

COVID-19 Pandemic's Effects on Disease and Psychological Outcomes of People With Inflammatory Bowel Disease in Portugal: A Preliminary Research

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Aims: No empirical research on the psychological impact of the coronavirus disease 2019 (COVID-19) pandemic on people living with IBD, a population known to typically present high levels of anxiety and depression and to be potentially vulnerable to COVID-19, has yet been conducted. This study aimed to explore the links between contextual variables related to the COVID-19 pandemic and disease and psychological outcomes.

Methods: The sample included 124 Portuguese patients with Crohn's disease or ulcerative colitis (85.48% women) who completed self-reported measures in an online survey during April 2020.

Results: Fear of contracting COVID-19 and medication adherence were both high and unrelated. About half of the sample presented moderate (37.10%) to severe (14.50%) anxiety. Normal and mild anxiety levels were at 29.80% and 18.50%, respectively. Regarding depressive symptoms, 51.60% of the sample presented normal levels, 27.40% mild severity, 16.10% moderate, and 4.8% severe. No differences were found between Crohn's disease and ulcerative colitis patients. Regression analyses showed that anxiety explained IBD symptom perception ($\beta = 0.29$; $P = 0.022$); fear of contracting COVID-19 ($\beta = 0.35$; $P < 0.001$) and IBD symptom perception ($\beta = -0.22$; $P = 0.009$) explained depressive symptoms; and fear of contracting COVID-19 ($\beta = 0.41$; $P < 0.001$), IBD symptom perception ($\beta = 0.26$, $P < 0.001$), and being in isolation ($\beta = -0.16$, $P = 0.041$) explained anxiety. Type of medication was not linked to these outcomes.

Conclusions: The COVID-19 pandemic does not seem to be affecting adherence to medication but seems to present relevant effects on psychological well-being. Inflammatory bowel disease health care professionals should be attentive of patients' psychological response to this pandemic and of its possible consequences on disease expression. This study additionally provided a psychometrically sound measure of fear of contracting COVID-19.

Key Words: COVID-19, inflammatory bowel disease, medication adherence, mental health, pandemic

INTRODUCTION

In a recent comment,¹ a group of colleagues alerted us to the implications of coronavirus disease 2019 (COVID-19) for patients with inflammatory bowel disease (IBD), whose risks of infection or of development of this disease are not yet clear.² However, nothing is mentioned about the possible psychological impact of the current pandemic, and no empirical research has been conducted on this topic within this population.

The uncertainty caused by the COVID-19 pandemic is likely to lead to negative emotional, cognitive, and behavioral reactions and poorer quality of life. The literature has shown that akin phenomena, such as intolerance of uncertainty, have

consistently shown to be a key variable in the development of anxiety and depressive disorder.³ This is likely to compound on the already studied effect of unpredictability of IBD episodes on a patient's mental health.⁴ Finally, it was shown in a recent review, that people in self-isolation or under quarantine measures are more likely to develop mental health problems such as depression and anxiety.⁵

Anxiety and depression disorders are generally prevalent among people living with IBD (41% for anxiety and 34.7% for depression in patients with active disease)⁶ and are thought to be predictors of active disease and relapses. Depression, in particular, is considered to be pro-inflammatory and influence the clinical expression of IBD. In turn, inflammatory processes and related symptomatology seem to lead to increased levels of depression, leading the patient into a self-perpetuating cycle of inflammation and depression.⁷

It can be postulated that in the current context, in which uncertainty and social isolation are likely to take place, patients are at risk of developing or experiencing an exacerbation of anxiety and depressive symptomatology, which may consequently restart or increase IBD activity. Further, behavior is likely to be affected. Adaptive behavior might be enhanced through fear of contamination with the virus (eg, better self-care practices, increased social distancing) or

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toward strengthening one's body to prepare for infection (eg, greater care in diet, exercise). But it may also lead to maladaptive behaviors such as poor medication adherence—especially to biologics, immunosuppressors, and corticosteroids—given a possible perception by patients that these therapies are risky during this pandemic context.⁸ In fact, this situation may compound an already significant issue with adherence to these medications outside of the context of COVID-19.⁹

The aims of this study were to evaluate, during the current pandemic context, IBD patients' fear of contracting COVID-19, adherence to medication, IBD symptom perception, and anxiety and depression severity, in addition to analyzing the relationships among these variables.

MATERIALS AND METHODS

Procedures

Participants were recruited through adverts posted in Portuguese online IBD patient groups (eg, Doença de Crohn/Colite Portugal). Informed consent was obtained from all participants. Data were collected through an online survey that comprised validated self-report measures in April of 2020. At this time in Portugal, a state of emergency due to the COVID-19 pandemic that required the mandatory confinement of the majority of the population was taking place since March 19, 2020, and was expected to continue at least until the end of April.

Participants

The sample included 124 Portuguese people living with IBD (85.48% women and 14.52% men) between 18 and 64 years old ($M = 39.93$; $SD = 9.87$). Education ranged from fourth grade to PhD ($M_{\text{years of education}} = 13.96$; $SD = 3.59$). Most participants were married or cohabitating (62.90%), 17.70% were single, 10.50% were divorced, and 1.6% were in a noncohabitating relationship. The majority of participants was employed (82.30%), 8.90% were unemployed, 4.90% were students, and 3.30% retired.

Regarding diagnosis, 68.10% of the participants had been diagnosed with Crohn's disease (CD) and 31.90% with ulcerative colitis (UC). Time since diagnosis presented an average of 11.84 years ($SD = 9.18$). The majority of the sample (75.80%) was taking immunosuppressants, biologics, or cortisone.

Most participants (79.84%) were in social isolation, leaving home only for the absolute necessary, whereas 8.90% were in quarantine, and 11.30% were neither in isolation nor quarantine because they were essential workers. Participants in isolation or quarantine had been in that situation for an average of 15.96 days ($SD = 9.78$) at the time of data collection and were mostly isolating with 2 to 4 other people (47.60%) or 1 other person (23.40%). Due to the pandemic and the country's state of emergency, 46% of the participants had to stop working, 37.70% were working from home, and 4% lost their job.

Measures

Participants were asked to report demographic and clinical data, information about their isolation context, contact with COVID-19, and socioeconomic impact of the pandemic. Additionally, participants reported their perception of experienced IBD symptomatology during the previous month through a checklist with 16 IBD symptoms (eg, loose stools, blood or mucus in stools, fatigue, urgency to evacuate, frequent bowel movements, abdominal pain, involuntary passing of gas or stools, fever), rated on a 7-point scale, from 0 (never) to 6 (always); total score ranged between 0 and 96.¹⁰ Participants additionally completed the following 3 measures.

The scale for Fear of Contracting COVID-19 (Table 1) was specifically developed for this study. It was based on the Fear of Aids Scale¹¹ and asks participants to indicate the level of fear/concern they are experiencing regarding each presented situation. The 9 items this scale comprises are rated on a 5-point scale from 1 (no fear) to 5 (very much fear), with higher scores indicating more fear/concern about contracting COVID-19; the total score ranges between 9 and 45.

The Medication Adherence Report Scale (MARS-5)¹² assesses patients' adherence to medications. Participants are asked to report how often they engage in nonadherent behavior on a 5-point Likert scale (1, always; 5, never), with higher scores revealing higher levels of adherence (possible scores between 5 and 25). Both the original ($\alpha = 0.70$)¹² and the Portuguese ($\alpha = 0.74$)¹³ validation studies showed that the MARS presents acceptable Cronbach alphas.

The Hospital Anxiety and Depression Scale (HADS)¹⁴ is a robust 14-item instrument with 2 separate subscales: anxiety and depression, each with 7 items. Each item is rated on a 4-point scale (from 0 to 3), with higher scores indicating higher levels of anxiety and depressive symptoms (possible scores between 0 and 21). A review¹⁵ has demonstrated the reliability of both scales of the HADS (mean Cronbach alpha of 0.83 for the anxiety subscale and of 0.82 for the depression subscale), which has also been validated in the Portuguese population (anxiety subscale: $\alpha = 0.76$; depression subscale: $\alpha = 0.81$).¹⁶

Fear of contaminating others with COVID-19 was also assessed with a single-item rated on a 10-point scale (1, no fear at all; 10, extreme fear of infecting others), created for the purpose of this study.

Cronbach alphas for each measure in the current study are presented in Table 2.

Statistical Analysis

A principal component analysis (PCA) was conducted to examine the factorial structure of the Fear of Contracting COVID-19 Scale. A confirmatory factor analysis (CFA) with maximum likelihood as estimation method was performed using structural equation modelling (SEM)¹⁷ to confirm the obtained structure. Data from the CFA were examined through

TABLE 1. Fear of Contracting COVID-19 Scale - Please indicate the *level of fear/concern* you are experiencing regarding each of the following situations

No fear	A little fear	A fair amount of fear	Much fear	Very much fear		
1	2	3	4	5		
1. Contracting COVID-19.		1	2	3	4	5
2. Going outside.		1	2	3	4	5
3. Meeting people.		1	2	3	4	5
4. Having contact with someone with respiratory symptoms.		1	2	3	4	5
5. Having contact with someone who was in contact with an infected patient.		1	2	3	4	5
6. Having contact with health care professionals.		1	2	3	4	5
7. Having contact with someone infected with COVID-19.		1	2	3	4	5
8. Having severe complications due to COVID-19.		1	2	3	4	5
9. Dying from COVID-19.		1	2	3	4	5

the analysis of Relative chi-square (χ^2/df) (<5 indicates that the model presents a good fit to empirical data),¹⁸ standardized root mean square residual (SRMR) (<0.08 indicates an acceptable fit),¹⁹ and the Comparative Fit Index (CFI) and the Tucker and Lewis Index (TLI) (>0.90 shows a good fit).¹⁸ The local adjustment of the model was analyzed by standardized regression weights and squared multiple correlations (≥ 0.50 and ≥ 0.25 , respectively, to indicate good local adjustment).²⁰

Descriptive and frequency analyses were then performed to analyze the variable's means, standard deviations, and frequencies in the studied sample. Student *t* tests were conducted to explore differences between CD and UC patients. Correlation and linear regression analyses were performed to examine the relationship between variables, in particular, which variables explain a significant amount of variance of IBD symptom perception, depressive symptomatology, and anxiety.

RESULTS

Psychometric Properties of the Fear of Contracting Covid-19 Scale

Results from the PCA showed satisfactory scores on the Kaiser-Meyer-Olkin test (0.89) and the Bartlett sphericity test ($\chi^2_{(36)} = 682.415$; $P < 0.001$). Two factors with eigenvalues ≥ 1 were identified. Because the second factor only accounted for 11.76% of the variance and all of the 9 items loaded on the first factor, the analysis was repeated forcing a 1-factor structure, which explained 59.75% of the variance. Results from the CFA confirmed the adequacy of the scale. With the intercorrelation of the error terms of items 2 and 3, 7 and 8, and 8 and 9, the model presented a good model fit (CMIN/DF, 2.37; CFI, 0.95; TLI, 0.93; SRMR, 0.05). The obtained local adjustment indices were also good: standardized regression weights varied between

0.69 and 0.84, and squared multiple correlations ranged from 0.47 to 0.70. The scale presented excellent internal reliability, with a Cronbach alpha of 0.91.

Descriptive Analyses

Table 2 presents the means and standard deviations of the studied variables. It is interesting to note that although fear of contaminating others (M = 7.17; SD = 3.05) and fear of contracting COVID-19 (M = 35.59; SD = 6.21) seemed to be elevated, adherence to medication as measured by the MARS was also high (M = 22.73; SD = 3.53). Further, though most participants (51.60%) presented normal (nonclinically significant) levels of depressive symptoms, with 27.40% presenting mild severity, 16.10% moderate, and 4.8% severe,¹⁵ the scenario was different regarding anxiety. The percentage of participants that presented normal and mild anxiety levels was at 29.80% and 18.50%, respectively. About half of the sample presented moderate (37.10%) to severe (14.50%) anxiety.¹⁵ No differences were found between CD patients and UC patients regarding perception of IBD symptoms ($t_{(122)} = -0.731$; $P = 0.466$), fear of contaminating others ($t_{(122)} = 0.345$; $P = 0.730$), fear of contracting COVID-19 ($t_{(122)} = 0.418$; $P = 0.677$), adherence to medication ($t_{(122)} = 0.197$; $P = 0.844$), depressive symptoms ($t_{(122)} = 0.880$; $P = 0.381$), and anxiety ($t_{(122)} = 0.406$; $P = 0.685$).

Correlation Analyses

Both depressive symptoms and anxiety were associated with higher IBD symptom perception, fear of infecting others, and fear of contracting COVID-19 (Table 2). Having lost one's job due to the pandemic was associated with higher depressive symptomatology severity, and being in isolation was linked to less anxiety. Being in isolation was additionally linked to less fear of contracting COVID-19 and more

TABLE 2. Means, Standard Deviations, Cronbach Alphas, and Correlation Scores Between Variables ($N = 124$)

	M (SD)	α	1	2	3	4	5	6	7	8	9	10	11
1. Isolating	—	—	—										
2. Isolation duration (days)	15.96 (9.78)	—	0.63 _c	—									
3. Stopped working	—	—	0.28 _b	0.17	—								
4. Lost job	—	—	0.07	0.13	0.22 _a	—							
5. Time since IBD diagnosis	11.89 (9.18)	—	0.00	-0.01	-0.11	-0.01	—						
6. IBD symptoms	36.71 (16.49)	—	-0.05	0.04	0.07	0.06	0.04	—					
7. Immunosuppressants, biologics, or corticosteroids current use	—	—	-0.02	-0.13	-0.08	-0.17	-0.08	-0.03	—				
8. Fear of infecting others with COVID-19	7.17 (3.05)	—	-0.22 _a	-0.14	0.03	0.03	-0.16	0.15	0.02	—			
9. Fear of contracting COVID-19	35.59 (6.21)	0.91	0.05	0.16	0.11	0.16	-0.06	0.24 _b	0.04	0.16	—		
10. Adherence to medication	22.73 (3.53)	0.87	0.22 _a	0.15	0.08	0.02	-0.09	0.01	0.32 _c	-0.12	0.15	—	
11. Depressive symptoms	7.27 (4.30)	0.82	-0.08	0.02	0.13	0.23 _a	0.08	0.32 _c	-0.06	0.19 _a	0.44 _c	-0.02	—
12. Anxiety	10.19 (3.99)	0.83	-0.18 _a	-0.08	0.01	0.10	0.17	0.38 _c	-0.03	0.28 _b	0.48 _c	-0.06	0.71 _c

_a $P < 0.05$; _b $P < 0.01$; _c $P < 0.001$

adherence to medication. The use of immunosuppressants, biologics, or corticosteroids was also—and solely—associated with more medication adherence. Fear of contracting COVID-19 was not related to medication adherence, being only positively linked to IBD symptom perception. Results did not show any other relevant associations.

Regression Analyses

To explore which variables explain perception of IBD symptoms in the studied sample, a linear regression analysis was conducted with fear of contracting COVID-19, depressive symptoms, and anxiety as independent variables (the variables that presented significant correlations with IBD symptom perception). The model ($F_{(3, 120)} = 7.28$; $P < 0.001$) accounted for 13% of IBD symptom perception's variance. Neither fear of contracting COVID-19 ($\beta = 0.06$; $P = 0.519$) nor depressive symptoms ($\beta = 0.09$; $P = 0.470$) accounted for this outcome's variance but anxiety did, with an effect of 0.29 ($P = 0.022$).

The same analysis was conducted with depressive symptomatology as dependent variable and fear of infecting others, job loss, IBD symptom perception, and fear of contracting COVID-19 as independent variables. The model was significant ($F_{(4, 119)} = 11.09$; $P < 0.001$) and explained 25% of depressive symptomatology's variance. Only 2 variables were demonstrated to significantly explain this variance: fear of contracting COVID-19 ($\beta = 0.35$; $P < 0.001$) and IBD symptom perception ($\beta = -0.22$, $P = 0.009$). Indeed, fear of infecting others did not explain depressive symptomatology severity's variance ($\beta = 0.09$, $P = 0.244$) and neither did job loss; although, this variable's effect was close to significance ($\beta = 0.15$; $P = 0.067$).

To examine anxiety's variance predictors, being in isolation, fear of infecting others, IBD symptom perception, and fear of contracting COVID-19 were inserted as independent variables. The model ($F_{(4, 119)} = 16.96$; $P < 0.001$) accounted for 34% of anxiety's variance and presented 3 significant independent variables: fear of contracting COVID-19, which presented an effect of 0.41 ($P < 0.001$); IBD symptom perception, with had an effect of 0.26 ($P < 0.001$); and being in isolation, which had an effect of -0.16 ($P = 0.041$). Fear of infecting others' explanation of anxiety's variance was close to significance ($\beta = 0.14$; $P = 0.064$).

DISCUSSION

This study aimed to investigate the relationship between depressive symptoms, anxiety, IBD symptom perception, medication adherence, fear of contracting COVID-19, and contextual variables related to the COVID-19 pandemic and confinement.

Crohn's disease and ulcerative colitis patients seem to be reacting the same way to the pandemic, revealing similar levels of depressive symptoms, anxiety, fear of contracting COVID-19, fear of contaminating others, adherence to medication, and IBD symptom perception. This finding is not surprising, as CD and UC patients tend to have a similar mental health profiles in nonpandemic circumstances, with increased anxiety and depression when compared with controls but not distinct between the 2 types of IBD.²¹

Although this study expected to find potential issues with medication adherence (particularly adherence to biologics or immunosuppressors), the contrary was observed. Medication adherence was high, even though fear of contaminating others

and fear of contracting COVID-19 were also high. These findings go in line with the ones found by an international study⁸ published during the time this article was being revised, which demonstrated with a sample of 3815 European IBD patients that although most respondents feared contracting COVID-19 and nearly two-thirds stated that immunosuppressive drugs were associated with a higher risk of infection, almost all respondents (96%) had continued taking their IBD medications on their own initiative. This corroboration is suggestive that the present study's correlational findings, although based on a Portuguese sample, may be observed in other IBD populations across the globe.

Results about depressive symptomatology and anxiety were more concerning. About half of the participants presented mild to severe depressive symptomatology, and anxiety was at a moderate level for about 37% of the sample and severe for 15%. High anxiety thus seems to be common among IBD patients during this time, which may be impactful not only to patients' mental health and well-being but also to the disease itself, as anxiety may be associated with clinical recurrence²² and was the only variable that significantly explained IBD symptom perception's variance in the model tested in the present study. Even though anxiety and depressive symptoms were relevant, these do not seem to be linked to poorer or better medication adherence. Being able to self-isolate and taking immunosuppressants, biologics, or corticosteroids were the only variables associated with how well patients are using their medication.

Depressive symptoms seem to be mainly explained by fear of contracting COVID-19 and IBD symptom perception. The effect of IBD symptom perception on depressive symptoms is already well known⁷; however, at this moment, the isolation created by the fear of contracting COVID-19 might be causing an additional burden on these patients, leading to a higher expression of depressive symptoms. Additionally, job loss due to the pandemic was close to significance (and may have not achieved it due to the small proportion of participants that had lost their job), which goes in line with the known links between job loss and depression.²³

Fear of contracting COVID-19 also seems to have an important role on the presentation of anxiety. It may be possible that IBD patients are afraid to get infected and suffer particular medical complications due to the preexisting IBD diagnosis.¹ This however does not seem to be related to type of medication patients are using because the use of immunosuppressive, biologics, or steroid medication was not correlated with fear of contracting COVID-19. It is patients with higher IBD symptom perception that seem to be more afraid, as evidenced by the association found between perception of IBD symptoms and fear of contracting COVID-19 and by the significant anxiety's variance explained by IBD symptom perception. More frequent symptomatology is also more likely to lead to hospital visits for treatment and management of IBD; however,

patients may be afraid of using the health system for fear of contagion. Inflammatory bowel disease patients who have increased symptomatology might experience more anxiety for seeing themselves at increased risk of contracting COVID-19 during a medical visit and of developing complications in case of infection.

Findings also demonstrated that being in isolation seems to be linked with decreased anxiety. This is an interesting finding, given that being in isolation was not associated with fear of contracting COVID-19, and yet it explains less anxiety. This seems to indicate that although patients in isolation reported the same level of fear of contracting the virus as patients who are essential workers (and therefore were not in isolation), the former presented less anxiety.

This study additionally provided a scale for the assessment of fear of contracting COVID-19. This scale performed well psychometrically and could potentially be used in other studies with IBD or other populations.

The present study nonetheless presents some limitations, such as the use of online self-selection recruitment methods (which may have resulted in a nonrepresentative sample of Portuguese IBD patients), reliance on self-reported outcomes and not on objective indicators of disease activity, and the lack of data on the studied variables' levels before the start of the pandemic, which precludes assumptions of causality. Depression and anxiety levels were high but there are not sufficient data to effectively know whether this was due to the pandemic or due to the cross-sectional nature of this study. Longitudinal studies should thus be performed to explore causal relationships between the studied variables. Nevertheless, given that fear of contracting COVID-19 was the most relevant variable for depressive symptomatology and anxiety severity, it seems that the pandemic context might have significantly contributed to increases in these outcomes. Furthermore, having limited access to medical care and fear of having an IBD flare during a pandemic might have explained the high adherence to medication reported by participants. These variables were nonetheless not assessed and should be considered in future studies on this topic. The singularity of the situation in Portugal at the time of data collection should also be acknowledged. During data collection (April 2020) and by the time this article was written (May 2020), Portugal was one of the countries that seemed to be dealing with the pandemic more effectively, with expressively low numbers of infected people and deaths due to COVID-19 per million in comparison with other European countries or the United States.²⁴ Inflammatory bowel disease patients from other countries might present increased levels of psychopathology and fear of contracting COVID-19 compared to this study's sample.

Data from this study indicate that IBD health care professionals should be attentive of patients' psychological response to this pandemic and of its possible consequences on disease expression. It may be useful to provide additional psychological

assessment and psychotherapeutic resources to IBD patients during the course of the COVID-19 pandemic.

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