

**ORIGINAL ARTICLE** 

INFLAMMATORY DISEASE

# HIGHLIGHTS

- Most inflammatory bowel diseases and COVID-19 patients were symptomatic, and fever was the main symptom.
- Patients with inflammatory bowel diseases and COVID-19 had more gastrointestinal symptoms than the general population with COVID-19.
- Use of salicylates, female gender and asthma were associated with COVID-19.
- Use of immunosuppressants or immunobiological drugs did not alter the clinical presentation of COVID-19.

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# COVID-19 in inflammatory bowel disease: should we be more careful with the use of salicylates?

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ABSTRACT - Backgrounds - Fortunately, much has been studied about COVID-19 in patients with inflammatory bowel diseases (IBD). Evidence suggests that these patients do not appear to be at increased risk of severe COVID-19. However, there are still some uncertainties regarding the clinical manifestations of COVID-19 in patients with immune-mediated diseases. Objective - This study aimed to describe the main symptoms of COVID-19 and their frequency in IBD patients and evaluate the impact of the IBD therapeutic drugs on clinical presentation of COVID-19 and to determine factors associated with COVID-19 in this population. Methods - Adult patients with IBD from three tertiary-care public, teaching hospitals in Ceará, Northeastern Brazil, were evaluated during one scheduled appointment from March to December 2020. Patients with possible or confirmed COVID-19 were compared with patients without COVID-19. Furthermore, incidences of each symptom were evaluated based on the use of IBD therapeutic drugs. Results - A total of 515 patients with IBD were included in the study: 234 with CD, and 281 with UC. Of these, 174 patients (34%) had possible/confirmed COVID-19 of whom 156 (90%) were symptomatic. Main symptoms were fever (65%) and headache (65%); gastrointestinal symptoms occurred in one third of patients and were higher than COVID-19 in general population. The factors associated with having COVID-19 were female gender (OR 1.71, 95%CI: 1.17-2.50); contact at home (OR 5.07, 95%CI: 3.31-7.78) and outside the home (OR 3.14, 95%CI: 2.10-4.71) with a case of COVID-19; work outside of the home (OR 1.87, 95%CI: 1.26-2.78); family history of COVID-19 (OR 2.29, 95%CI 1.58-3.33) use of salicylate (OR 1.71, 95%CI: 1.17-4.28); and asthma (OR 7.10, 95%CI: 1.46-34.57). Conclusion - IBD patients at high risk of COVID-19 infection may need to avoid salicylate therapy but further studies are necessary to confirm this association.

Keywords - Inflammatory bowel disease; COVID-19; salicylates.

#### INTRODUCTION

COVID-19 is the disease caused by the SARS-CoV-2, a coronavirus first reported in December 2019, which quickly spread to several countries and was declared a pandemic<sup>(1)</sup>. The most common symptoms are fever, cough, dyspnea, myalgia, fatigue, chest tightness, headache, hemoptysis, and diarrhea<sup>(2)</sup>. Until March 2023, more than 700 million confirmed cases had been reported worldwide (with more than 37 million cases in Brazil), with a total death count of over 6 million<sup>(3)</sup>. In Ceará (a state in the Brazilian Northeast), almost 1.5 million cases of COVID-19 were confirmed, with more than 28,000 deaths<sup>(4)</sup>.

As the pandemic expanded, concern on the impact of COVID-19 on immunosuppressed patients, such as those with inflammatory bowel diseases (IBD) grew. IBD includes Crohn's disease (CD) and ulcerative colitis (UC) that are chronic, immune-mediated diseases, whose pathogenesis involves a complex interaction between environmental factors and genetic susceptibility<sup>(5)</sup>. Symptoms of IBD are heterogeneous and may include symptoms related to the gastrointestinal tract and also systemic symptoms<sup>(6)</sup>. Study from a reference center located in Brazil<sup>(7)</sup>, showed that the main clinical manifestations of IBD patients were weight loss, followed by diarrhea, abdominal pain, fecal urgency, asthenia and blood in the stool.

Most IBD patients are currently exposed to immunosuppressive drugs, including corticosteroids, immunomodulators, and immunobiologicals for prolonged periods which can increase the risk of infection<sup>(8,9)</sup>. These drugs have been associated with higher rates of serious viral and bacterial infections<sup>(10)</sup>.

Little is known about the impact of COVID-19 on patients with chronic inflammatory diseases such as IBD, particularly those requiring the use of systemic immunosuppressant drugs. Older age, increased number of comorbidities, and the use of systemic corticosteroid are risk factors for adverse COVID-19 outcomes in patients with IBD. However, TNF-antagonist therapy does not seem to be associated with severe COVID-19<sup>(11)</sup>.

COVID-19 can cause gastrointestinal (GI) symptoms. A meta-analysis suggested that up to 17.6% of COVID-19 patients have these symptoms<sup>(12)</sup>. Data are

conflicting with some reports suggesting worse prognosis among those with GI symptoms while others found better outcomes<sup>(13)</sup>. There are limited data on COVID-19 and GI symptoms among IBD patients.

The aims of this study were to describe the main symptoms of COVID-19 in IBD patients, including the frequency of GI symptoms during COVID; to evaluate the impact of immunosuppressants and immunobiological drugs on clinical presentation of COVID-19; and to determine factors associated with COVID-19 in this population.

#### METHODS

#### Setting and patients

Adult patients with IBD from three tertiary-care, public, teaching hospitals, reference centers for IBD in Ceará, Brazil were evaluated.

#### Study design and data collection

This is a retrospective study. Patients with IBD were evaluated during one scheduled appointment from March to December 2020. Their clinical and epidemiological data including associated factors and COVID-19 presentation and outcomes, as well as data on their underlying disease and its treatment were collected. In this cross-sectional design, the patient assessment was made by in-person care, after the application of an informed consent.

During the appointment, the attending gastroenterologists obtained data from the patients' medical records and data collected from the patients' interviews. Patients were evaluated for socio-demographic, and epidemiological data, underlying diseases, information on IBD, such as extension and severity, hospitalization for reasons other than COVID-19, and procedures undergone during the COVID-19pandemic, laboratory data (including PCR for SARS-CoV-2 or serological result), and treatment of IBD. We considered the following drugs used during the pandemic to be immunosuppressants: thiopurines (azathioprine), methotrexate, calcineurin inhibitors (cyclosporine), and mycophenolate. Immunobiological drugs were: infliximab, adalimumab, golimumab, certolizumab, vedolizumab and ustekinumab. The COVID-19 pandemic period was established as starting on 1 March 2020 until the date of completion of the questionnaire. Physical activity was considered to be regular when performed more than three times a week. Family history of COVID-19 was established if a consanguineous relative had COVID-19. Exposure to COVID-19 at home was defined as living with any person who had become ill with COVID-19. Only mask use outside of the home was considered. The evaluation of the impact of COVID-19 on IBD was based on the patients' perception (symptoms improved, worsened, or unchanged during/after COVID-19).

The extent of UC was evaluated according to the Montreal classification<sup>(14)</sup>: rectitis (disease limited to the rectum), left colitis (involvement up to the splenic flexure of the colon), and extensive colitis (involvement proximal to the splenic flexure). The behavior (phenotype) of CD was classified according to Montreal Classification<sup>(14)</sup>: non-stricturing non-penetrating disease (B1), stricturing disease (B2) and penetrating disease (B3). UC activity was evaluated using the partial Mayo score<sup>(15)</sup>  $\geq$ 2 and CD activity was evaluated using the Harvey-Bradshaw Index<sup>(16)</sup> (HBI)  $\geq$ 5.

# Data analysis

For the analyses, the following definitions were used:

- Possible COVID-19: symptoms compatible with COVID-19 (fever, nasal obstruction, sore throat, cough, dyspnea, headache, diarrhea, nausea or vomiting, anosmia, ageusia, and fatigue) during the period of the pandemic, plus the patient was untested for SARS-CoV-2 infection.
- Confirmed COVID-19: symptomatic or asymptomatic patient with positive PCR for SARS-CoV-2 or positive serological result (the study was carried out in the pre-vaccination period).
- Without COVID-19: tested negative or untested asymptomatic patient.

We compared data between the groups of patients with COVID-19 (possible or confirmed) and without. We also compared the frequency of each symptom of COVID-19 in the group of patients using immunosuppressants and/or immunobiological drugs with the group that did not use these drugs. For these comparisons, we used Fisher's exact test. Variables that presented a P value <0.2 in the bivariate analysis were included in the multivariate analysis done using stepwise logistic regression.

# **Ethical issues**

This study was approved by the ethics committee of the hospitals involved. There are no conflicts of interest between the authors and the objectives of this study.

# RESULTS

A total of 515 patients with IBD were included: 234 with CD, and 281 with UC (TABLE 1). Most patients were in their 4th decade of life and were female. Median number of years of formal education was 14. Most had been vaccinated against influenza in 2020. Sixteen percent (n=84/515) engaged in regular physical activity. The most frequent comorbidity in addition to IBD, was hypertension, followed by diabetes mellitus. The most frequent means of transportation were car (31%); public transport (27%); and motorcycle (25%). Ninety-four percent reported that they always used a mask outside of the home. Exposure to COVID-19 cases at home and outside home occurred in 25% and 29%, respectively; 28% worked outside the home during the pandemic. Family cases of COVID-19 were reported by 47%. The mean time since the diagnosis of IBD was approximately 9 years. Salicylates were the most frequent drugs in use, followed by immunobiological drugs, and immunosuppressants.

Among the CD patients, 80% were considered to be in remission. Among the UC patients, 60% were in remission, and 28% (80/281) had mild disease. During pandemic, 235 procedures were undergone, mostly endoscopic (71%). A total of 49 hospital admissions for reasons other than COVID-19 were recorded during the pandemic, 63% due to IBD activity. The location of IBD can be seen in TABLE 1.

One hundred and seventy-four patients (34%) had possible or confirmed COVID-19. Of the 68 confirmed, 74% had only a positive serology, 19% had only a positive PCR, and 7% had both tests positive. Among the confirmed cases, 74% had been symptomatic.

Demographic data (n=515)	
Female n (%)	303 (59%)
Age in years - mean (SD)	45.8 (16.42)
Influenza vaccination in 2020	342 (66%)
Number of residents in the household n (%)	
1	37 (7%)
2	126 (24%)
3	150 (29%)
4 or more	202 (39%)
Clinical data (n=515)	
Comorbidities n (%)	
Hypertension	106 (21%)
Non-insulin dependent diabetes mellitus	52 (10%)
Hypothyroidism	12 (2%)
Asthma	9 (2%)
Insulin dependent diabetes mellitus	8 (2%)
Drugs in use for IBD n (%)	
Salicylate	284 (55%)
Immunobiological drugs	168 (33%)
Immunosuppressants	156 (30%)
Steroids	67 (13%)
None	36 (7%)
Characteristics of Crohn's disease (n=234) Location n (%)	
lleum and colon	80 (34%)
Only colon	74 (32%)
Only ileum	64 (27%)
Behaviour n (%)	
Non-stricturing non-penetrating disease	97 (41%)
Stricturing disease	64 (27%)
Penetrating disease	73 (31%)
Characteristics of ulcerative colitis (n=281)	
Extent n (%)	
Left-sided	127 (45%)
Extensive	93 (33%)
Ulcerative proctitis	61 (22%)

**TABLE 1.** Characteristics of 515 patients with IBD evaluated duringthe COVID-19 pandemic (March-December 2020).

IBD: inflammatory bowel disease; SD: standard deviation.

Considering only the 156 symptomatic patients, (confirmed or possible), most did not discontinue their medication for IBD during symptoms (77%), and 72% reported that COVID-19 had no impact on their IBD. Of patients with COVID-19, 2 (1.15%) required hospitalization.

Among the 156 symptomatic patients the main symptoms were: fever (65%), and headache (65%), with a median duration of 3 days and 4 days, respectively. Anosmia (63%), ageusia (60%), and fati-

gue (53%) were also frequent. GI symptoms were diarrhea (33%), and nausea/vomiting (19%), with a median duration of 3 days. There was no difference in clinical presentation of COVID-19 in patients who used immunosuppressants or immunobiological drugs except for less frequent nasal obstruction (SUPPLEMENTARY TABLE S1).

In the bivariate analysis, the following factors were associated with having COVID-19 (possible or confirmed): female sex, contact with a case of COVID-19 at home; contact with a case of COVID-19 outside of the home; working outside of the home; having a family history of COVID-19; using a salicylate; and asthma. These variables remained significant in the multivariate analysis (TABLE 2).

CD was not associated with a higher risk of CO-VID-19 when compared to UC. Active disease, use of immunosuppressants, immunobiological, and corticosteroids did not increase the risk of having COVID-19.

Only two patients required hospitalization for COVID-19. Neither required intensive care. Both had CD, one was using corticosteroid and an immunobiological drug (vedolizumab), and during COVID-19 the use of the steroid was suspended, and the next dose of vedolizumab was postponed. The other was using salicylate and corticosteroid during COVID-19 and did not stop these medications.

# DISCUSSION

Among 515 patients with IBD treated at tertiary-care centers in Ceará, Brazil, the prevalence infection caused by SARS-CoV-2 was 34% of which 90% were symptomatic. The most frequent symptoms of COVID-19 were fever and headache, and GI symptoms occurred in at least one third of patients (diarrhea, and nausea/vomiting). The use of immunosuppressants or immunobiologicals drugs did not change the clinical presentation of COVID-19. Factors associated with COVID-19 were female sex, contact with a case of COVID-19 at home; contact with a case of COVID-19 outside of the home; working outside home; having a family history of COVID-19; and asthma. Activity of IBD and type of treatment of IBD did not increase the risk of having COVID-19, except for the use of a salicylate which was associated with COVID-19, independently of age.

Symptom	Used immuno suppressantdrugs (n=52)	Did not use immuno suppressant drugs (n=122)	ODDS RATIO (95%Cl)	P value	Used immuno biological drugs (n=50)	Did not use immuno biological drugs (n=124)	ODDS RATIO (95%Cl)	P value
Fever	30 (57%)	72 (60%)	0.947 (0.490–01.828)	0.8688	26 (52%)	76 (61%)	0.684 (0.353 <b>–</b> 1.327)	0.308
Nasal obstruction	17 (33%)	49 (40%)	0.724 (0.365 <b>–</b> 1.433)	0.396	12 (24%)	54 (43%)	0.409 (0.195–0.858)	0.017
Sore throat	19 (36%)	53 (43%)	0.750 (0.384 <b>–</b> 1.462)	0.501	17 (34%)	55 (43%)	0.646 (0.326 <b>–</b> 1.281)	0.237
Cough	20 (38%)	43 (35%)	1.148 (0.587 <b>–</b> 2.246)	0.732	14 (52%)	49 (40%)	0.595 (0.291 <b>–</b> 1.216)	0.167
Dyspnea	14 (27%)	30 (24%)	1.130 (0.540 <b>–</b> 2.364)	0.849	11 (22%)	33 (27%)	0.778 (0.357 <b>-</b> 1.694)	0.569
Headache	27 (52%)	74 (60%)	0.701 (0.364 <b>–</b> 1.347)	0.316	28 (56%)	73 (59%)	0.889 (0.458 <b>–</b> 1.726)	0.737
Diarrhea	12 (23%)	39 (32%)	0.638 (0.302–1.350)	0.2783	14 (52%)	37 (30%)	0.914 (0.442 <b>–</b> 1.893)	0.856
Nausea or vomiting	9 (17%)	21 (17%)	1.007 (0.427 <b>–</b> 2.375)	1.000	8 (16%)	22 (17%)	0.883 (0.364 <b>–</b> 2.141)	1.000
Anosmia	28 (54%)	70 (57%)	0.867 (0.451–1.665)	0.739	27 (54%)	71 (57%)	0.876 (0.453 <b>–</b> 1.696)	0.737
Ageusia	27 (52%)	67 (55%)	0.887 (0.463 <b>–</b> 1.699)	0.742	25 (50%)	69 (56%)	0.797 (0.413 <b>–</b> 1.539)	0.507
Fatigue	26 (50%)	57 (47%)	1.140 (0.596 <b>–</b> 2.184)	0.742	23 (46%)	60 (48%)	0.909 (0.470 <b>–</b> 1.755)	0.867

**SUPPLEMENTARY TABLE S1.** Frequency of symptoms of COVID-19 in patients with inflammatory bowel diseases distributed according to the use of immunosuppressant and immunobiological drugs (March-December 2020).

#### TABLE 2. Factors associated with acquiring COVID-19 among 515 patients with IBD (March-December 2020).

	Had	Did not have	Bivariate analysis		Multivariate analysis	
	COVID-19 (n=174)	COVID-19 (n=341)	ODDS RATIO (95%CI)	P value	ODDS RATIO (95%CI)	P value
Female gender	117 (68%)	186 (55%)	1.71 (1.17–2.50)	0.006	1.67 (1.05–2.67)	0.03
Age over 60 years (mean)	30 (40%)	81 (23%)	0.67 (0.42–1.06)	0.09	1.01 (0.53 <b>–</b> 1.92	0.97
Influenza vaccination in 2020	106 (61%)	236 (69%)	0.69 (0.47–1.02)	0.06	0.73 (0.45 <b>-</b> 1.19)	0.21
Exposure to COVID-19 case at home	78 (45%)	49 (14%)	5.07 (3.31-7.78)	<0.001	3.55 (2.18–5.80)	<0.001
Exposure to COVID-19 case outside of the home	76 (43%)	72 (21%)	3.14 (2.10–4.71)	<0.001	2.41 (1.49–3.90)	<0.001
Use of public transportation	47 (27%)	90 (26%)	1.03 (0.68–1.56)	0.881	-	-
Work outside of the home	64 (36%)	81 (23%)	1.87 (1.26–2.78)	0.002	1.91 (1.15–3.16)	0.012
Physical activity >3 times a week	26 (15%)	58 (17%)	0.86 (0.52–1.42)	0.548	-	-
Family history of COVID-19	105 (61%)	136 (40%)	2.29 (1.58–3.33)	<0.001	1.70 (1.07–2.68)	0.02
Underwent colonoscopy	43 (24%)	82 (24%)	1.04 (0.68 <b>–</b> 1.58)	0.868	-	-
Hospitalization for reasons other than COVID-19	12 (6%)	36 (10%)	0.63 (0.32–1.24)	0.177	0.71 (0.29 <b>–</b> 1.74)	0.45
Underwent surgery	7 (4%)	12 (0.03%)	1.15 (0.44 <b>–</b> 2.97)	0.774	-	-
Use of corticosteroid	65 (37%)	106 (31%)	1.32 (0.90 <b>-</b> 1.94)	0.153	1.18 (0.73 <b>–</b> 1.90)	0.49
Use of salicylate	117 (67%)	186 (54%)	1.71 (1.17–2.50)	0.006	2.24 (1.17–4.28)	0.01
Use of immunosuppressant drugs	52 (29%)	128 (37%)	0.71 (0.48 <del>-</del> 1.05)	0.085	0.65 (0.36–1.16)	0.14
Use of immunobiological drugs	50 (28%)	122 (35%)	0.72 (0.49 <del>-</del> 1.08)	0.110	1.23 (0.60 <b>–</b> 2.49)	0.56
Concomitant use of immunobiological and immunosuppressant drugs	17 (10%)	49 (14%)	0.64 (0.36–1.16)	0.140	0.84 (0.31–2.29)	0.74
Active IBD	55 (31%)	103 (30%)	1.06 (0.72 <b>–</b> 1.58)	0.74	-	-
Arterial hypertension	30 (17%)	76 (22%)	0.73 (0.45 <b>–</b> 1.16)	0.180	0.79 (0.43–1.46)	0.46
Diabetes mellitus	20 (11%)	40 (11%)	0.97 (0.55–1.73)	0.937	-	-
Asthma	7 (4%)	2 (0.5%)	7.10 (1.46–34.5)	0.005	9.21 (1.53–55.4)	0.01
Hypothyroidism	10 (5%)	11 (3%)	1.83 (0.76–4.40)	0.171	2.66 (0.98-7.22)	0.052
Crohn's disease	74 (42%)	160 (47%)	1.19 (0.83–1.73)	0.344	1.34 (0.73 <b>–</b> 2.47)	0.33

IBD: inflammatory bowel diseases; CI: confidence interval.

We found that patients with IBD and COVID-19 had a clinical presentation similar to the general population, as previously described, except for a higher frequency of GI symptoms such as diarrhea (33%) and nausea/vomiting (19%)<sup>(17)</sup>. In the general population with COVID-19 these GI symptoms were reported to be around 10%(12,18,19). The greater presence of GI symptoms in IBD patients with COVID-19 has been described previously but was less frequent than in our patients<sup>(20-22)</sup>. Our study showed that the main COVID-19 GI symptom in patients with IBD is diarrhea, present in about a third of patients. This is important as GI symptoms may be erroneously interpreted as a flare of IBD. Activity of IBD was not associated with having COVID-19. The clinical presentation of COVID-19 was not affected by immunosuppressants or immunobiologicals. Transplanted immunosuppressed patients have experienced a different clinical presentation of COVID-19, with more dyspnea and myalgia and a lower frequency of fever, but contrary to these other immunosuppressed patients, in IBD patients, the use of immunosuppressant and immunobiologicals does not seem to affect the clinical manifestations of COVID-19(23,24). Studies and meta-analyses about COVID-19 in patients with IBD were performed, but they did not study correlation among symptoms and the use of immunosuppressants and immunobiologicals<sup>(22,25)</sup>. In the state of Ceará, where the study was carried out, until March 2023, 0.64% of population with COVID-19 required hospitalization (9,384 hospitalizations among 1,451,847 cases). Among our 174 SARS-CoV-2-infected IBD patients, 2 (1.15%) required hospitalization. Although our numbers are too small to draw conclusions, it may suggest that these patients are at higher risk of severe COVID-19. More studies are necessary to clarify this issue.

Although in our IBD patients, females were more frequent, we found that being female was independently associated with COVID-19, unlike the general population where COVID-19 affected men and women equally<sup>(26)</sup>. We also found an association between asthma and COVID-19, which is in line with recently published studies associating asthma with severe forms of COVID-19<sup>(27)</sup>. Other factors associated with COVID-19 were contact with COVID-19 cases (at home and outside, and in the family), working outside the home, and the use of salicylates. Use of immunosuppressants, immunobiological, and corticosteroids were not associated with COVID-19, and there was no higher hospitalization rate in this group, findings consistent with other studies<sup>(20,28,29)</sup>.

The association between salicylates and CO-VID-19 is controversial. Studies that found this association were prone to selection bias. Salicylates have a better safety profile and are preferred in elderly patients who also have a higher risk for CO-VID-19<sup>(20,22,30)</sup>. Our study, however, included a young population, with a mean age of 45 years. In order to evaluate the influence of age we performed a multivariate analysis that included the variable age and observed that the association between the use of salicylate and COVID-19 was independent.

Also, we adjusted for factors such as sex, comorbidities (hypertension, asthma and hypothyroidism), activity disease, and type of IBD and the association of salicylates and COVID-19 remained. Similar to corticosteroids, salicylate may impair the initial immune response to COVID-19, leading to adverse outcomes<sup>(31)</sup>. Furthermore, some studies have shown that the use of immunosuppressants for patients with IBD helps to suppress COVID-19 activity, avoiding cytokine storm, and acting as a protective factor<sup>(32,33)</sup>.

Although some comorbidities (diabetes mellitus, hypertension, chronic kidney disease, obesity, and cancer) are associated with worse COVID-19 outcomes, we found no association between hypertension, diabetes and COVID-19<sup>(34)</sup>. Most of our patients reported that COVID-19 had no impact on the activity of IBD, contrary to a study carried out by Salvatori S et al. that showed that 81% of patients had IBD exacerbation after SARS-COV-2 infection<sup>(25)</sup>.

Our study has limitations. It is a retrospective study with data collection based on the information given by the patients. We assumed that patients with respiratory symptoms in the critical period of the pandemic (lockdown period) had COVID-19, since we still did not have tests widely available at that time. Unfortunately, we were unable to assess CO-VID-19-related mortality, as data were collected at the outpatient clinic after resolution of the infection.

#### CONCLUSION

In conclusion, the clinical presentation of CO-VID-19 in patients with IBD was not affected by immunosuppressants and immunobiologicals, and was similar to that of the general population, however, GI manifestations, mainly diarrhea, seemed to be more common. This is important so that health professionals and patients can know what to expect from COVID-19 in IBD patients avoiding confusion with an IBD flare. Female gender was independently associated with COVID-19, as was the use of salicylates. Immunosuppressants, immunobiologicals and corticosteroids did not influence the risk of COVID-19. IBD patients at high risk for SARS-CoV-2 infection may need to avoid salicylate therapy, but further studies are necessary to confirm this association.

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#### Authors' contribution

Conceptualization of this study, including methodology and study design, was done by Macedo MRF, Sobreira CAF, Farias LABG, Perdigão Neto LV, and Levin AS. Patient recruitment and data collection was done by Macedo MRF, Lavor CB, Rôla CR, Rolim TML, Pessoa FSRP, Girão MS, Freire CCF and Siebra RCB. Souza MHLP, Braga LLBC and Mello LP performed the data analysis and statistics. All authors contributed to data interpretation. Macedo MRF, Farias LABG and Perdigão Neto LV wrote the manuscript; Oliveira MS, Melo ISS, Souza MHLP, Braga LLBC, Mello LP, Silva DB, Farias LABG, Oliveira MS, Perdigão, Levin AS were responsible to review and supervision the manuscript. All authors had access to the study data and reviewed and approved the final manuscript.

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RESUMO - Contexto - Felizmente, muito se tem estudado sobre a COVID-19 em pacientes com doenças inflamatórias intestinais (DII). As evidências sugerem que esses pacientes não parecem ter risco aumentado de COVID-19 grave. Mas ainda se tem algumas incertezas com relação às manifestações clínicas da COVID-19 em portadores de doenças imunomediadas. Objetivo - Este estudo teve como objetivo descrever os principais sintomas da COVID-19 e sua frequência em pacientes com DII e avaliar o impacto dos medicamentos utilizados no tratamento das DII na apresentação clínica da COVID-19. Métodos - Pacientes adultos com DII de três hospitais públicos terciários de ensino do Ceará, Nordeste do Brasil, foram avaliados em consulta ambulatorial no período de março a dezembro de 2020. Pacientes com COVID-19 possível ou confirmada foram comparados com pacientes sem COVID-19. Além disso, as incidências de cada sintoma foram avaliadas com base no uso de medicamentos utilizados para tratamento da DII. Resultados - Foram incluídos no estudo 515 pacientes com DII: 234 com DC e 281 com RCU. Destes, 174 pacientes (34%) tinham COVID-19 possível/confirmado, dos quais 156 (90%) eram sintomáticos. Os principais sintomas foram febre (65%) e dor de cabeça (65%); sintomas gastrointestinais ocorreram em um terço dos pacientes, sendo mais frequentes do que na população geral com CO-VID-19. Os fatores associados a ter COVID-19 foram sexo feminino (OR 1,71, IC95%: 1,17–2,50); ter contato com caso de COVID-19, tanto intradomiciliar (OR 5,07; IC95%: 3,31-7,78) como fora do domicílio (OR 3,14; IC95%: 2,10-4,71); trabalhar fora de casa (OR 1,87; IC95%: 1,26–2,78); história familiar de COVID-19 (OR 2,29, IC95% 1,58–3,33), uso de salicilato (OR 1,71, IC95%: 1,17–4,28) e asma (OR 7,10; IC95%: 1,46-34,57). Conclusão - Pacientes com DII com alto risco de infecção por COVID-19 podem precisar evitar a terapia com salicilatos, mas mais estudos são necessários para confirmar esta associação.

Palavras-chave - Doença inflamatória intestinal; COVID-19; salicilatos.

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