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INFLAMMATORY BOWEL DISEASE: EPIDEMIOLOGICAL ASPECTS OF HOSPITALIZATION IN A STATE IN THE AMAZON REGION

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Abstract: Introduction: Inflammatory bowel disease (IBD) is a term that encompasses Crohn's disease (CD) and ulcerative colitis (UC), recognized for causing chronic inflammation of the gastrointestinal tract. In Brazil, in 2020, they represented 0.5% of hospitalizations due to digestive diseases. IBD does not show gender preference, has a higher incidence between 20 and 40 years and low mortality. CD and UC present similar clinical aspects, with emphasis on diarrhea, digestive bleeding and abdominal pain. Objectives: To analyze the epidemiological aspects of hospital admissions for IBD in the State of Amapá, through the ICD-10 morbidity list (K50/K51), in the period from 1998 to 2022, considering sociodemographic aspects, deaths and length of hospital stay. Method: An ecological study, the data source of the Hospital Information System (SIH-SUS) of the Unified Health System was used. Results: 357 admissions were registered. Macapá had the highest number of hospitalizations (190). The most affected age group was 20 to 39 years old (110). There were 7. The mean length of stay was 7.4 days. Conclusion: CD and UC have low incidence and lethality. Hospitalizations are more common in the age group with greater work activity and the average length of stay is significant.

INTRODUCTION

EPIDEMIOLOGY

Inflammatory bowel disease (IBD) is a medical term that encompasses Crohn's disease (CD) and ulcerative colitis (UC), recognized for causing chronic inflammation of the gastrointestinal tract (GIT) (VILELA et al., 2020). Despite being present in the same pathological group and sharing important characteristics, CD and UC present markedly different aspects, mainly according to the regional extent of inflammation (VILELA et al., 2020). CD is known for inflammatory processes that can settle from the oral cavity to the anus, while UC has symptoms restricted to the colon and rectum (FLORES; CALIXTO; FRANCESCONI, 2013).

CD and UC receive more attention in Europe and the United States, with incidences of 7 per 100,000 inhabitants and 11 per 10,000 inhabitants, respectively. In Brazil, IBD has a low incidence, despite the progressive increase in recent years (FLORES; CALIXTO; FRANCESCONI, 2013). In 2020, in Brazil, 4,405 hospitalizations for CD and UC were registered, representing 0.5% of all hospitalizations for diseases of the digestive system (FLORES; CALIXTO; FRANCESCONI, 2013). There is no preference between genders, with regularity in the number of cases between men and women. Regarding the age group, the incidence of CD and UC is more common in young adults, comprising ages between 20 and 40 years. Mortality, however, is more present in elderly patients (ABOU; PEREIRA; FATURI, 2003).

ETIOLOGY AND PATHOPHYSIOLOGY

CD and UC do not have a fully understood etiology, however, genetic, environmental and immunological aspects involved in the genesis of these diseases are known (SANTOS et al., 2015). The genetic influence is highlighted as an etiological factor due to the higher occurrence of IBD in families with members with these diseases. Mutations in the NOD2/CARD5 gene, responsible for maintaining the nonspecific immune system in the gastrointestinal epithelium, decrease protection against antigenic components and increase the susceptibility and development of the chronic inflammatory process, characteristic of CD and UC (STUCCHI; BECKER, 1999).

CLINICAL CONDITION

In CD, the inflammatory process can manifest itself in all regions of the digestive tract and is characterized by discontinuous ulcerative lesions that can compromise all histological layers of the gastrointestinal tract. In contrast, in UC the inflammation of the intestinal mucosa is continuous and well demarcated, restricted to the colon and rectum (KLEINUBING-JÚNIOR et al., 2011).

CD and UC present similar clinical signs, with emphasis on diarrhea, lower digestive bleeding, chronic anemia, weight loss and abdominal pain. IBD, in some cases, course with extraintestinal manifestations, such as arthritis, sacroiliitis, hepatic steatosis, cirrhosis and cutaneous manifestations, such as opioderma gangrenosum (KLEINUBING-JÚNIOR et al., 2011).

DIAGNOSIS

There is no diagnostic gold standard for IBD, only finding the diagnosis through endoscopic, radiological and histopathological examinations, therefore, the real number of IBD is not known (SARLO; BARRETO; DOMINGUES, 2008). In Brazil, there is no survey of the number of patients diagnosed with IBD, but there is concern in the scientific community due to the growth of regionalized epidemiological studies that show an increase in IBD cases (SARLO; BARRETO; DOMINGUES, 2008).

Due to its similarity with other IBD such as ulcerative colitis (UC), in the early stages CD can be misdiagnosed as irritable bowel syndrome, which is why it requires high clinical training for its complex and difficult clinical investigation, in which it has an average time of diagnosis from 9 to 18 months (MOUGALIAN et al., 2015). As a result, the analysis of endoscopic, histological and radiological data are the most used techniques currently for diagnosis, showing focal, asymmetric, transmural or granulomatous involvement (MOUGALIAN et al., 2015).

With endoscopy, it is possible to visualize the ulcerated lesions, interspersed with areas with normal mucosa, focal, asymmetrical and discontinuous involvement, allowing the collection of material for analysis. Histological analysis, in turn, evaluates the presence of non-caseating granulomas, transmural involvement and segmental pattern (MOUGALIAN et al., 2015).

The histological study of the biopsies obtained by colonoscopy enables diagnostic confirmation, through the differential diagnosis between CD and UC, and the diagnosis of dysplasia and cancer in cases of long-standing colitis (ABOU; PEREIRA; FATURI, 2003). Capsule endoscopy (CE), magnetic resonance enterography (MRE) and contrast-enhanced ultrasound are evaluated as similar diagnoses in determining CD and the risk of surgery (KOPYLOV et al., 2017).

Colonoscopy with ileoscopy allows the visualization and biopsy of the mucosa of the colon, rectum and terminal ileum, thus being considered fundamental in differentiating the diagnosis of ulcerative colitis (UC) from CD with an efficiency of 90% (ALEXANDRE et al, 2018).

Conventional enteroclysis and CT have good diagnostic accuracy, but are limited by exposure to ionizing radiation. Ultrasound, on the other hand, does not contain radiation, but it is limited, because the image quality depends on the technician's experience and it has difficult access to some visualization areas (BARATTA et al., 2022). The main CT findings that indicate Crohn's disease are intestinal wall thickening, mural hyperenhancement, mural stratification, comb sign caused by engorged vasa recta and higher density perineral fat (BARATTA et al., 2022).

It must be noted that, due to the immunological intolerance of patients with

CD against non-pathogenic microorganisms, a large number of patients develop anti-Saccharomyces cerevisiae (ASCA) antibodies, a yeast present in various foods. Thus, in some cases the detection of ASCA has been used as a marker in the differential diagnosis of CD in both adult and pediatric populations (KIM et al., 2021).

TREATMENT

As it is a disease of unknown etiology, the clinical treatment of CD is largely empirical, individualized and guided by the patient's risk stratification (SARLO; BARRETO; DOMINGUES, 2008).

Clinical therapy aims to reduce and control the level of inflammation in the gastrointestinal system, which generate various symptoms (OLIVEIRA, 2015). The patient must be accompanied by specialists, and sometimes involves the need for surgical intervention (OLIVEIRA, 2015). From the symptoms presented by the patient, it is possible to measure the degree of the disease in mild, moderate or severe, and the treatment can be carried out in stages, making it easier for the clinician to choose the best way to treat the patient. This contributes to the reduction of symptoms and induces the patient to remission of the disease (OLIVEIRA, 2015). In the active stages of the disease, support, psychological control, and adherence to drug therapy are extremely important for the treatment and control of the disease (OLIVEIRA, 2015).

Aminosalicylates such as sulfasalazine and mesalazine are used for an initial clinical approach for mild cases. Sulfasalazine, when degraded by bacterial action, is divided into sulfapyridine and 5-aminosalicylic acid, which has topical anti-inflammatory action. Regarding administration, sulfasalazine must be prescribed at a dose of 2 to 6 g/day and, at each use, folic acid at 2 to 5 mg/day must be used to prevent the risk of macrocytic anemia. In addition, mesalazine has been shown to be effective in protecting against the onset of dysplasia and colorectal cancer in patients with colitis (SOBRADO; LEAL; SOBRADO, 2016).

Antibiotics are used to prevent acute exacerbations with systemic repercussions triggered by toxic megacolon, abscesses, fistulas, and sepsis. The two most used antibiotics are ciprofloxacin (1g/day) and metronidazole (10-30 mg/kg) that can be administered for up to three months (DA SILVA; SILVA; RODRIGUES, 1996).

Corticosteroids can be used in cases of moderate and severe active CD. In the oral form, prednisone or prednisolone can be administered, while hydrocortisone can be administered parenterally. Prednisone at a dose of 0.75 to 1 mg/kg/day (maximum 60 mg/day) is indicated to induce clinical remission that occurs 2 to 4 weeks after initiation. This corticosteroid is intended to reduce disease activity, but does not change the natural course. Furthermore, patients who do not respond to corticosteroids or who are dependent on corticosteroids must be treated in phases, with the introduction of immunosuppressants or biological therapy. This phased therapy is indicated in the following situations: clinical worsening within 6 weeks after withdrawal of steroids; need for more than two courses of corticosteroids within a year; and recurrence of symptoms whenever the dose is reduced below 15 mg (SOBRADO; LEAL; SOBRADO, 2016).

Immunosuppressants are indicated to maintain the remission achieved after the use of corticosteroids, with the immunosuppressants used being azathioprine and 6-mercaptopurine (SOBRADO; LEAL; SOBRADO, 2016).

Biological therapy, introduced in the treatment of CD two decades ago, has been

shown to be efficient in healing the mucosa, in addition to clinical response and remission. Furthermore, patients with severe CD and poor prognosis may benefit from the use of these antibodies. Monoclonal antibodies such as infliximab (INX) and adalimumab (ADA) are used. These drugs act by inhibiting alpha tumor necrosis factors and, consequently, inhibiting their pro-inflammatory actions (PAGNINI; SIAKAVELLAS; BAMIAS, 2018).

Regarding surgical treatment, depending on the intensity and intestinal segment affected by the inflammation, the appearance of fistulas and obstructions may occur so that surgical treatment becomes necessary (MEIMA-VAN PRAAG et al., 2021). About 70 to 90% of patients will need some form of surgical treatment throughout their lives, ranging from simple drainage of anal abscesses to resections of intestinal segments, and 80% of operated patients suffer surgical recurrence (MEIMA -VAN PRAAG et al., 2021).

The increase in the incidence of CD worldwide makes it necessary to develop treatments (clinical or surgical) with a focus on the quality of life of these patients, with methods that reduce intestinal inflammation and promote the healing of this mucosa. With this, the therapy will be as personalized as possible (SOFIA; PINTO, 2021).

OBJECTIVES AND METHODOLOGY

This work aims to study the epidemiological aspects of hospitalizations for Crohn's disease and ulcerative colitis in the state of Amapá, from 2008 to 2022, based on the following parameters: number of hospitalizations, sex, age, municipality, death and average time of hospitalization.

This is an observational, aggregated and cross-sectional epidemiological study, using data referring to hospitalizations for inflammatory bowel diseases (Crohn's disease and ulcerative colitis, according to the ICD-10 Morbidity List) in the state of Amapá from January 1998 to December from 2022.

Data were taken from the hospital information system (www.datasus.gov.br). As it related to a database that is in the public domain, it was not necessary to submit the study to the Research Ethics Committee. The following were analyzed as parameters for tracing the epidemiological profile: gender, age group, city of hospitalization, number of deaths and average length of hospitalization.

The study period comprises the years between 1998 – the year in which records of these diseases began – and 2022 – the year with the most recent data available. Data were analyzed from absolute, proportional and percentage numbers. For trend analysis and graphic construction, the software GraphPad Prism version 9.0 was used.

RESULTS

In the state of Amapá, hospitalizations due to Crohn's disease and ulcerative colitis, in the period from 1998 to 2022, represented approximately 0.62% of all hospitalizations due to digestive system diseases in the state. During this period, there were 357 hospitalizations, of which 202 (56.58%) were male cases and 155 (43.42%) were female cases, demonstrating that there is a small prevalence of prominence for males. The highest number occurred in 2003, with a total of 50 hospitalizations, corresponding to 14%, in these 25 years of the study period. Graph 1 shows the number of hospitalizations for IBD in Amapá per year, according to the period studied.

Analyzing the number of hospitalizations in the years studied, a peak was observed in 2001 (31 cases, 8.68%), 2002 (33 cases, 9.24%), 2003 (50 cases, 14.00%), 2004 (48 cases, 13.44%), followed by a drop in the number of hospitalizations from 2005 (16 cases, 4.48%)

to 2013 (8 cases, 2.24%). From 2014 to 2020 there was a good drop in hospitalizations, with an average of 4.5 hospitalizations per year. An increase was observed in the last two years, 2021 (8 cases, 2.24%) and 2022 (12 cases, 3.36%).

When data are analyzed by municipality, a prevalence can be observed over those with the largest population. Among the municipalities in Amapa, the state capital stands out with more than half of the hospitalizations, the municipality of Macapá with 190 (53.22%) cases, followed by Porto Grande with 75 (21.00%) cases, Santana with 44 (12.32%) cases and Laranjal do Jari with 40 (11.20%) cases, corresponding together to a percentage of 97.74% of admissions (graph 2).

According to the age group, there was a greater number of hospitalizations in the corresponding ages between 30 and 39 years. Thus, the smallest number of cases is in the age group of 05 to 09 years (02 cases, 0.57%), followed by 10 to 14 years (06 cases, 1.69%) and less than 01 years (09 cases, 2.53%), respectively. From that point onwards, an increase is observed as the age group rises, in the groups from 01 to 04 years old (18 cases,

5.05%), 15 to 19 years old (24 cases, 6.73%), a significant increase between 20 and 29 years old (54 cases, 15.14%), with a peak in the age group of 30 to 39 years old (70 cases, 19.62%). Thereafter, a reduction can be seen in the following age groups, between 40 and 49 years old (50 cases, 14.01%), between 50 and 59 years old (37 cases, 10.37%), between 60 and 69 years old (35 cases, 9.81%), between 70 and 79 years old (32 cases, 8.87%) and over 80 years old (20 cases, 5.61%). Confirming middle age as the age range for diagnosis of the disease.

During the study period, there was an average stay of 8.3 days of hospitalization, with emphasis on the years 2017 and 2022, obtaining an average of 27.6 and 25.5 respectively.

It must also be noted that there were 07 deaths in the analyzed period, demonstrating that the low lethality in the region studied is in line with the national average. Of these deaths, 06 affected males, corresponding to 85.72% of deaths and 01 affected females, corresponding to 14.28% of deaths. It was observed that the highest lethality occurred in the age group above 60 years old, totaling 04 deaths.
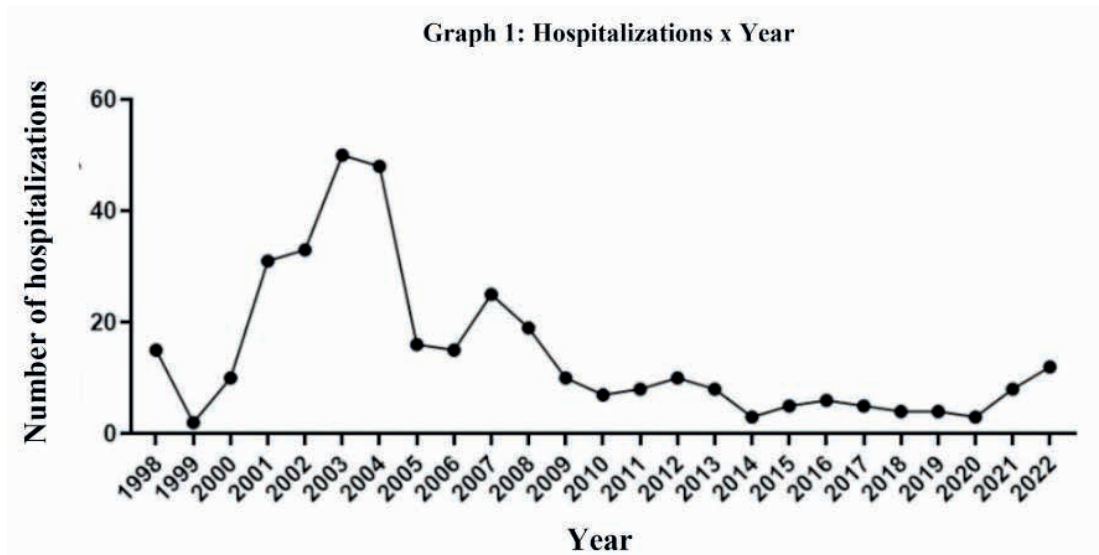
Graphic 1. Hospitalizations for Crohn's disease and ulcerative colitis in the State of Amapá, Brazil.1998-2022.
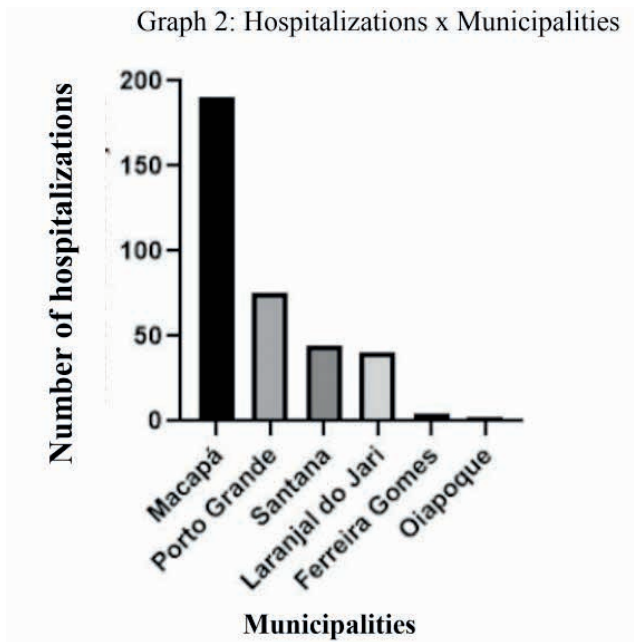
Graph 2. Hospitalizations for Crohn's disease and ulcerative colitis in the State of Amapá by municipality.1998-2022.
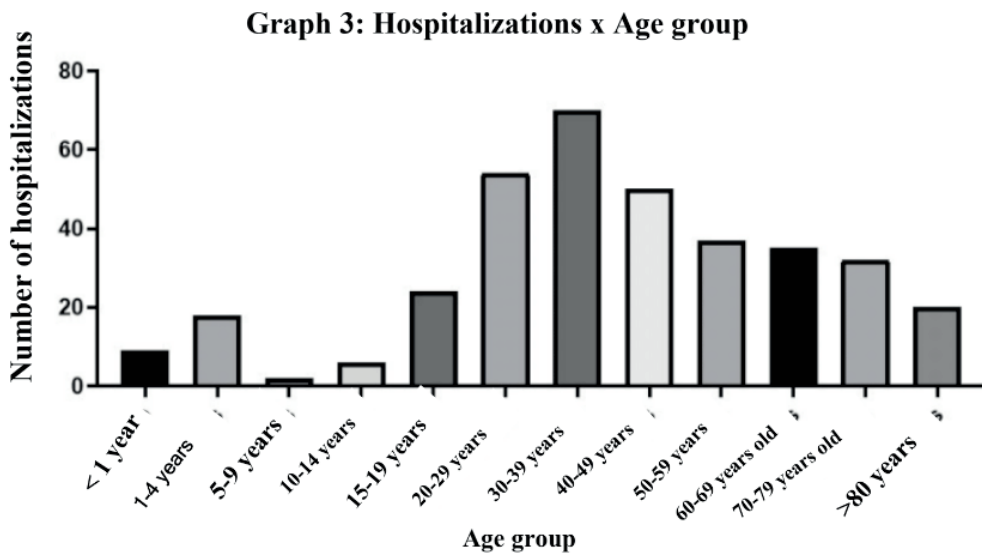
Graph 3. Hospitalizations for Crohn's disease and ulcerative colitis in the State of Amapá by age group. 1998-2022.

DISCUSSION

Inflammatory bowel diseases (IBD) have shown a change in their epidemiological profile in recent years (PALMIRO et al., 2021). IBD were more common in Northern Europe and the USA, but with the socioeconomic improvements of the population of underdeveloped countries, with new westernization and smoking habits, the incidence of IBD increased worldwide (PALMIRO et al., 2021). Brazil also follows this trend and has seen an increase in the number of cases in recent years (SELINGER et al., 2019). In the state of Amapá, there was a significant increase in hospitalizations from

the year 2001, with a peak in the years 2003 and 2004, followed by a decrease until the year 2013, from then on there is a plateau with an average of 05 hospitalizations per year. This growth in hospitalizations in the state of Amapá from 2001 onwards coincides with the period of greatest development and demographic growth in the state and corroborates the causes of incidence mentioned above (SELINGER et al., 2019).

In the State of Amapá, the regions with the most hospitalizations are the most urbanized, collaborating with the most current studies that IBD have a strong influence on residents of urbanized areas (PALMIRO et al., 2021). On a global scale, this epidemiology is also demonstrated, since more industrialized countries are the ones with more cases, such as North America, the United Kingdom and Australia (SELINGER et al., 2019). Most likely, it may be related to the Western diet, based on foods rich in fats and sugars (MARQUES; PATRÍCIO, 2019).

As for age, the age group from 20 to 69 years old has the highest number of hospitalizations, the same occurred in a study carried out in Minas Gerais, with 70% of hospitalizations in the age group from 20 to 69 years old (BRITO; PINTO, 2019). In a national study, the age group with the highest number of records was 20 to 59 years old (PALMIRO et al., 2021). Along the same lines, in a study carried out in a hospital in Amazonas, where diagnoses with 70% of cases occurred in the age group of 20 to 69 years, there is no doubt that the age group of IBD prevalence, both in the diagnosis and in the hospitalizations, are from 20 to 69 years old (SANTOS; et al, 2015).

In pediatric age, the most prevalent age group was 01 to 04 years in the state of Amapá. Most pediatric patients are diagnosed in late childhood, since cases below this age are difficult to diagnose (SELINGER et al., 2019).

Regarding gender, data from the state of Amapá show a prevalence of hospitalizations by males (56.58%) compared to females (43.42%). In the study carried out in a reference center in the city of Salvador, the prevalence of diagnoses was for females (60.90%) compared to males (39.10%) (MARQUES; PATRÍCIO, 2019). In a study carried out in the eastern macro-region of the state of Minas Gerais, there was no gender prevalence, of the 363 hospitalizations, 50.70% were male and 49.30% were male (OLIVEIRA et al, 2008). In the national study, a prevalence for females (53.55%) compared to males (46.45%), corroborating the study by Salvador (PALMIRO et al., 2021). Unlike the study's proportion of hospitalizations in the state of Amapá, a possible explanation would be a greater demand for health services by women, which leads to underreporting in the case of men.

The average length of hospital stay in Brazil is 7.1 days and in the state of Amapá 8.3 days, the latter being within the national proportion, these data reveal a high degree of morbidity from the disease, in addition to high costs for health services (PALMIRO et al., 2021).

In Brazil, IBD has a low death rate. In the national study, there were 1,169 deaths (2.51%), with the North region having the lowest rate (0.13%), peak in the age group of 70 to 79 years (0.47%) and a slight prevalence for the men (51.83%) compared to women (48.16%) (PALMIRO et al., 2021). The data from the state of Amapá follows the data from the national study, low mortality rate (1.96%) with a predominance of men (85.72%) in relation to women, with only one death out of seven that occurred in the study period.

FINAL CONSIDERATIONS

Inflammatory bowel diseases, Crohn's disease and ulcerative colitis, present in the period studied, a higher prevalence of hospitalizations in the most populous

municipalities, Macapá, Porto Grande, Santana and Laranjal do Jarí. In the age group, the highest number of hospitalizations was between 20 and 49 years old. In hospitalizations by gender, there was a slight predominance for men and a high prevalence of deaths compared to women. In addition, during the study period, the average number of hospitalized days was 8.3. There are still not many studies on these diseases in Brazil, a likely reason is that IBD is not compulsory notification. Of the few studies we have, there is a greater number of cases in more urbanized and industrialized regions.

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