



## Original article

# The epidemiological profile of inflammatory bowel disease patients on biologic therapy at a public hospital in Alagoas



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## ABSTRACT

**Introduction:** Inflammatory Bowel Diseases (IBD), represented by Crohn's disease (CD) and ulcerative colitis (UC) are chronic and idiopathic inflammatory conditions involving the gastrointestinal tract. There are several epidemiological studies that have shown an increased incidence of IBD worldwide.

**Objective:** To analyze the epidemiological profile of patients with IBD under biologic therapy, treated in a coloproctology outpatient clinic, Hospital Universitario Professor Alberto Antunes, Alagoas.

**Methods:** Retrospective observational clinical study, conducted by collecting patients' records and interviewing them at the time of follow-up.

**Results:** 40 patients were evaluated: 70% female, 27 patients (67.5%) with CD and 13 (32.5%) with UC, mean age of 37.8 years and predominance of white ethnicity. The ileocolonic area was more frequently affected among patients with CD (33.3%), whereas the extensive colitis presentation predominated among UC patients (61.5%). 95% of the patients received some medication before using biologicals. 70% of the respondents remain in deep remission in the period of 6–60 months.

**Conclusion:** The socioeconomic profile of patients was similar to that described in the literature. Crohn's disease was more frequent in our study, while extensive colitis was more common among UC patients. Most patients used biologicals after failure of other treatment options.

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## Perfil epidemiológico dos pacientes portadores de Doença Inflamatória Intestinal, que fazem uso da terapia biológica, atendidos em um hospital da rede pública de Alagoas

### R E S U M O

#### Palavras-chave:

Doença intestinal inflamatória  
Perfil epidemiológico  
Colite ulcerativa  
Doença de Crohn  
Medicamentos biológicos

**Introdução:** As Doenças Inflamatórias Intestinais (DII), representadas pela Doença de Crohn (CD) e Retocolite Ulcerativa Inespecífica (RCUI), são condições inflamatórias crônicas, idiopáticas, que envolvem o trato gastrointestinal. Vários são os estudos epidemiológicos que vêm demonstrando o aumento na incidência da DII em todo o mundo.

**Objetivo:** Analisar o perfil epidemiológico dos pacientes portadores de DII, que fazem uso da terapia biológica, atendidos no Serviço de Coloproctologia do Hospital Universitário Professor Alberto Antunes da Universidade Federal de Alagoas.

**Métodos:** Estudo clínico descritivo observacional transversal, realizado através da coleta dos prontuários dos pacientes e entrevista com os mesmos no momento da consulta de acompanhamento.

**Resultados:** Foram avaliados 40 pacientes, sendo 28 do gênero feminino e 12 do gênero masculino. 27 pacientes (67,5%) apresentavam DC e 13 (32,5%) apresentavam RCUI, com uma média de idade de 37,8 anos com predominância da etnia branca. A região íleo-colônica foi a localização mais frequente entre os pacientes com DC (33,3%), enquanto que a colite extensiva predominou entre os portadores de RCUI (61,5%). 95% dos pacientes fizeram uso de algum medicamento antes do uso dos biológicos. 70% dos entrevistados permanecem com remissão profunda no período de 6 a 60 meses.

**Conclusão:** O perfil socioeconômico dos pacientes foi semelhante ao descrito na literatura. Doença de Crohn foi mais freqüente em nosso estudo, enquanto que colite extensiva foi a forma mais comum entre os portadores de RCUI. A maioria dos pacientes fez uso dos biológicos após falha das outras opções de tratamento clínico.

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## Introduction

Inflammatory Bowel Disease (IBD), represented by Crohn's disease (CD) and Ulcerative Colitis (UC), are chronic, idiopathic inflammatory conditions, which probably involve an immune reaction of the body against its own gastrointestinal tract.<sup>1,2</sup> Considering that these are chronic conditions that affect preferably young people in the productive phase and contribute to long-term morbidity, thus causing changes in the social, psychological and professional realms, IBDs are gaining importance, constituting a public health problem in many countries, with a large financial impact on the health-care system.<sup>3-6</sup>

There are several epidemiological studies showing an increased incidence of IBD in the world.<sup>1-8</sup> A recent epidemiological research estimates that about 4 million people worldwide have either UC or CD, with 1.4 million of these cases occurring in the United States.<sup>9</sup> The male/female ratio is similar for both UC and CD, with women showing a slightly higher incidence. Both diseases are more commonly diagnosed in young adults. The vast majority of new diagnoses are detected in the age ranging between 15-40 years, with the peak incidence occurring early in the second decade of life.<sup>2</sup>

Brazil is still considered an area of low prevalence of IBD, despite the significant increase in the incidence of these

diseases in reports of the national literature. In our environment, these diseases are not considered of compulsory notification, which leads us to think that perhaps IBDs are being underdiagnosed.<sup>4</sup>

The management of IBD will depend on its severity and of the extent and anatomical region involved. A large number of drugs have been used, achieving remission, but not a cure for the disease. Among the classes used in conventional therapy, aminosalicylates, glucocorticoids, immunomodulators and antibiotics are mentioned.<sup>10,11</sup> However, the conventional therapeutic options for IBD are limited, both by the inability to maintain clinical remission, and by their side effects.<sup>10</sup> In this context, a new therapeutic approach emerges based on the use of antagonists of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ): the so-called biological therapy.

The evidence for use of biological therapy comes from large-scale randomized clinical trials. The class of anti-TNF- $\alpha$  agents, in general, has demonstrated considerable effectiveness in moderate to severe intraluminal CD.<sup>12</sup> It is not completely clear whether the biologic therapy approach would be most effective when used at an early stage, with possible beneficial impacts on the natural course of the disease, or would be indicated later, after a failure to respond to traditional drugs.<sup>13</sup> Therefore, the lack of national epidemiological data on IBD, in association with the currently existing paradigm regarding the early use of biological therapy in the

treatment of these diseases, corroborates the relevance of this study.

## Objective

To analyze the epidemiological profile of patients with inflammatory bowel disease using biological therapy treated at the Coloproctology Service, Hospital Universitário Professor Alberto Antunes, with characterization of patients according to social, clinical and disease-related aspects.

## Method

This is an observational cross-sectional descriptive study that was conducted from March 2012 to March 2013 in the coloproctology outpatient clinic, Hospital Universitário Professor Alberto Antunes (HUPAA), a reference service in colorectal diseases' care.

The study population involved all patients with inflammatory bowel disease (IBD): Crohn's disease, ulcerative colitis or indeterminate colitis, seen, registered and followed up in the coloproctology outpatient clinic, HUPAA, with a total of 44 patients. The sample consisted of forty (40) patients, in view of the withdrawal or exclusion of some individuals in the population.

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Patients of both genders, regardless of age, diagnosed with IBD, seen at the coloproctology outpatient clinic, HUPAA – UFAL, and currently in biological therapy were enrolled. On the other hand, patients who, for some reason, had to stop their biologic therapy, in addition to patients using biologicals for different pathologies of IBD, were excluded from the study.

The medical records of the subjects were acquired by consultation of HUPAA – UFAL files, under authorization by the institution proposing the study, with assurance of complete confidentiality in relation to personal data and clinical information, according to the standards proposed by the Resolution CNS/MS 196/96.

In cases where information from medical records was insufficient for implementation of the Research Protocol for IBD, patients were approached during routine consultations, to conduct an interview aimed at complementing this protocol.

After collecting the clinical records, the social aspects, medical history and current history of the disease were analyzed, in order to adapt these data to the research objectives (by inclusion and exclusion criteria) and to implement the Research Protocol for Inflammatory Bowel Disease. In the event that the information contained in medical records was insufficient, the Protocol was complemented with interviews with the patient itself.

After data collection, the material was scanned into a database and processed.

The following project was approved by the Ethics and Research Committee, Centro de Ensino Superior de Maceió (CESMAC), and registered under protocol number 1419/12. All patients interviewed were informed about the study objectives and signed two (2) copies of a Free and Informed Consent Term

**Table 1 – Disease location according to the Montreal classification between March 2012 and March 2013, Alagoas.**

Location	Number of patients	Percentage (%)
Colon	9	33.3
Ileum and colon	9	33.3
Terminal ileum	7	25.9
Upper gastrointestinal tract	2	7.5

– FICT. For those cases in which the analysis of medical records was done, FICT exemption was requested.

## Results

After conducting all methodological steps, with interviews and medical records' analysis, a final number of 40 patients was reached; of those, 12 (30%) were male and 28 (70%) were female patients. The patients' age ranged from seven to 67 years, with a mean of 37.8 years (for male patients, the mean was 35.6 years and for female patients, 38.8 years). Regarding ethnicity: 22 (55%) were white, 16 (40%) mixed race and 2 (5%) were black.

Regarding the patients' diagnosis, it was observed that 27 (67.5%) patients had CD, while 13 (32.5%) had UC. This diagnosis was defined before age 40 in 32 patients (80%) (2 patients >16 years and 30 patients >20 years). Eight (20%) patients, of more than 40 years of age had their diagnosis confirmed.

In our study, 27 patients (67.5%) did not undergo any surgical procedure related to their condition, but 13 (32.5%) patients had been submitted to some type of surgery.

Among the patients evaluated, it was found that 38 (95%) already had undergone some type of drug therapy prior to the use of biologicals, whereas two (5%) were on biological therapy as first choice of treatment for IBD. Among the commonly used alternative therapies (aminosalicylates, antibiotics, corticosteroids and immunosuppressive agents), 13 patients (34.2%) had made use of them all, followed by 10 individuals (26.3%) who had used three of these drugs and nine (23.7%) who used only two of them. Four (10.5%) patients were on monotherapy with immunosuppressive agents, while two (5.3%) had used only aminosalicylates before the biologicals.

Regarding the social and family history, 22 (55%) patients reported no smoking habit throughout life, while eight (20%) had been smokers and 10 (25%) did not answer. Familial recurrence was present in four (10%) patients, compared to 25 (62.5%) individuals who did not have any relative with a diagnosis for IBD and 11 (27.5%) patients who could not inform about the occurrence of these diseases in their families.

The location of the disease was diagnosed and established by means of upper gastrointestinal endoscopy, colonoscopy and CT (enterography) (Table 1).

Crohn's disease manifested itself in a non-stenosing/non-penetrating inflammatory presentation in 15 (55.5%), in a stenotic presentation in nine (33.3%) and in a penetrating presentation in three (11.1%) subjects.

In patients with UC, the predominant location, according to the Montreal classification, was an extensive colitis in eight cases (61.5%), followed by left colitis in five cases (38.5%). In our

sample, no cases of ulcerative proctitis or proctosigmoiditis were found.

Extra-intestinal manifestations were present in 28 (70%) patients. It was noted that these manifestations were more frequently found in patients with UC (76.9%) when compared with patients with CD (66.7%).

With respect to medication duration of use, 23 patients (57.5%) use biological agents between 2 and 5 years and 17 (42.5%) for less than two years. Thirty-three patients (82.5%) showed no adverse effects during the biological therapy, whereas seven (17.5%) subjects had some type of reaction with the use of this medication (erythema, pain at the infusion site, tuberculosis in two patients, herpes simplex, acne).

Regarding the course of the clinical picture, it was observed that 28 (70%) patients achieved complete remission, while 12 (30%) remained with symptoms.

## Discussion

We demonstrated in this study a predominance of female gender (70%) among patients with IBD, consistent with the national and international literature.<sup>1,2,4,14,15</sup> Regarding the age of our patients, a distribution pattern similar to that described in the literature was observed, with a minimum of seven and a maximum of 67 years old, with a mean age corresponding to the peak incidence among young adults (mean age, 37.8 years).<sup>1-5,7,10,14,15</sup> Regarding ethnicity, there was predominance of white subjects (55%) when compared to other races, a fact that agrees with the epidemiology of IBD.<sup>1,2,7</sup>

Other factors associated with the etiology of IBD are familial recurrence and smoking.<sup>2,7,16</sup> The hereditary character was present in four patients (10%). However, it is noteworthy that 11 patients (27.5%) were not certain about relatives possibly affected, which may have contributed to an underestimation of this variable. Regarding smoking, eight patients (20%) reported that were smokers at some point in their life. However, 10 patients (25%) declined to answer this question, underestimating, again, the statistical results of this variable.

According to studies recently published,<sup>4-6,8,10,15</sup> UC is the most prevalent disease among IBDs – a finding that goes against the statistics of our study, where 67.5% of the participants were CD patients. Most patients were diagnosed between 17 and 39 years, agreeing with the literature, most likely because the peak incidence of IBD covers this age group.<sup>1,2</sup>

With regard to the location of the disease, we observed that in patients with CD, the most affected area in the digestive tract (ileocolonic area) corresponds to that found in the literature.<sup>2,4,5,10,15</sup> As for its behavior, non-stenosing/non-penetrating CD was the more prevalent presentation among the patients studied (55.5%), which is consistent with Souza et al.<sup>4</sup> findings.

On the other hand, these studies reveal that ulcerative proctitis is the most common clinical presentation among patients with UC. This goes against our study findings of extensive colitis as the more prevalent presentation and localization.<sup>2,4,5,10,15</sup>

According to some studies,<sup>6,12</sup> the extra-intestinal manifestations are highly prevalent among patients with IBD. In our

study, we observed a prevalence of 70%, occurring more often in patients with UC (76.9%) compared with patients with CD (66.7%). This latter finding is at odds with our findings, which show that such events are more common in patients with CD.

Pharmacological treatment has been extensively researched, aiming to decrease the symptoms and inflammation.<sup>3,5,7,10,11</sup> The early use of biologic therapy was not yet adopted; this option is reserved only for cases of moderate or severe bowel disease in patients refractory to conventional treatment.<sup>13</sup> In the present study we found that 95% of the patients used another type of drug therapy before starting the use of biologicals, which speaks in favor of the referenced studies. Of these patients, 34.2% used all drug classes prescribed in the treatment of IBD, without clinical improvement.

Regarding surgical treatment, 32.5% of the patients required some form of surgical intervention during the course of the disease, all of them being patients with CD, which is similar to results in the literature that show a higher prevalence of surgical procedures among CD patients when compared to UC.<sup>4,5</sup>

With respect to the use of biological therapy, most patients evaluated (57.5%) made use of this medication for more than two years. The remission of the disease was obtained in most cases (70%), which is consistent with recently published studies.<sup>10,14</sup>

## Conclusion

Patient characteristics were similar to those found in the literature, with a predominance of women (70%), young adults (mean age, 37.8 years) and presence of CD (67.5%). In relation to this condition, the ileocolonic manifestation was the most frequent presentation (33.3%), while extensive colitis or pancolitis was more common among patients with UC (61.5%). The vast majority of patients (95%) made use of biologicals as late therapy and 70% progressed with remission of their symptoms.

## Conflicts of interest

The authors declare no conflicts of interest.

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