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## CLINICAL PROFILE OF PATIENTS WITH IBD ASSISTED AT SUS (UNIFIED HEALTH SYSTEM) IN AMAZONAS

#### Leury Max Santos Ferreira

Coloproctologist, Master in Surgery from the: Universidade Federal do Amazonas Manaus - AM

#### Gerson Suguiyama Nakajima

Surgeon of the Digestive System, Doctor of Medicine by: Universidade de São Paulo Manaus - AM

#### Iolanda Samanta Souza Amoedo

General Surgeon, at: Hospital Adventista de Manaus Manaus - AM



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**Abstract: INTRODUCTION:** Inflammatory bowel disease (IBD) is defined as a chronic intestinal inflammation, whose main forms, Crohn's Disease (CD) and Ulcerative Colitis (UC), are distinct chronic inflammatory bowel disorders. Data on Inflammatory Bowel Disease in the state of Amazonas are scarce, with no official number of diagnosed patients, although we know that many of these patients are treated in the Unified Health System (SUS) Amazonas. GOALS: General: to outline the profile of patients with IBD assisted by specialists in Amazonas. Specific: analyze the profile of patients assisted by specialists, clinical, laboratory and imaging findings most seen by these specialists; compare the data found with the relevant literature. METHOD: equalitative, prospective and non-probabilistic study, in which electronic questionnaires were prepared containing questions about the clinical practice of coloproctologists, gastroenterologists digestive system surgeons related to the profile of patients with IBD treated, clinical status, physical examination and complementary examinations of these patients by they attended in the Unified Health System of Amazonas. RESULTS: of the 17 specialists who agreed to participate, 6 were gastroenterologists, 5 coloproctologists and 6 digestive system surgeons. Patients treated at SUS Amazonas with IBD are mostly young adults (18-40 years old) female. The most common symptoms seen in UC are diarrhea with mucus and blood. Abdominal pain and weight loss are more common in CD. About 25% of patients have already been operated on due to IBD complications; the segment from the rectum to the sigmoid is the most affected in UC and the ileum is the most affected in CD. C-reactive protein (CRP) continues to be widely used in follow-up and flexible rectosigmoidoscopy has been used to initiate diagnostic investigation, complemented by colonoscopy. later

**DISCUSSION**: in the researched literature, the age group is similar to that pointed out by the specialists, in relation to gender, there are divergent points even in the literature. The segments commonly affected in the practice of specialists are consistent with the literature, but some points are divergent. Clinical, laboratory and endoscopic findings considered important by specialists are consistent with the researched literature. CONCLUSIONS: the view of specialists from Amazonas on the clinical, laboratory and endoscopic findings in patients with IBD was confronted with the specialized literature, in order to identify the profile of these patients assisted in the State's SUS. These data can serve as a basis for the development of other studies that contribute to better care for these patients.

**Keywords:** 1. Profile; 2. Inflammatory bowel disease; 3. Colitis; 4. Crohn's; 5. Amazon.

#### INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic intestinal inflammation that has Crohn's Disease (CD) and Ulcerative Colitis (UC) as its main representatives. Although both are chronic inflammatory bowel disorders, they are two distinct diseases whose etiology is not completely elucidated (ZHANG & LI, 2014; LODDO & ROMANO, 2015).

Crohn's disease (CD) has as its main characteristics the inflammation of any segment of the digestive tract, in a noncontinuous way, in all its layers, which can lead to strictures, perforations and fistulas (ZALTMAN et al., 2018).

Ulcerative colitis (UC) is characterized by inflammation of the mucosa, which starts in the rectum and extends continuously through the colon, leading to diarrhea, rectal bleeding and abdominal pain (CONRAD; ROGGENBUCK; LAASS, 2014; DAMIÃO et al., 2019).

IBD can manifest extra-intestinally, leading to symptoms in other organs and systems such as: skeletal muscle, integumentary, hepatobiliary, endocrine and ocular systems. Extraintestinal manifestations can occur in up to 40% of these patients, even with the disease under control (UNGARO et al., 2017; VIDE et al., 2018; DAMIÃO et al., 2019).

The incidence of IBD has increased in Asia, Eastern Europe and South America. In Brazil, from 2008 to 2017, 162,894 patients with IBD registered in the Datasus system were identified, of which 59% with UC and 41% with CD. These numbers are higher in the South and Southeast regions, with the North having the lowest rates (ZHANG & LI, 2014; BURISCH & MUNKHOLM, 2015; LODDO & ROMANO, 2015; NG; WONG; NG, 2016; MOREIRA; LOBATO; SOUZA, 2019).

The diagnosis of IBD is established after a joint assessment of anamnesis, physical examination, laboratory, endoscopic, histopathological and imaging findings (YAMAMOTO-FURUSHO et al., LICHTENSTEIN et al., 2018; VIEIRA et al., 2018). Diarrhea is the most common clinical manifestation, but the spectrum of clinical manifestations is very variable depending on the inflamed segment, and may include abdominal distension and pain, weight loss, anemia, malnutrition (CABRAL & ABBY, 2012; LICHTENSTEIN et al., 2018; FLYNN & EISENSTEIN, 2019; GAJENDRAN et al., 2019; MACDOWELL et al., 2021).

In the State of Amazonas, as in Brazil, the public health system is divided into levels of care. The gateway for its users is through the Primary Care Units or the Emergency Care Units, from where they are referred to specialized care, which is carried out in Polyclinics and Hospitals (BACKES et al., 2009). It was based on this context that we idealized this study.

#### **JUSTIFICATION**

In the State of Amazonas, data on Inflammatory Bowel Disease are scarce, so we do not have the official number of diagnosed individuals. Without these data, it is difficult to plan actions to improve diagnosis and treatment. In Manaus, service is not centralized. The best-known places for the care of these patients in the SUS are: Hospital Universitário Getúlio Vargas (HUGV), which has specialized care and a unit for biological therapy; Danilo Correia and Codajás State Polyclinics, which offer specialized care.

As there is no reference unit, it is difficult to identify who these patients are to draw their profile, so we chose to seek this data from the specialists who assist and conduct these patients in the SUS.

#### **OBJECTIVES**

#### **GENERAL**

A. Elaborate the profile of patients with IBD treated by specialists in Amazonas.

#### **SPECIFICS**

The. Analyze the profile of patients assisted by specialists, clinical, laboratory and imaging findings most seen and used by these specialist physicians;

B. Compare the data found with the relevant literature.

#### **METHODOLOGY**

#### **TYPE OF STUDY**

Qualitative, prospective, non-probabilistic study, in which two rounds of electronic questionnaires were developed and applied according to the Delphi Method (MERCEDES & MERCEDES, 2016). The doctors selected were specialists in gastroenterology, coloproctology and digestive system surgeons,

who treat and monitor patients with IBD in the Amazon, with regular registration in the specialty at the Regional Council of Medicine of Amazonas (CREMAM) and who agreed to participate in the study. Consensus among specialists was considered when options were chosen by more than 50% of the specialists. Data were collected through questionnaires applied via the Internet using the research site SURVEY MONKEY\*, using descriptive statistics for the items of each question and calculating the percentage between the answers considered valid. We considered consensus when at least 60% of the experts selected the same option.

## TERMS OF FREE AND INFORMED CONSENT

Before being included in the study, the invited specialist physicians must accept the Informed Consent Form (TCLE), with information about the objectives of the study, the method chosen and the guarantee of confidentiality of their personal data (APPENDIX A).

The project was approved by the Research Ethics Committee (CEP) of ``Universidade Federal do Amazonas``, with CAAE 29434219.2.0000.5020.

#### **RESULTS**

Of the 71 specialists registered with regular enrollment at CREMAM, 37 were gastroenterologists, nine coloproctologists and 26 digestive system surgeons (Graphic 1).

Of the specialists who treated patients with IBD in the SUS and who agreed to participate, 6 were gastroenterologists, 5 coloproctologists and 6 digestive system surgeons, totaling 17 participants.

17 questions were selected with questions about the profile of patients seen by these specialists, symptoms considered most important, what to look for in the physical

examination, the most affected intestinal segments and the most used complementary exams.

The age group between 18 and 40 years is the most attended in the opinion of more than 70% of the specialists, both in the UC and in the CD (Graphic 2). There was no need for a new round, due to the significant majority selecting the same option.

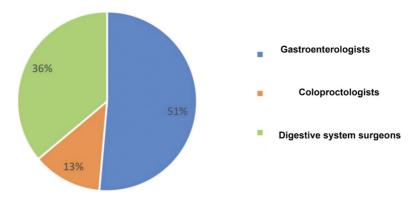
Regarding gender, two rounds of questions were necessary, as no option was chosen by more than 60% of the experts. In the first round, 47.06% of the specialists selected that they more frequently assist women and 35.29% of the specialists approximately assist both genders with UC. In DC, 41.18% of the specialists assist approximately both sexes, while 35.29% assist more women (Graphic 3).

In the second round, we excluded the least selected option in the UC (male sex) and kept the same options in the DC, as there was an almost homogeneous distribution in the specialists' responses. The result was like this for RCU: 70.59% assist more women and 29.41% both sexes. For DC, the result was as follows: 52.94% assist more women, 47.06% both genders and no specialist selected the option for men in this round (Graphic 4).

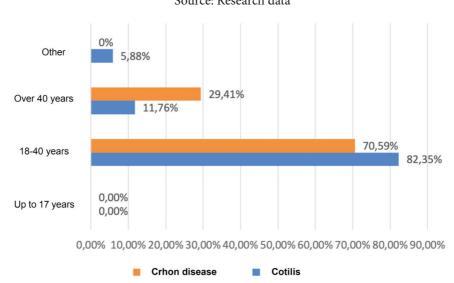
Patients seen by 70.59% of specialists arrive at their first consultation with suspected IBD (Graphic 5).

Among the exams that the patients had in the first consultation with the specialists, two rounds of questions were necessary, as no option was chosen by more than 60% of the specialists in the first round. In the second round, we repeated the question, leaving only the two most chosen options in the first round, with endoscopic examination being chosen by 82.35% of the specialists (Graphic 6).

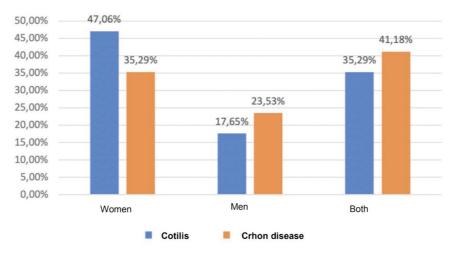
For 76.47% of the specialists, up to 25% of their patients have already undergone surgical procedures resulting from IBD complications (Graphic 7).



**Graphic 1** – Total doctors by specialty registered with CREMAM Source: Research data

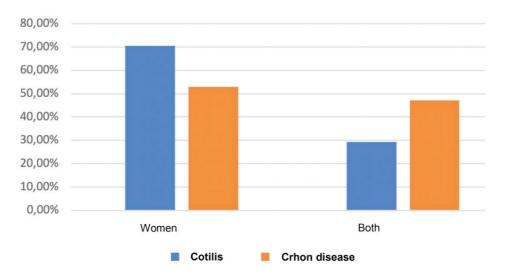


**Graphic 2** – Age range of patients seen with IBD Source: Research data



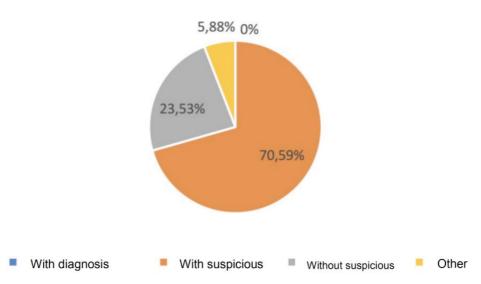
**Graphic 3** – Gender of patients treated with IBD (1st round)

Source: Research data

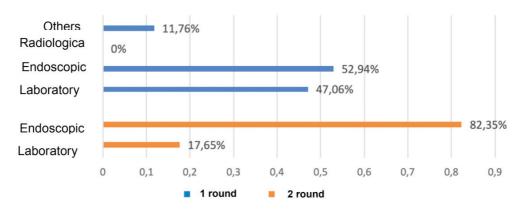


**Graphic 4** – Gender of patients treated with IBD (2nd round)

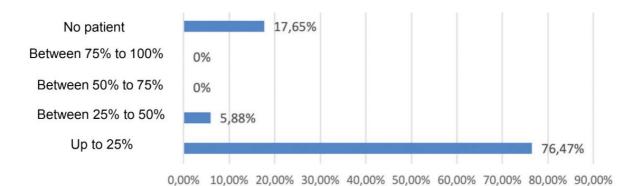
Source: Research data



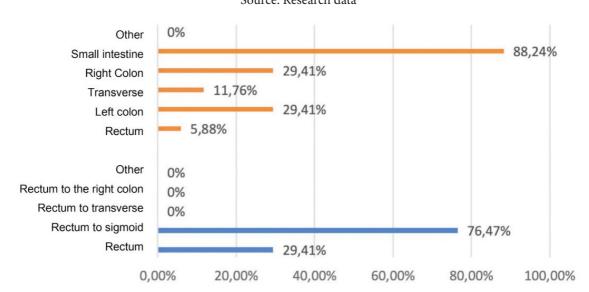
**Graphic 5** – Stage of the investigation that patients with IBD arrive at the specialists' clinic Source: Research data



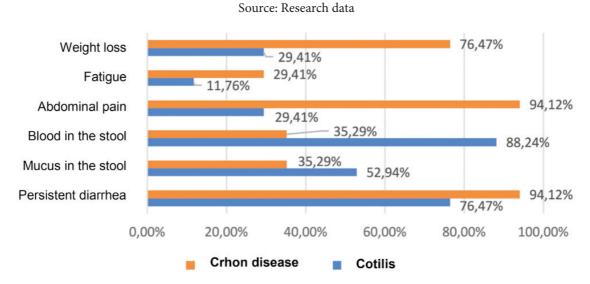
**Graphic 6** – Complementary exams that patients with IBD had in the first consultation with specialists Source: Research data



**Graphic 7** – Percentage of patients seen by specialists with surgical complications due to IBD Source: Research data

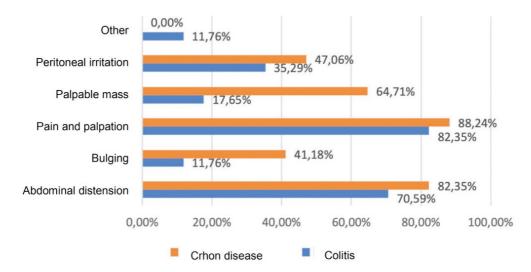


**Graphic 8** – Most common inflamed segments in patients with IBD



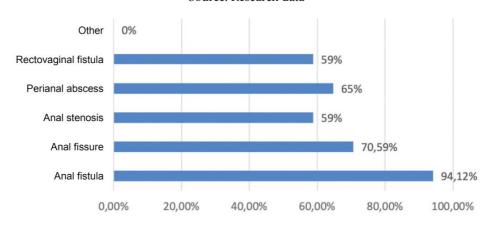
**Graphic 10** – IBD symptoms considered most important by experts

Source: Research data

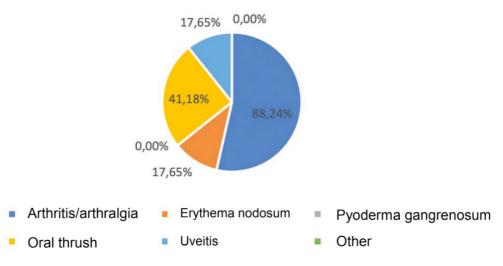


**Graphic 11** – Physical examination findings of patients with IBD considered most important by specialists

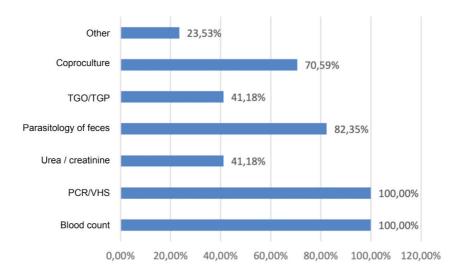
Source: Research data



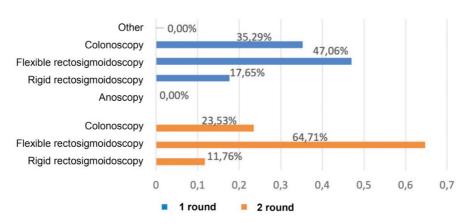
**Graphic 12** – Findings considered most important by specialists in the perianal region of patients with CD Source: Research data



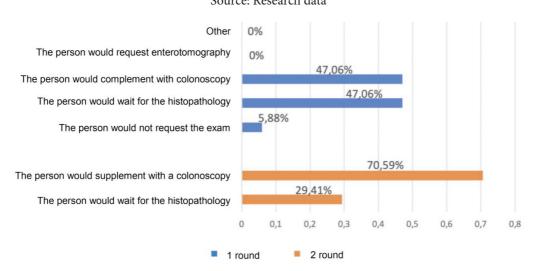
**Graphic 13** – Extra intestinal manifestations most seen by specialists in patients with IBD Source: Research data



**Graphic 14** – Laboratory tests considered most important by specialists to initiate investigation of IBD Source: Research data



**Graphic 15** – Endoscopic exams considered most important by specialists for the diagnosis of UC Source: Research data



**Graphic 16** – Conduct of specialists in the face of the result suggestive of IBD in the flexible rectosigmoidoscopy exam

Source: Research data

As for the inflamed intestinal segments that are most seen in patients with IBD, the specialists indicated the following: in UC, the segment that goes from the rectum to the sigmoid was chosen by 76.47% of the specialists; in CD, the small intestine was chosen by 88.24% of the specialists (Graphic 8).

Among the symptoms that specialists consider most important to aid the diagnosis of UC, persistent diarrhea and the presence of mucus in the stool were chosen by more than 70% of specialists. In CD, persistent diarrhea and abdominal pain were chosen by more than 90% of specialists (Graphic 10).

Among the findings on physical examination of the abdomen of patients with IBD, abdominal pain on palpation was chosen by more than 80% of specialists as the most important (Graphic 11).

In perianal CD, 94.12% of specialists chose perianal fistula as the most important manifestation in this region, with anal fissure being the second most chosen (Graphic 12).

The extra-intestinal manifestations of IBD that specialists most observe in their patients are arthritis/arthralgia, chosen by 88.24% (Graphic 13).

Regarding the laboratory tests available at SUS, which experts consider most important to start the investigation, blood count, C-reactive protein (CRP) and erythrocyte sedimentation rate were chosen by 100% of them (Graphic 14).

Among the endoscopic exams considered by specialists as the most important for the diagnosis of CD and which are available in the SUS, colonoscopy was the only exam chosen. As for the diagnosis of UC, there was a need for two rounds of questions, as no option was chosen by more than 60% of the specialists in the first round. In the second round, we repeated the question, leaving only the three most chosen options from the first round,

with flexible rectosigmoidoscopy chosen by 64.71% of the specialists (Graphic 15). All experts agree that anoscopy with visualization of the lower rectum can be a practical method to aid in the diagnosis of IBD.

The specialists were asked what their conduct would be in the face of a patient who had a continuous inflammatory process in his rectosigmoidoscopy report in all evaluated segments. Two options were the most chosen, but by less than 60% of the specialists, requiring a 2nd round of questions with only these two options, the option "complementary with colonoscopy" was chosen by 70.59% of the specialists (Graphic 16).

#### **DISCUSSION**

## GENERAL PROFILE OF PATIENTS SERVED AT SUS BY SPECIALISTS

For more than 70% of specialists, the age group most affected by patients with CD and UC is between 18 and 40 years. These data are similar to the researched national and international studies, in which the peak age of incidence of IBD is between the second and fourth decades of life, although CD can affect at an earlier age (between 15 and 25 years). Some works consider that in UC there is a second peak of incidence between 50 and 80 years. In the world there seems to be a predominance of UC in relation to CD (SAIRENJI; COLLINS; EVANS, 2017; GASPARINI, 2018; FEUERSTEIN; MOSS; FARRAYE, 2019; GAJENDRAN et al., 2019; SANTOS et al., 2021).

For 70.59% of the specialists, females are the most affected by UC in clinical practice. In CD, 52.94% of experts also believe that females are the most affected in clinical practice, but there was no consensus among them. In the world literature, some studies suggest a predominance of UC in men, however there seems to be no predominance by sex. In

CD, there are studies reporting that there is no predominance by sex, as well as studies in which there is a greater predominance of females, that is, there does not seem to be a consensus (TORRES et al., 2017; UNGARO et al., 2017; GAJENDRAN et al, 2019; SEYEDIAN; NOKHOSTIN; MALAMIR, 2019; RANASINGHE & HSU, 2020; RODA et al., 2020).

In Brazil, some studies indicate a higher frequency of UC and CD in women, consistent with what was observed by specialists in clinical practice (GASPARINI, 2018; NÓBREGA et al., 2018). In the study by Moreira et al. (2019), in the period between 2008 and 2017, evaluating data in the DATASUS of patients treated with a diagnosis of IBD, 162,894 patients with IBD were identified, of which 59% with UC and 41% with CD; the average age was 42 years, with a predominance of 59% in women. These are general data and do not specify the profile of patients with CD and UC.

For 70.59% of the specialists, most of their patients are already referred with suspicion of the disease, and for 82.35% of these specialists, most of their patients already bring an endoscopic examination suggestive of IBD in the first consultation. In Brazil, the mean time between the onset of symptoms and diagnosis was 23 months for UC and 28 months for CD. In Peru, the average time for the diagnosis of IBD is 14.6 months (NÓBREGA et al., 2018). In Europe, this time is less than 12 months. In Asia, this time is very variable, ranging from 12 to 24 months, and may be even longer in CD (RODRÍGUEZ-LAGO; ZABANA; BARREIRO-DE, 2020).

For 76.47% of the specialists, up to 25% of their patients have already undergone surgery due to IBD complications, which is similar to the researched literature. About 25% of patients with CD may require surgical intervention due to disease complications within five years of diagnosis, and this rate

may double in 10 years. The average rate in the West of colectomy in UC in 10 years is 20% and in the East 10%. With the advent of biological therapy, in these patients, the tendency is for this rate to be lower and lower (SAIRENJ; COLLINS; EVANS, 2017; AKIYAMA; RAI; RUBIN, 2021; PORTER; KALLA; HO, 2020).

#### AFFECTED SEGMENTS OBSERVED BY THE EXPERTS

For 76.47% of the specialists, the most affected segment in UC is that which goes from the rectum to the sigmoid, with the isolated involvement of the rectum being the second most seen in clinical practice (29.41%). In the researched world literature, there is an inversion in the order that the specialists observed, with the rectum being the most affected site and then the segment that goes from the rectum to the sigmoid (UNGARO et al., 2017; GAJENDRAN et al., 2019; SEYEDIAN et al, 2019; MACDOWELL et al., 2021; RODRÍGUEZ-LAGO; ZABANA; BARREIRO-DE, 2020).

For 88.24% of specialists, the small intestine is the most common site of involvement in CD, and this data is compatible with the researched world literature and the terminal ileum, the most affected segment of the small intestine (TORRES et al., 2017; GASPARINI 2018; ZALTMAN et al. 2018; RANASINGHE & HSU 2020; RODA et al., 2020). In Brazil, the ileocolic segment seems to be the most affected by inflammation; however, the exclusive disease in the colon is also seen with high frequency (SANTOS et al., 2021). Still in CD, for 94.12% of the specialists, the perianal fistula is the most common manifestation in this region, and this is considered in the literature a perianal manifestation present in up to 40% of the patients, being considered an indicator of worse prognosis (GASPARINI, LICHTENSTEIN 2018: et al.. 2018: RODRÍGUEZ-LAGO et al., 2020).

## CLINICAL MANIFESTATIONS AND PHYSICAL EXAMINATION

#### **CLINICAL MANIFESTATIONS**

The most important symptoms of UC for specialists were persistent diarrhea, blood and mucus in the stool. These are also the main symptoms found in the literature (UNGARO et al., 2017; GASPARINI, 2018; NÓBREGA et al.; 2018; MACDOWELL et al., 2021). Some studies consider only bloody diarrhea as the main symptoms, not citing the presence of mucus. Other common symptoms found in the literature are: tenesmus, urgency and abdominal pain (MARANHÃO; VIEIRA; CAMPOS, 2015; UNGARO et al., 2017; KUCHARZIK et al., 2020).

In CD, experts also consider persistent diarrhea as one of the most important symptoms, followed by abdominal pain and weight loss. In the literature, these are also the most cited symptoms. Other common symptoms found in the literature are: fatigue, anorexia and growth deficit (MARANHÃO; VIEIRA; CAMPOS, 2015; TORRES et al., 2017; LICHTENSTEIN et al., 2018; VEAUTHIER & HORNECKER, 2018; ZALTMAN et al., 2018; KEDIA et al., 2019; MACDOWELL et al., 2021).

#### ABDOMEN EXAM

In the evaluation of the abdomen, pain during palpation and abdominal distension are the most important findings for more than 70% of specialists. In UC, these pains are more common in the lower or upper left quadrant (MARANHÃO; VIEIRA; CAMPOS, 2015; MACDOWELL et al., 2021). In CD, the right lower quadrant is the most common place to find pain on abdominal palpation (MACDOWELL et al., 2021)

## EXTRA-INTESTINAL MANIFESTATIONS

Of the extra-intestinal manifestations most observed in clinical practice, arthritis/ arthralgias are the most seen in the opinion of 88.24% of the consulted specialists, which is in line with the literature (MARANHÃO; VIEIRA; CAMPOS, 2015; LICHTENSTEIN et al, 2018; SU et al., 2019; MACDOWELL et al., 2021). In the literature, this joint manifestation can be in two main patterns: peripheral arthritis and sacroiliitis, with divergence in the literature which would be the most common, but both are more seen in CR (MARANHÃO; VIEIRA; CAMPOS, 2015; UNGARO et al., 2017).

## LABORATORY AND ENDOSCOPIC EXAMS

#### LABORATORY TESTS

Regarding laboratory tests, 100% of the specialists request blood count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) when IBD is suspected. These data are consistent with the literature. The blood count may show anemia, leukocytosis and thrombocytosis (MARANHÃO; VIEIRA; CAMPOS, 2015; UNGARO et al., 2016; LICHTENSTEIN et al., 2018; VEAUTHIER & HORNECKER 2018; MACDOWELL et al., 2021). CRP is considered the most sensitive serological marker to detect IBD, however it has low specificity and can be altered in several situations such as: infections, arthritis, pancreatitis, acute myocardial infarction, pregnancy and use of oral contraceptives (YAMAMOTO-FURUSHO et al, 2017). Two other tests were selected by more than 60% of the specialists, stool culture and fecal parasitology. The researched literature considers these exams important for the differential diagnosis with infectious enterocolitis and intestinal parasites

(UNGARO et al., 2016; LICHTENSTEIN et al., 2018; MACDOWELL et al., 2021).

Fecal calprotectin and fecal lactoferrin were not included in the questionnaire rounds as they are not available in the local SUS. It is noteworthy that its use is more indicated in the monitoring of the treatment of IBD and in the differentiation between Irritable Bowel Syndrome and IBD.

#### **ENDOSCOPIC EXAMS**

Colonoscopy was considered by specialists as the endoscopic examination that most aids in the diagnosis of CD, recommends and literature the terminal ileum be evaluated in this examination (LICHTENSTEIN et al., 2018; VEAUTHIER & HORNECKER, 2018;). In UC, 64.71% of specialists considered flexible rectosigmoidoscopy the as endoscopic examination that most aids in the diagnosis. When flexible sigmoidoscopy with biopsy continuous inflammation evaluated segments, 70.59% of specialists prefer to complement the investigation with colonoscopy, not needing to wait for the result of the biopsies performed. In the researched literature, colonoscopy must preferably be performed both for diagnosis and to assess the extent of inflammation. Isolated histopathological analysis has little

value for diagnosis (UNGARO et al., 2016; YAMAMOTO-FURUSHO et al., 2017; DAMIÃO et al., 2019). When there is an urgent need to rule out IBD in a patient with bloody diarrhea, flexible sigmoidoscopy with biopsies is the most appropriate endoscopic examination, which is later complemented by colonoscopy. An interesting fact is that all the specialists considered that the observation of the distal rectum through anoscopy is a practical way that can help in the diagnosis of IBD, not being found this evaluation in the researched literature.

#### **CONCLUSIONS**

The view of specialists from the State of Amazonas on clinical, laboratory and endoscopic findings in patients with IBD was confronted with the specialized literature, in order to identify the profile of patients treated at SUS in Amazonas and which data specialists consider important for the diagnosis of IBD in the local setting.

The clinical, laboratory, imaging and endoscopic findings pointed out by specialists in the Amazon are similar to those in the researched literature, with little divergence. These data can serve as a basis for the development of other studies that contribute to better care for these patients.

#### REFERENCES

AKIYAMA, Shintaro; RAI, Victoria; RUBIN, David T. Pouchitis in inflammatory bowel disease: a review of diagnosis, prognosis, and treatment. **Intestinal Research**, v. 19, n. 1, p. 1–11, 2021. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7873408/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7873408/</a>. Acesso em 14 novembro 2021.

BACKES, Dirce Stein; KOERICH, Magda Santos; RODRIGUES, Anna Carolina Ribeiro Lopes; DRAGO, Livia Crespo; KLOCK, Patrícia; ERDMANN, Alacoque Lorenzini. O que os usuários pensam e falam do Sistema Único de Saúde? Uma análise dos significados à luz da carta dos direitos dos usuários. **Ciênc. Saúde Coletiva**, Rio de Janeiro, v. 14, n. 3, p. 903-910, 2009. Disponível em: <a href="http://www.scielo.br/scielo.php?script=sci\_arttext&pid=S1413-81232009000300026&lng=en&nrm=iso">http://www.scielo.br/scielo.php?script=sci\_arttext&pid=S1413-81232009000300026&lng=en&nrm=iso</a>. Acesso em 13 novembro 2019.

BURISCH, J. & MUNKHOLM, P. The epidemiology of inflammatory bowel disease. **Scandinavian J of Gastroenterol.**, v. 50, n. 8, p.942–951, 2015. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pubmed/25687629">https://www.ncbi.nlm.nih.gov/pubmed/25687629</a>>. Acesso em: 14 abril 2019.

CABRAL, M. G.; ABBY, F. Diagnóstico das Doenças Inflamatórias Intestinais. **Rev Hospital Universitário Pedro Ernesto**, v. 11, n. 4, p. 17-21, Rio de Janeiro, 2012. Disponível em: <a href="https://www.e-publicacoes.uerj.br/index.php/revistahupe/article/view/9001/6886">https://www.e-publicacoes.uerj.br/index.php/revistahupe/article/view/9001/6886</a>>. Acesso em 14 abril 2019.

CONRAD, K.; ROGGENBUCK, D.; LAASS, M. W. Diagnosis and classification of ulcerative colitis. **Autoimmunity. Reviews**, v. 13, n. 4-5, p.463–466, 2014. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/24424198/">https://pubmed.ncbi.nlm.nih.gov/24424198/</a>. Acesso em 14 abril 2019.

DAMIÃO, Adérson Omar Mourão Cintra; VIEIRA, Andrea; VILELA, Eduardo Garcia; TEIXEIRA, Fábio Vieira; ALBUQUERQUE, Idblan Carvalho de; PARENTE, José Miguel Luz; CHEBLI, Júlio Maria Fonseca; JÜNIOR, Orlando Ambrogini; HOSSNE-SAAD, Rogerio; MISZPUTEN, Sender Jankiel. Guideline on Ulcerative Colitis. International Journal of Inflamatory Bowel Disease, v. 5, n. 1, p. 12-20, 2019. Disponível em: <a href="https://gediib.org.br/wp-content/uploads/2019/10/REVISTA-INTERNATIONAL-JOURNAL\_VOL5-N1-2.pdf">https://gediib.org.br/wp-content/uploads/2019/10/REVISTA-INTERNATIONAL-JOURNAL\_VOL5-N1-2.pdf</a>>. Acesso em 16 novembro 2019.

FEUERSTEIN, Joseph D.; MOSS, Alan C.; FARRAYE, Francis A. Ulcerative Colitis. **Mayo Clinic Proceedings**, v. 94, n. 7, p. 1357–1373, 2019. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/31272578/">https://pubmed.ncbi.nlm.nih.gov/31272578/</a>>. Acesso em: 14 de fevereiro 2021.

FLYNN, Sean; EISENSTEIN Samuel. Inflammatory Bowel Disease Presentation and Diagnosis. **Surg Clin North Am.**, v. 99, n. 6, p.1051-1062, 2019. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/31676047/">https://pubmed.ncbi.nlm.nih.gov/31676047/</a>. Acesso em 20 de fevereiro 2021.

GAJENDRAN, Mahesh; LOGANATHAN, Priyadarshini Loganathan; JIMENEZ, Guillermo; CATINELLA, Anthony P.; NG, Nathaniel; UMAPATHY, Chandraprakash; ZIADE, Nathalie; HASHASH, Jana G. A comprehensive review and update on ulcerative colitis. **Disease-a-Month**, v. 65, n. 12, 2019. Disponível em: <a href="https://www.sciencedirect.com/science/article/abs/pii/50011502919300318">https://www.sciencedirect.com/science/article/abs/pii/50011502919300318</a>>. Acesso em 20 agosto 2020.

GASPARINI, Rodrigo Galhardi. Incidência e P de Doenças Inflamatórias Intestinais no Estado de São Paulo - Brasil. 2018. Tese (Doutorado) - Bases Gerais da Cirurgia, Universidade Estadual Paulista, Botucatu, 2018. <a href="https://repositorio.unesp.br/bitstream/handle/11449/152905/gasparini\_rg\_dr\_bot.pdf?sequence=3">https://repositorio.unesp.br/bitstream/handle/11449/152905/gasparini\_rg\_dr\_bot.pdf?sequence=3</a>. Acesso em 05 de fevereiro de 2021.

KEDIA, Saurabh; DAS, Prasenjit; MADHUSUDHAN, Kumble Seetharama; DATTAGUPTA, Siddhartha; SHARMA, Raju; SAHNI, Peush; MAKHARIA, Govind; AHUJA, Vineet. "Differentiating Crohn's disease from intestinal tuberculosis." **World J. of Gastroenterol.**, v. *25*, *n*. 4, p. 418-432, 2019. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6350172/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6350172/</a>. Acesso em 14 de janeiro 2022.

KUCHARZIK, Torsten; KOLETZKO, Sibylle; KANNENGIESSER, Klaus; DIGNASS, Axel. Colite Ulcerativa-Diagnóstico e Algoritmos Terapêuticos. **Dtsch Arztebl Int.**, v. 117, n. 33-34, p. 564-574, 2020. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8171548/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8171548/</a>. Acesso em 14 janeiro 2022.

LICHTENSTEIN, Gary R.; LOFTUS, Edward V.; ISAACS, Kim I.; REGUEIRO, Miguel D.; GERSON, Lauren B.; SANDS, Bruce E. ACG Clinical Guideline: Management of Crohn's Disease in Adults, *Americ J Gastroenterol*, v. 113, n. 4, p. 481-517, 2018. Disponível em: <a href="https://journals.lww.com/ajg/Fulltext/2018/04000/ACG\_Clinical\_Guideline\_Management\_of\_Crohn\_s.10">https://journals.lww.com/ajg/Fulltext/2018/04000/ACG\_Clinical\_Guideline\_Management\_of\_Crohn\_s.10</a>. aspx?context=FeaturedArticles&collectionId=2>. Acesso em 20 agosto 2020.

LODDO, I.; ROMANO, C. Inflammatory Bowel Disease: Genetics, Epigenetics, and Pathogenesis. **Frontiers in Immunology**, v. 6, p. 551, 2015. Disponível em: < https://www.frontiersin.org/articles/10.3389/fimmu.2015.00551/full>. Acesso em 14 abril 2019.

MARANHÃO, Débora Davalos Albuquerque.; VIEIRA, Andrea; CAMPOS, Tércio de. Características e diagnóstico diferencial das doenças inflamatórias intestinais. **J. Bras. Med.**, v. 103, n. 1, 2015. Disponível em: <a href="http://files.bvs.br/upload/S/0047-2077/2015/v103n1/a4920.pdf">http://files.bvs.br/upload/S/0047-2077/2015/v103n1/a4920.pdf</a>. Acesso em 14 maio 2019.

MCDOWELL, Christopher; FAROOQ, Umer; HASEEB, Muhammad. Inflammatory Bowel Disease. [Atualizado em 28 de junho de 2020]. In: StatPearls [Internet]. **Treasure Island (FL):** StatPearls Publishing, 2021. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/books/NBK470312/">https://www.ncbi.nlm.nih.gov/books/NBK470312/</a>. Acesso em 21 de maio 2021.

MERCEDES R. A.; MERCEDES, T. F. El método Delphi. **REIRE Rev. d'Inov. i Recerca em educació, Universitat de Barcelona, Institut de Ciencies de l'Educacion**, v. 9, n. 1, p. 88-102, 2016. Disponível em: <a href="http://www.ub.edu/ice/reire.htm">http://www.ub.edu/ice/reire.htm</a>. Acesso em 12 junho 2020.

MOREIRA, André da Luz; LOBATO, Luiz. Felipe de Campos.; SOUZA, Heitor S. de. IBD Epidemiology: What is Going on in the Developing World? Results from 163,000 Patients. **Gastroenterology,** V. 156, ed. 6, suplemento 1, S-73, 2019. Disponível em: <a href="https://www.gastrojournal.org/article/S0016-5085(19)36968-9/pdf">https://www.gastrojournal.org/article/S0016-5085(19)36968-9/pdf</a>. Acesso em 29 out 2019.

NG, W. K.; WONG, S. H.; NG, S. C. Changing epidemiological trends of inflammatory bowel disease in Asia. **Intest Res.** v. 14 (2), p.111–119, 2016. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4863044/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4863044/</a>. Acesso em 14 abril 2019.

NÓBREGA, Viviane Gomes; SILVA, Isaac Neri de Novaes; BRITO, Beatriz Silva; SILVA, Juliana; SILVA, Maria Carolina Martins da; SANTANA, Genoile Oliveira. O INÍCIO DAS MANIFESTAÇÕES CLÍNICAS EM PACIENTES COM DOENÇA INFLAMATÓRIA. **Arq de Gastroenterol [online]**, v. 55, n. 03, p. 290-295, 2018. Disponível em: <a href="https://www.scielo.br/j/ag/a/GJPykqyP38drZjHTrVjSbwL/?lang=en#ModalArticles">https://www.scielo.br/j/ag/a/GJPykqyP38drZjHTrVjSbwL/?lang=en#ModalArticles</a>. Acesso em 25 de maio de 2021.

PORTER, Ross J.; KALLA, Rahul; HO, Gwo-Tzer. Ulcerative colitis: Recent advances in the understanding of disease pathogenesis. **F1000Res**, v. 9, 2020. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194476/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194476/</a>. Acesso em 18 feveiro 2021.

RANASINGHE, I.R., HSU, R. Crohn Disease. 2020 Jun 9. In: StatPearls [Internet]. **Treasure Island (FL):** StatPearls Publishing; 2021 Jan-. PMID: 28613792. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/books/NBK436021/#article-20133.s2">https://www.ncbi.nlm.nih.gov/books/NBK436021/#article-20133.s2</a>. Acesso em 18 abril 2021.

RODA, Giulia; CHIEN, Siew Ng; KOTZE, Paulo Gustavo; ARGOLLO, Marjorie; PANACCIONE, Remo; SPINELLI, Antonio; KASER, Arthur; PEYRIN-BIROULET, Laurente; DANESE, Silvio. Crohn's disease. **Nat Rev Dis Primers**, v. 6, n. 1, 2020. *Erratum in*: Nat Rev Dis Primers. 2020 Apr 6;6(1):26. *Erratum in*: Nat Rev Dis Primers. 2020 May 20;6(1):42. *Erratum in*: Nat Rev Dis Primers. 2020 Jun 19;6(1):51. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/32242028/">https://pubmed.ncbi.nlm.nih.gov/32242028/</a>. Acesso em 18 abril 2021.

RODRÍGUEZ-LAGO, Iago; ZABANA, Yamile; BARREIRO-DE, Manuel Acosta. Diagnosis and natural history of preclinical and early inflammatory bowel disease. **Ann Gastroenterol.**, v. 3, n. 5, p. 443-452, 2020. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7406806/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7406806/</a>>. Acesso em 14 de janeiro 2022.

SAIRENJI, Tomoko; COLLINS, Kimberly L.; EVANS, David V. An Update on Inflammatory Bowel Disease. Primary Care: Clinics in Office Practice, v. 44, n. 4, p. 673–692, 2017. Disponível em: <a href="https://www.sciencedirect.com/science/article/abs/pii/S0095454317301045?via%3Dihub">https://www.sciencedirect.com/science/article/abs/pii/S0095454317301045?via%3Dihub</a>. Acesso em 18 fevereiro 2021.

SANTOS, Monique Costa de Assunção; OLIVEIRA, Fernanda de Araújo; ANDRADE, Laíla Damasceno; MARIANO, Victor Dias; PIMENTEL, Andrea Maia; SURLO, Valdiana Cristina; MOTA, Jaciane Araújo; SANTANA, Genoile Oliveira. Perfil clínico-epidemiológico de pacientes com Doença de Crohn em uso de terapia biológica de um centro de referência em Salvador, Bahia. **Brazilian J of Development**, v.7, n.3, p. 32489-32502, 2021. Disponível em: <a href="https://brazilianjournals.com/ojs/index.php/BRJD/article/view/27334">https://brazilianjournals.com/ojs/index.php/BRJD/article/view/27334</a>. Acesso em 12 de novembro 2021.

SEYEDIAN, Seyed Saeid; NOKHOSTIN, Forogh; MALAMIR, Mehrdad Dargahi. A review of the diagnosis, prevention, and treatment methods of inflammatory bowel disease. **J Med Life**, v. 12, n. 2, p. 113-122, 2019. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6685307/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6685307/</a>. Acesso em 14 de fevereiro 2021.

TORRES, Joana; MEHANDRU, Saurabh; COLOMBEL, Jean-Frédéric; PEYRIN-BIROULET, Laurent. Crohn's disease. Lancet, v. 389, n. 10080, p. 1741-1755, 2017. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/27914655/">https://pubmed.ncbi.nlm.nih.gov/27914655/</a>. Acesso em 17 abril 2021.

UNGARO, Ryan; MEHANDRU, Saurabh; ALLEN, Patrick B.; PEYRIN-BIROULET, Laurent; COLOMBEL, Jean-Frédéric. Ulcerative colitis. **Lancet**, v. 389, n. 10080, p.1756-1770, 2017. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6487890/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6487890/</a>>. Acesso em 10 de fevereiro 2021.

VEAUTHIER, Brian; HORNECKER, Jaime R. Crohn's Disease: Diagnosis and Management. Am Fam Physician, v. 98, n. 11, p. 661-669, 2018. Disponível em: <a href="https://www.aafp.org/afp/2018/1201/p661.html">https://www.aafp.org/afp/2018/1201/p661.html</a>. Acesso em 9 de dezembro 2021.

VIDE, Julia *et al.* Cutaneous Morbidity Among Inflammatory Bowel Disease Patients: A Cohort Study. **J Crohn's Colitis**, v. 12, n. 4, p. 442-45, 2018. Disponível em: <a href="https://pubmed.ncbi.nlm.nih.gov/29300856/">https://pubmed.ncbi.nlm.nih.gov/29300856/</a>>. Acesso em 12 de nov de 2019.

YAMAMOTO-FURUSHO, J.K.; BOSQUES-PADILLA, F.; DE-PAULA, J.; GALIANO, M.T.; IBAÑEZ, P.; JULIAO, F.; KOTZE, P.G.; ROCHA, J.L.; STEINWURZ, F.; VEITIA, G.; ZALTMAN, C. Diagnosis and treatment of inflammatory bowel disease: First Latin American Consensus of the Pan American Crohn's and Colitis Organisation. **Rev Gastroenterol Mex**, v. 82, n. 1, p. 46-84, 2017. Disponível em: <a href="https://www.sciencedirect.com/science/article/pii/S0375090616300829?via%3Dihu">https://www.sciencedirect.com/science/article/pii/S0375090616300829?via%3Dihu</a>. Acesso em 14 de feveiro 2021.

ZALTMAN, Cyrla *et al.* Crohn's Disease Guidelines. **International Journal of Inflamatory Bowel Disease**, v. 4, n. 1, p. 10-18, 2018. Disponível em: <a href="https://gediib.org.br/wp-content/uploads/2019/10/REVISTA-INTERNATIONAL-JOURNAL\_VOL4-N1\_31-10-2018-1.pdf">https://gediib.org.br/wp-content/uploads/2019/10/REVISTA-INTERNATIONAL-JOURNAL\_VOL4-N1\_31-10-2018-1.pdf</a>. Acesso em 16 novembro 2019.

ZHANG, Y.; LI, Y. Inflammatory bowel disease: pathogenesis. **World J. Gastroenterol.**, v. 20(1), p. 91–99, 2014. Disponível em: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3886036/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3886036/</a>>. Acesso em 14 abril 2019.