatory bowel diseases patients in this area.

HEADINGS - Inflammatory bowel disease, epidemiology. Colitis, ulcerative, epidemiology. Crohn disease, epidemiology. São Paulo (Brasil).

INTRODUCTION

Ulcerative colitis (UC) and Crohn's disease (CD) represent an important public health problem as they tend to afflict young people and have a protracted and relapsing clinical course, affecting education, working abilities, long-term productivity, social life, and quality of life[25, 28, 30]. Both forms of inflammatory bowel diseases (IBD) are complex clinical entities whose etiopathogenesis involves conditioning factors that are permissive for IBD – genes, environment, enteric flora and possible infectious agents, and effectors mechanisms that mediate damaged tissues – natural intestinal immune and non-immune systems. Components in both categories must coalesce to induce the clinical manifestation of IBD, but which and how conditioning factors trigger mediator systems are yet unknown[7, 10].

Epidemiologic studies of a disease are a powerful research tools. They may yield clues about the contribution of environmental factors to the disease etiology, or at least, provide important information about its behavior, enabling the identification of the geographical areas that should be further investigated by policy makers and healthcare insurers[30].

The conduction of epidemiologic studies on IBD can be particularly difficult due to the onset of the disease may be gradual, and medical care may not be sought at once, making it hard to determine the agents that possibly acted at the beginning of the disease activity. The lack of universally accepted criteria for IBD diagnosis, and the fact that the differential diagnosis is broad, including intestinal infections, intestinal infestations and functional diseases frequently found in the population of many countries, can lead to misdiagnosis. Also, comparing the incidence and prevalence rates of this diseases in different areas is not easy and of difficult epidemiological interpretation.

The currently available epidemiological data of intestinal inflammatory diseases show that these

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diseases are more frequent in industrialized countries where incidence rates range from 6.5 to 16.0/100,000 persons/year and prevalence rates range from 26 to 214 patients/100,000 persons/year. On the other hand, in countries where industrial development is not so strong, IBD are less frequent with incidence and prevalence rates ranging from 0.08 to 5.0 and from 3.6 to 70.0 patients/100,000 persons/year, respectively[4]. Today, IBD incidence is somewhat stable in areas where it was formerly high, and continuously rising where it used to be low[16]. According to the European IBD Study Group, the incidence rates are 40 to 80 per cent higher in northern Europe[27]. Incidence and prevalence rates in Eastern European countries remain very low, but in Hungary and Croatia are as high as in Western Europe. Furthermore, UC predominance is diminishing as CD is becoming more prevalent. A French group has recently reported a 23% increase in CD incidence alongside a 17% decrease in the incidence of UC between 1988 and 1999[9, 14, 20]. In addition, IBD are more common in young people, with women slightly more likely to develop CD while men are more likely to develop UC[4, 25].

In Central and South America, epidemiologic data on IBD are still scarce, demonstrating the rarity of these diseases or their insufficient registries in these appraised areas[1, 6, 15]. Nonetheless, a tendency toward increase, mainly of CD has been reported in Puerto Rico[1].

In Brazil, few are the studies regarding the epidemiologic aspects of IBD. Most of them just describe clinic IBD characteristics and the frequency of hospital admission due to IBD, with no reference to the incidence and prevalence of these diseases in population terms. Recent data shows that hospital admissions due to IBD have become more frequent with predominance of CD in comparison with UC[8, 29].

In brief, IBD frequency rates have constantly changed worldwide. The causes of the continuous and rapid changes in IBD incidence are still unknown, but there are evidence to support the possible sharing of environmental factors such as dietary habits, lifestyle and other factors associated to industrial development. The initial step to understand the real medical importance of IBD is to determine its incidence and prevalence rates in most areas of a country. Therefore, this work aimed at estimating the incidence and prevalence rates of UC, CD, and NCC in the population from a specific are in the Midwest region of São Paulo State, Brazil.

METHODS

Population

The target region of the study – located in the Midwest region of São Paulo State – estimated at 533,508 inhabitants in 2005 (IBGE)[13] presents a population density of 37 inhabitants per km². The urban population in this area is bigger than the rural population (urban/rural relation = 3) with a male predominance over the female population (male/female relation = 1,04) and prevalence of the white race. The region is well geographically defined and consist of 30 municipal districts that – until 2006 - composed the 11th health's region of São Paulo State (DIR 11) (Figure 1).

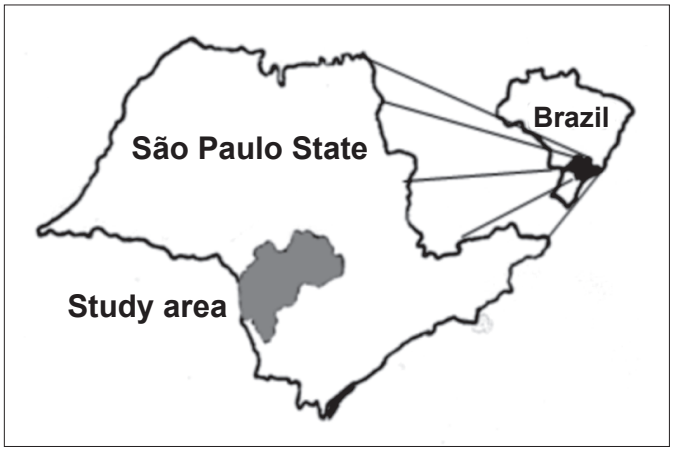

FIGURE 1. Study area (formerly named São Paulo health region DIR 11) and study population. (Population: 533,508 inhabitants (2005); area: 14,504 km²; urban/rural population ratio: 3; male/female population ratio: 1.04)

Identification and inclusion of cases

The IBD cases coming from exclusively from the studied region were sequentially identified from 1986 to 2005 by the medical records from the hospital, and putted together in a database created for this purpose at the Intestinal Inflammatory Diseases at University Hospital of Botucatu School of Medicine – UNESP – a referral medical center for the 30 municipal districts that compose the study region. The patient inclusion criteria in study was: patients adults (over 15 years of age), male or female with IBD, living in area (urban or rural) located in the study area attended during a 20-year period (1986 to 2005). Were excluded all other patients with IBD attended in this Hospital that are not living in this target region. The diagnostics of UC, CD, and non-classified colitis (NCC) was based on clinical, endoscopies and histological findings[22, 26]. The term NCC was used when the differential diagnosis between UC and CD remained uncertain[18, 24].

No centralized IBD database were available in the study area, also was necessary the construction of a database based on inpatient and outpatient reports for patients residing in this study area for the conduction of this epidemiologic investigation.

Epidemiological data (age, reported race, gender and residence) were extracted from the hospital database containing the registry of 115 patients with IBD living on the target region.

To calculate the incidence rates (new cases/100,000 inhabitants/period) and prevalence rates (existing cases/100,000 inhabitants/period) of total IBD, UC, CD and NCC, the patients were grouped according to the year of entrance in the service, in four consecutive periods of 5-years each. Male, female and total population of the middle year of each period was used as standard to compute the incidence and prevalence rates of IBD for that period into which the patients were grouped. The annual adult male, female and total populations were estimated based on data published by the Brazilian Institute of Geography and Statistics[13].

This work was approved by the Research Ethics Committee from Botucatu School of Medicine – UNESP (CEP – OF.535-12/01/2003).

Statistical analysis

Descriptive and inferential analyses of the distribution of patients with IBD according to race and residence were performed using the proportion test[21]. Differences among proportions in all the tests were considered significant when $P \leq 0,05$. The Poisson regression model[4, 20] was used to find the best adjustment of linear equations for the parameters gender and time of entrance of patients in study considering total IBD, UC, CD and NCC in overall intervals studied. The Akaike Information Criterion (AIC) was used to check the adjustment levels of linear regression equation models for nonaligned alternatives[4]. The smallest AIC provided the best linear equation model. Software used: SPSS vs. 12.0 for Windows; S-Plus v 6.2 for Windows; Excel for data mining and validation.

RESULTS

The majority of the IBD patients, in the study area, was white and lived in urban districts (Table 1).

TABLE 1. Distribution of patients with inflammatory bowel diseases in study area according to residence (urban or rural) and reported race

Demographic variables		%	*P* statistic values	
Area	Urban	90.51		
	Rural	9.49	*P*<0.001	
Race	White[a]	91.07	a x b	*P*<0.01
	Black[b]	8.04	b x c	*P* = 0.023
	Asiatic[c]	0.89	a x c	*P*<0.001

IBD patients were aged between 15 to 74 years, with a mean age of 37.95 years and standard deviation of mean of 13.96 years. Among the 115 patients with IBD the frequency of disease diagnostics was: UC = 65.22%, CD = 25.22% and NCC = 9.56%. The age distribution was similar in the UC, CD and NCC groups with a mean age of 35-36 years, respectively.

The adjustment of total IBD (UC+CD+NCC) incidence for gender in all 5-year intervals, by Poisson regression model showed a significantly higher incidence among females (gender: RR = 0.44; 95% CI = 0.29; 0.67; *P*< 0.001) (Table 2).

TABLE 2. Total IBD (UC+CD+NCC) incidence adjusted for gender and 5 year interval by Poisson modeling

Parameters	β	$se^{(\beta)}$	Z	*P*	RR	CI
Intercept	-340.40	108.04	-3.15	0.001		
Log (population)	27.99	8.82	3.17	0.001		
Gender	-0.81	0.21	-3.79	<0.001	0.44	(0.29;0.67)
(5-year interval)^2	-0.28	0.20	-2.40	0.016	0.75	(0.51;1.11)

Residual deviance = 1.87 and χ^2 = 1.78 with 4 degree of freedom; AIC = 42.83; β = estimated parameters; $se^{(\beta)}$ = estimated parameter standard error; z = statistic test value; *P* = values of significante statistic of model parameters, in punctual and at intervals estimates; RR = ratio risk; CI = 95% confidence interval

The incidence of total IBD (UC+CD+NCC) changed significantly according to the 5-year interval study. It exhibited an initial rapid increase (Figure 2) followed by a plateau over the last study intervals (5-years interval^2: RR= 0,75; 95% CI= 0,51-1,11; *P* = 0.016).

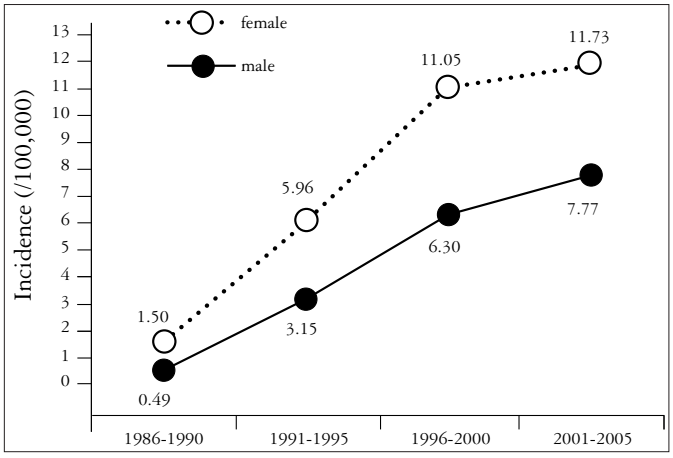

FIGURE 2. Incidence rates (new cases/100,000 people) of inflammatory bowel diseases distributed by gender, over the four study intervals (1986-2005)

The adjustment, by Poisson regression model, of time of entrance in the study of patients with UC, CD and NCC, in accord with gender (Table 3), showed that incidence rates differed according to disease type (IBD:RR=11.47;95% CI= 7.17-18.35;*P*<0.001). So, the incidence of UC was significantly higher than that of CD, which in turn was significantly higher than NCC incidence in all periods. In addition, there was a female preponderance in all types of diseases (gender: RR=0,50; 95%CI=0,10-0,62; *P*<0.001). The incidence of UC, CD and NCC showed an increased in a different way along the study (Figure 3). The CD and NCC incidence rates increased progressively from the first 5-year interval (1986 to 1990) to the last (2001 to 2005), whereas UC incidence rate dropped in the last interval [IBD* (time entrance)^2: RR=0,88; 95% CI=0,86-0,91; *P*<0.001)].

TABLE 3. Incidence of ulcerative colitis (UC), Crohn's disease (CD) and non classified colitis (NCC) adjusted to gender, time of entrance and 5-year interval by Poisson modeling

Parameters	β	$se^{(\beta)}$	Z	*P*	RR	CI
Intercept	-414.37	115.50	-3.58	<0.001		
Log (population)	33.43	9.42	3.54	<0.001		
IBD	2.44	0.47	5.13	<0.001	11.47	(7.17;18.35)
Gender	-0.68	-0.21	-3.21	<0.001	0.50	(0.10;0.62)
(Time of entrance)^2	-0.03	0.14	-0.25	0.795	0.97	(0.84;1.11)
IBD*(time of entrance)	-0.12	0.03	-3.58	<0.001	0.88	(0.86;0.91)

Residual deviance = 6.68 and χ^2 = 8.54 with 18 degrees of freedom. AIC:80.62; IBD= inflammatory bowel disease; β=estimated parameters; se $^{(\beta)}$ = estimated parameter standard-error; z = statistic test values; *P* = values of significance statistic associates to parameters of the model, estimates punctual and at intervals; RR = ratio risk; CI = 95% confidence interval

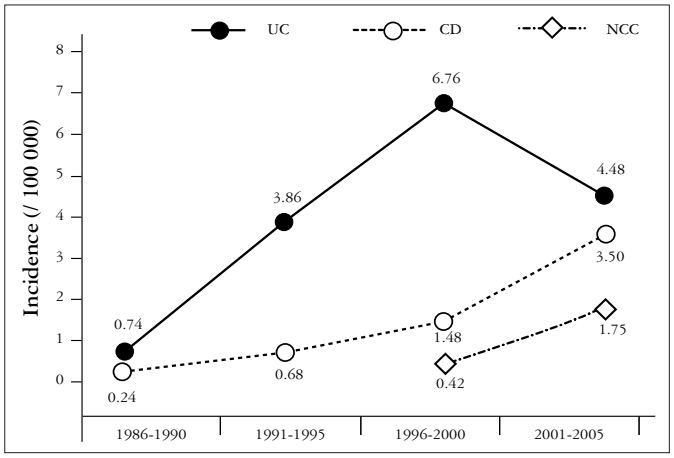

FIGURE 3. Incidence rates of ulcerative colitis (UC), Crohn's disease (CD) and non-classified colitis (NCC) over the four study periods (1986-2005)

Between 1986 and 2005, the prevalence rates of UC, CD and NCC in the entire studied population increased more in the first 2 intervals than in the last one (Figure 4).

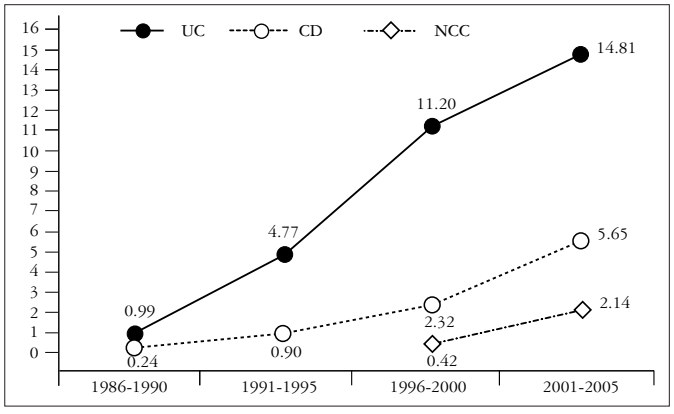

FIGURE 4. Prevalence rates (existing cases/100,000 inhabitants) of ulcerative colitis (UC), Crohn's disease (CD) and of non-classified colitis (NCC) over the four study periods (1986-2005)

DISCUSSION

The medical services in the study area have been limited regarding IBD management. Thus, a specific medical service to manage patients with IBD was started in 1986 at University Hospital at Botucatu School of Medicine, in Midwestern region of São Paulo State (Brazil). In this service, IBD patients are attended by a specialized group of gastroenterologists, nutritionists and psychologists. The attendance of the group is weekly and a follow up visit is obligatory every 6 months for all patients in remission of disease. In the event of an acute crisis, the patient is guided to the Hospital service, as soon as possible, in any time. As a result, the relationship between IBD patients and the specialists group is very close. This service utilizes the Brazilian government assistance program for patients with IBD, and consequently is able to provide free medical care, free laboratory tests and treatment with high cost drugs. These conditions have significantly improved the care delivered to IBD patients in this region, with good results as already observed by others[17, 19].

The dates used in this study were based mainly on sequential register of cases of patients from a single general hospital, but limiting the results to cases coming from the investigated area. Due to the population data from this area is known, the computation of new and existing cases was possible. The set of cases studied reflects, therefore, just a part of the total number of IBD patients seen at this service. Differently from other Brazilian investigations, that utilized dates of patients coming from distinct regions, this work utilized data collected from patients coming from a single and well-limited target region with known population density and so can reflect the comportment of IBD on it. However, patients from the studied area, with milder symptoms, who were misdiagnosed or did not seek medical advice, might have gone unnoticed and not referred to this service, causing underestimated incidence and prevalence rates. Nevertheless, since this study covered a long time period, and because these disorders develop into chronic conditions with many acute periods of variable severity, and most patients cannot afford continuous and expensive medications, they end up by seeking free public reference hospital of ours area, for better treatment, in some moment of their life, as frequently observed in many medical services.

Thus, total IBD, UC, CD and NCC incidence adjusted for female, male and total population computed for the four periods allowed to appraise the growth and evolution of these diseases in this area. The dates showed the incidence rates of IBD to be similar to that observed in other countries of Latin America[6, 15] and Southern and Eastern Europe[9, 14, 16, 23], where industrial development is as low as in the study area.

Among all IBD studied, UC had the highest incidence rate. These results are in line with European dates. However, the European studies report that UC is slightly more frequent in men that differ from dates showed in this work[16].

The data of the present work also showed that women were the most affected by CD, in agreement with the data obtained in Chile and in Brazil[5, 6]. Notwithstanding, they are in disagreement with another study also conducted in Brazil and others performed in Canada and Puerto Rico where CD was found to be more frequent in males[1, 2, 8]. Moreover, in Ribeirão Preto city – an urban district of high industrial development located North of the study area – the number of patients of both genders with CD has increased over the past years, based on hospital statistics[29]. The explanation for these differences are not easy to be found due to the different methodologies used in some these works and the great regional diversity of environmental and social factors that were not appraised in this study. Nonetheless, we can suppose that as women — mainly in the less development countries — in order to help the home budget, are taking even more and more jobs in industries and factories located in urban

areas, where they become more frequently exposed to factors closely associated with the etiology of IBD.

In this study, a high IBD incidence was observed in city dwellers. Over the last years, people have left the countryside to live in the periphery of urban areas more frequently. Three out of four inhabitants of the study were urban dwellers[12]. This has produced important changes in lifestyle, particularly in dietary habits and more exposition to pollution agents. Theses facts may explain why IBD incidence was found to be higher in urban districts than in rural areas.

In the study area, IBD incidence was higher in individuals of the white race. Racial composition in Brazil shows significant regional differences. In the more developed areas (South and Southeast), most inhabitants are white while in the less developed areas (North and Northeast) the black predominates. The largest part of the population (43,7%) is concentrated in the Southeast, where 64% of population are white and 34% are black[11]. The study area is located in the Southeast of Brazil, with white race predominance and, where a great number of white European immigrants — mostly Italians — settled in the past (1890-1940). The highest incidence of IBD observed in white people of the studied region could be explained like this, and the epidemiological data collected were expected to be similar to those seen in the immigrants' home countries. However, the IBD incidence in Italy is much higher, with UC being slightly more prevalent in males, which differs from dates of this work[3, 31]. This could be explained by the great miscegenation that occurred in the study area, as well as by the environmental effect, caused by its poorer industrial development. Nevertheless, in other areas in Brazil with similar development as in study area, the level of CD is more frequent among in black than in white people, like showed at hospital statistics[5]. This is probably due to the wide regional racial differences found in our country and pointing to the fact that industrial development and genetic race penetration could not be the only causal agents of these complex diseases.

The great increase of IBD incidence rates, initially observed over the first two intervals of the study, diminished and reached a plateau over the last one. This behavior can be attributed to an initial greater patient demand that later stabilized at regular levels and advances in the criteria used to diagnosis IBD in the region. The increased prevalence of non-classified colitis over the latter study time intervals, now reaching 0.42 cases/100.000/year, may be also attributed to an advance in the criteria used to confirm the diagnosis of IBD in this service[24]. Based on these observations, and considering the reported prevalence in the last period of study, we can expect about 240 patients with IBD every 5 years or at least 48 patients/year. A large number of these patients will require an approach involving very high costs treatment[30], which shall be supplied by the government, due to the social conditions of most of the patients. Also, many patients will show a fall in their productive capacity as demonstrated in Germany[28]. Thus, even though IBD are still relatively rare in our region, workers with IBD are likely to require more assistance from the government than other workers[17]. Therefore, it is necessary to set policies to avoid the impact of the disease on the well being and the working power of these patients.

Victoria CR, Sassaki LY, Nunes HRC. Incidência e prevalência das doenças inflamatórias intestinais na região centro-oeste do Estado de São Paulo. Arq Gastroenterol. 2009;46(1): 20-25.

RESUMO – ***Contexto*** - No Brasil, a incidência e prevalência populacionais das doenças inflamatórias intestinais são desconhecidas. ***Objetivo*** - Neste trabalho, estimou-se esses parâmetros na área que abrange a antiga região de saúde DIR 11, no centro-oeste do Estado de São Paulo. ***Métodos*** - Usou-se um registro sequencial de 115 pacientes (>15 anos de idade) com doenças inflamatórias intestinais, residindo na área de estudo, atendidos durante período de 20 anos (1986-2005) em hospital de referência. Estimou-se, para quatro períodos consecutivos de 5 anos, as incidências e prevalências de acordo com os tipos de doença e do sexo de doentes. As suas inter-relações foram analisadas utilizando o modelo de regressão linear de Poisson. ***Resultados*** - Na região, as doenças inflamatórias intestinais foram predominantes em mulheres jovens, da raça branca, residindo na zona urbana.A incidência da retocolite foi maior que a da doença de Crohn e das colites não classificadas, e diferentemente dessas duas ultimas, mostrou decréscimo no último período (2001-2005). Neste mesmo período, a taxa da incidência para a retocolite foi de 4,48 casos/100.000 habitantes, para a doença de Crohn atingiu 3,50 casos/100.000 habitantes e a das colites não classificadas foi de 1,75 casos/100.000 habitantes. As prevalências atingiram os valores de 14,81 casos/100.000 habitantes para a retocolite, 5,65 casos/100.000 habitantes para a doenças de Crohn e 2,14 casos/100.000 habitantes. Considerando todas as doenças inflamatórias a prevalência atingiu o valor de 22,61 casos/100.000 habitantes. ***Conclusão*** - A incidência dessas doenças inflamatórias intestinais nessa região é baixa, igualando-se aos países da América Latina e do sul da Europa e sua crescente prevalência justifica políticas de saúde para as suas abordagens.

DESCRITORES – Enteropatias inflamatórias, epidemiologia. Colite ulcerativa, epidemiologia. Doença de Crohn, epidemiologia. São Paulo (Brasil).

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