ORIGINAL ARTICLE

Evolution of the emotional impact in patients with early inflammatory bowel disease during and after Covid-19 lockdown

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Abstract
Background: Patients with inflammatory bowel disease (IBD) are vulnerable to some psychological disorders. Here we describe the psychological impact of a COVID-19 pandemic lockdown in patients with IBD.
Methods: This multicenter prospective cohort study included 145 patients recently diagnosed with IBD. Data on clinical and demographic characteristics, anxiety and depression scales, and IBD activity were collected in two telephone surveys, during and after the first COVID-19 lockdown in Spain. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

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Results: During lockdown, 33.1% and 24.1% scored high on the anxiety and depression scales, respectively. Independent factors related to anxiety (all values ORs; 95% CIs) during lockdown were female sex (2; 1.2–5.4) and IBD activity (4.3; 1.8–10.4). Factors related to depression were comorbidity (3.3; 1.1–9.8), IBD activity (6; 1.9–18.1), use of biologics (2.9; 1.1–7.6), and living alone or with one person (3.1; 1.2–8.2). After lockdown, anxiety and depression symptoms showed significant improvement, with 24.8% and 15.2% having high scores for anxiety and depression, respectively. Factors related to post-lockdown anxiety were female sex (2.5; 1.01–6.3), Crohn's disease (3.3; 1.3–8.5), and active IBD (4.1; 1.2–13.7). Factors associated with depression were previous history of mood and/or anxiety disorders (6.3; 1.6–24.9), active IBD (7.5; 2.1–26.8), and steroid use (6.4; 1.4–29).

Conclusions: Lockdown during the COVID-19 pandemic had a significant psychological impact in patients with IBD. Disease activity was related to the presence of anxiety and depression symptoms during and after lockdown.

Evolución del impacto emocional en pacientes con enfermedad inflamatoria intestinal temprana durante y después del bloqueo de COVID-19

Resumen

Antecedentes: Los pacientes con enfermedad inflamatoria intestinal (EII) son vulnerables a sufrir trastornos psicológicos. En este estudio describimos el impacto psicológico que ha supuesto el confinamiento durante el COVID-19 en pacientes con EII.

Métodos: Este estudio de cohorte prospectivo multicéntrico se incluyeron 145 pacientes con diagnóstico de EII reciente. Los datos sobre las características clínicas y demográficas, las escalas de ansiedad y depresión y la actividad de la EII se recogieron en dos encuestas telefónicas, durante y después del primer confinamiento por COVID-19 en España. Se calcularon las odds ratios (OR) y los intervalos de confianza (IC) al 95%.

Resultados: Durante el confinamiento, el 33,1% y el 24,1% puntuaron alto en las escalas de ansiedad y depresión respectivamente. Los factores independientes relacionados con la ansiedad (todos los valores OR; IC del 95%) durante el confinamiento fueron el sexo femenino (2; 1,2-5,4) y la actividad de la EII (4,3; 1,8-10,4). Los factores relacionados con la depresión fueron la comorbilidad (3,3; 1,1-9,8), la actividad de la EII (6; 1,9-18,1), el uso de biológicos (2,9; 1,1-7,6) y el vivir solo o con una persona (3,1; 1,2-8,2). Tras el confinamiento, los síntomas de ansiedad y depresión mostraron una mejoría significativa, ya que el 24,8% y el 15,2% tenían puntuaciones altas en ansiedad y depresión, respectivamente. Los factores relacionados con la ansiedad tras el confinamiento fueron el sexo femenino (2,5; 1,01-6,3), enfermedad de Crohn (3,3; 1,3-8,5) y EII activa (4,1; 1,2-13,7). Los factores asociados con la depresión fueron los antecedentes de trastornos del estado de ánimo y/o de ansiedad (6,3; 1,6-24,9), EII activa (7,5; 2,1-26,8), y el uso de esteroides (6,4; 1,4-29).

Conclusiones: El confinamiento durante la pandemia de COVID-19 tuvo un impacto psicológico significativo en los pacientes con EII. La actividad de la enfermedad se relacionó con la presencia de síntomas de ansiedad y depresión durante y después del confinamiento.

Introduction

The COVID-19 pandemic has triggered important changes in the lifestyle and behavior of the general population, with an inevitable impact on mental health.[1,2] Lockdown of the population at home is a widely used measure during incidence peaks. Some surveys during the first wave of lockdown have identified anxiety symptoms in 23–37% and depression symptoms in 24–46% of the general population.[3–5]

Patients with inflammatory bowel disease (IBD) are vulnerable to some psychological disorders.[6,7] Although lockdown of a population with a comorbidity that makes them susceptible to infections can have protective effects, it can intensify their vulnerability to these disorders. Research is limited on the psychological impact of lockdown on the population with IBD. Available findings show a high prevalence of symptoms, but we do not know how much this psychological impact persists once lockdown ends.[8–10]

Our study aims were to assess the psychological impact of pandemic lockdown in patients with IBD and to evaluate factors related to the risk of developing anxiety and depression symptoms.

Patients and methods

Study population

We carried out a multicenter prospective study in a cohort of patients with IBD diagnosed during 2018 and 2019 in four hospitals in the Valencian community of Spain. These patients were participating in a prospective registry of new IBD cases. The inclusion criterion was diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) according to ECCO/ESGAR guidelines (clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical findings).[11] The exclusion criteria were age under 18 years; diagnosis of unclassified colitis, intellectual disability, dementia, bipolar disorder, or schizophrenia; and the presence of a language barrier.

Ethical considerations

The Ethics Committee of HGUA-ISABIAL approved the study (PI 2020-078). All patients included in the study read the patient information sheet and signed the informed consent form sent by e-mail.

Sample size calculation

We estimated the sample size for the multiple logistic regression analysis using standard methods, assuming the need for at least 10 cases for each independent variable. The anxiety/depression rate during COVID-19 lockdown was estimated to be 35%, and 142 patients thus were required to perform a multiple logistic regression analysis with five independent variables.[12]

Data collection

We extracted clinical characteristics from electronic medical records. Body mass index and medication adherence were checked in telephone surveys. Patients were evaluated at diagnosis for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).

Patients were contacted by telephone twice during the first wave of COVID-19 in Spain. The first contact was made between April 13 and May 17, 2020, during the last month of lockdown imposed by the Spanish government. The second telephone contact was made 2 months later, when the population had returned to its routines after a period of increasingly relaxed lockdown measures.

During lockdown, all patients were invited to answer questionnaires addressing anxiety and depression (HADS), IBD activity (the Modified Harvey Bradshaw Index [MHBI] for CD and Simple Clinical Colitis Activity Index [SCCAI] for CU),[13–15] medical treatment, and work status. In addition, a semi-structured interview was conducted, covering demographic characteristics and characteristics of lockdown.

After lockdown, all patients were invited to answer the same questionnaires covering anxiety and depression (HADS) and IBD activity (MHBI, SCCAI) and to complete a semi-structured interview.

Definitions

Predictive variables

Age was dichotomized as <40 years and ≥40 years according to other studies of IBD. Regular alcohol use was defined as alcohol intake ≥3 times/week. Education level was split into low level (secondary school or lower) and high level (college or higher). The definition of active employment included being an employee or self-employed and excluded temporary employment or cessation of being self-employed.

Comorbidity was characterized as coexisting diseases or conditions that affect an individual's physiologic reserve condition or require chronic treatment. A previous history of mood and/or anxiety disorders (MAD) was defined as the presence of an active MAD diagnosis in the medical records within 6 months before lockdown. Psychopharmacological treatment was defined as active intake of benzodiazepines and/or antidepressants.

Disease phenotype was classified according to the Montreal classification.[16] IBD was considered to be active when the MHBI or SCCAI score was ≥5.[14,15] Extra-intestinal manifestations of IBD were extracted from the confirmed diagnosis in medical records according to European Evidence-based Consensus on Extra-intestinal Manifestations in IBD.[17] Medications for IBD treatment during the interviews were classified as mesalazine, steroids (prednisone or equivalent, budesonide and beclomethasone), immunosuppressants (azathioprine, mercaptopurine, methotrexate, and cyclosporine), biologics (infliximab, adalimumab, certolizumab pegol, golimumab, ustekinumab, and vedolizumab), or small molecule inhibitors (tofacitinib).

Dependent variables

Symptoms of anxiety and depression were evaluated using HADS. The HADS-total consists of 14 items, divided into two 7-item subscales, one each for anxiety (HADS-A) and depression (HADS-D).[13] Patients were considered to have a high anxiety or depression scale scores based on a cut-off value of >7 for the respective subscale.[18]

Outcomes

The primary aim of the study was to evaluate anxiety and depression symptoms in the early IBD population during and after the COVID-19 pandemic lockdown. We also evaluated factors related to the risk that these symptoms would be present.

Statistical analysis

Descriptive statistics were used to examine the baseline characteristics. Variables with a probable relation to the presence of anxiety and depression symptoms were evaluated during and after the lockdown by univariate regression. Variables with $P < 0.05$ in univariate analysis were included
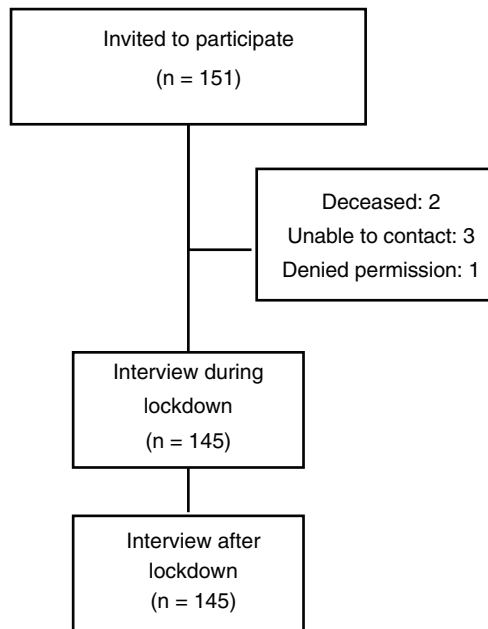
Figure 1   Flow diagram of the study.

in a multivariable logistic regression model. The statistical significance level for all variables was set at $P < 0.05$. We used the SPSS statistical package for Windows, version 25.0.

Results

A total of 145 patients were included in the study (Fig. 1). All participants completed the two telephone surveys. Demographic and clinical characteristics during and after lockdown are shown in Table 1.
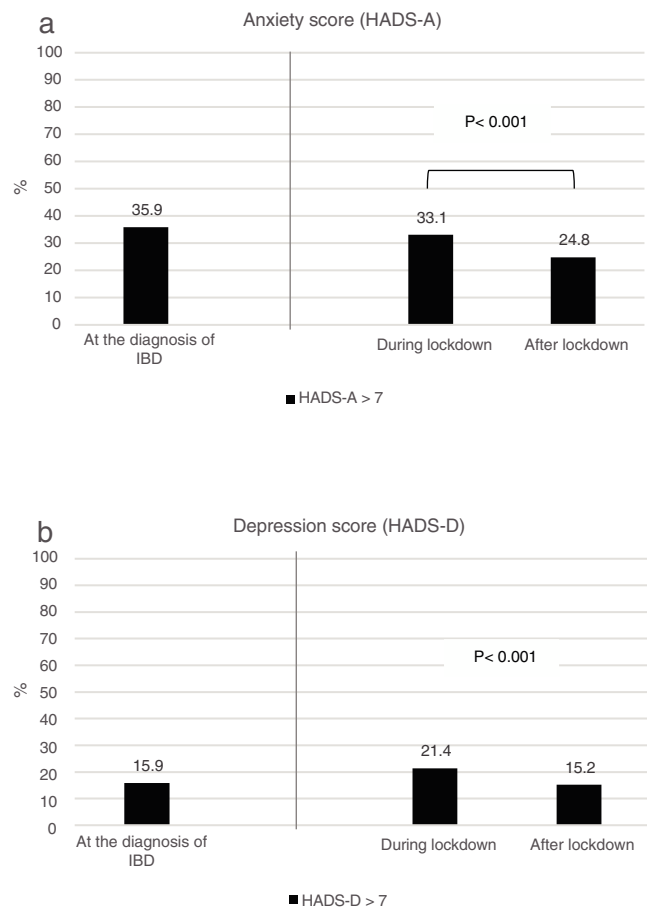
Anxiety

During lockdown, 48 (33.1%) patients had a high anxiety score (Fig. 2a). The factors found in the univariate analysis to be predictive of anxiety during lockdown are shown in Table 2. After multivariate analysis adjusted for all of the studied variables, female sex (odds ratio [OR], 2; 95% confidence interval [CI], 1.2–5.4; $P = 0.012$) and active IBD (OR, 4.3; 95% CI, 1.8–10.4; $P = 0.001$) were independently associated with the presence of anxiety symptoms (Table 4).

After lockdown, 36 (24.8%) patients had a high anxiety score, which was a significant improvement from the proportion during lockdown (Fig. 2a). Factors found in univariate analysis to be predictive of anxiety after lockdown are shown in Table 2. After multivariate analysis adjusted for all of the studied variables, female sex (OR, 2.5; 95% CI, 1.01–6.3; $P = 0.047$), Crohn's disease (OR, 3.3; 95% CI, 1.3–8.5; $P = 0.010$), and active IBD (OR, 4.1; 95% CI, 1.2–13.7; $P = 0.019$) were independently associated with the presence of anxiety symptoms (Table 4).

Depression

During lockdown, 31 (24.1%) patients had a high depression score (Fig. 2b). The factors found in the univariate analysis

Figure 2   Categorization of symptoms based on Hospital Anxiety and Depression Scale (HADS) scores at diagnosis of IBD and during the course of lockdown. (2a) HADS-anxiety. (2b) HADS-depression.

to be predictive of depression during lockdown are shown in Table 3. After multivariate analysis adjusted for all of the studied variables, comorbidity (OR, 3.3; 95% CI, 1.1–9.8; $P = 0.024$), active IBD (OR, 6; 95% CI, 1.9–18.1; $P = 0.001$), use of biologics (OR, 2.9; 95% CI, 1.1–7.6; $P = 0.031$), and living alone or with one person (OR, 3.1; 95% CI, 1.2–8.2; $P = 0.017$) were independently associated with the presence of depression symptoms (Table 4).

After lockdown, 22 (15.2%) patients had a high depression score, which was a significant improvement from the proportion during lockdown (Fig. 2b). Factors found in the univariate analysis to be predictive of depression after lockdown are shown in Table 4. After multivariate analysis adjusted for all of the studied variables, a previous history of MAD (OR, 6.3; 95% CI, 1.6–24.9; $P = 0.008$), active IBD (OR, 7.5; 95% CI, 2.1–26.8; $P = 0.002$), and use of steroids (OR, 7.5; 95% CI, 2.1–26.8; $P = 0.015$) were independently associated with the presence of depressive symptoms (Table 4).

Discussion

Our results show that a high proportion of patients with IBD suffered anxiety and depression during lockdown and that this proportion significantly decreased after lockdown

Table 1 Clinical and demographic characteristics of the study population.

	During lockdown	After lockdown
Sex, n (%)		
Male	79 (54.5)	
Female	66 (45.5)	
Age (mean in years, SD)	43 (16.3)	
Disease type, n (%)		
CD	72 (49.7)	
UC	73 (50.3)	
Duration of IBD, mean in months (SD)	17.3 (6.4)	
BMI, mean (SD)	25 (4.8)	
Current smoker, n (%)	22 (15.2)	
Regular alcohol use, n (%)	39 (26.9)	
Marital status		
Married/partner, *n* (%)	107 (73.8)	
Divorced, *n* (%)	9 (6.2)	
Single, *n* (%)	28 (19.3)	
Widowed, *n* (%)	1 (0.7)	
Education, n (%)		
Low level	97 (66.9)	
High level	48 (33.1)	
Active employment, n (%)	52 (35.9)	71 (49)
Comorbidity, n (%)	69 (47.6)	
Previous history of MAD, n (%)	15 (10.3)	
CD Montreal classification	72	
Age in years, n (%)		
A2: 17–40	42 (58.3)	
A3: ≥40	30 (41.7)	
Location of Crohn's (>1 location possible), n (%)		
L1: Ileal	37 (51.4)	
L2: Colonic	12 (16.7)	
L3: Ileocolonic	22 (30.6)	
L4: Upper GI	6 (8.3)	
Crohn's behavior, n (%)		
B1: Inflammatory	53 (73.6)	
B2: Stricturing	11 (15.3)	
B3: Penetrating	8 (11.1)	
Perianal involvement	4 (5.6)	
UC Montreal classification, n (%)	73	
E1: Proctitis	19 (26)	
E2: Distal colitis	29 (39.7)	
E3: Total colitis	25 (34.2)	
Active IBD, n (%)	29 (20)	18 (12.4)
EIM, n (%)	23 (15.9)	
IBD-related surgical history, n (%)	10 (6.9)	
Use of mesalazine, n (%)	86 (59.3)	86 (59.3)
Use of steroids, n (%)	7 (4.8)	12 (8.3)
Use of immunosuppressants, n (%)	33 (22.8)	32 (22.1)
Use of biologics, n (%)	44 (30.3)	46 (31.7)
Psychopharmacological treatment, n (%)	29 (20)	
Cohabitants during lockdown (n) 0-1	55 (37.9)	
≥2	90 (62.1)	

CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; BMI, body mass index; MAD, mood and/or anxiety disorders; EIM, extra-intestinal manifestations; GI, gastrointestinal

Table 2 Univariate analysis of risk factors for the presence of significant symptoms of anxiety during and after lockdown.

	During				After			
	HADS anxiety >7 n (%)	OR	95% confidence interval	P	HADS anxiety >7 n (%)	OR	95% confidence interval	P
Sex								
Male	18 (22.8)	1			11 (13.9)	1		
Female	30 (45.5)	2.8	1.3–5.7	0.004	25 (37.9)	3.7	1.6–8.4	0.001
Age								
<40 years	24 (35.8)	1			17 (25.4)	1		
≥40 years	24 (30.8)	0.79	0.39–1.5	0.519	19 (24.4)	0.94	0.44–2	0.888
Disease type								
CD	29 (40.3)	1.9	0.94–3.8	0.068	27 (37.5)	4.2	1.8–9.9	<0.001
UC	19 (26)	1			9 (12.3)	1		
BMI								
<30	40 (32)	1			30 (24)	1		
≥30	8 (40)	1.4	0.53–3.7	0.480	6 (30)	1.3	0.47–3.8	0.564
Current smoker								
Yes	8 (36.4)	1.1	0.46–3	0.724	6 (27.3)	1.1	0.41–3.2	0.773
No	40 (32.5)	1			30 (24.4)	1		
Regular alcohol use								
Yes	15 (38.5)	1.3	0.64–2.9	0.406	11 (28.2)	1.2	0.55–2.9	0.568
No	33 (31.1)	1			25 (23.6)	1		
Marital status								
Married/partner	38 (35.5)	0.64	0.28–1.7	0.301	26 (24.3)	1		
Divorced/single/widowed	10 (26.3)	1			10 (26.3)	1.1	0.47–2.5	0.805
Education								
Low level	33 (34)	1.1	0.54–2.3	0.739	26 (26.8)	1.3	0.6–3.1	0.434
High level	15 (31.1)	1			10 (20.8)	1		
Active employment								
Yes	16 (30.8)	0.84	0.4–1.7	0.655	19 (26.8)	1.2	0.57–2.2	0.598
No	32 (34.4)	1			17 (23)	1		
Comorbidity								
Yes	25 (36.2)	1.3	0.65–2.6	0.446	20 (29)	1.5	0.71–3.2	0.269
No	23 (30.3)	1			16 (21.1)	1		
Previous history of MAD								
Yes	8 (53.3)	2.5	0.87–7.5	0.089	9 (60)	5.7	1.8–17.4	0.001
No	40 (30.8)	1			27 (20.8)	1		
Active IBD								
Yes	18 (62.1)	4.6	1.9–11	<0.001	12 (66.7)	8.5	2.9–25.1	<0.001
No	30 (25.9)	1			24 (18.9)	1		
EIM								
Yes	10 (43.5)	1.7	0.68–4.2	0.249	7 (30.4)	1.4	0.52–3.7	0.497
No	38 (31.1)	1			29 (23.8)	1		
IBD-related surgical history								
Yes	3 (30)	0.85	0.21–3.4	1	3 (30)	1.3	0.32–5.4	0.71
No	45 (33.3)	1			33 (24.4)	1		

Table 2 (*Continued*)

	During				After			
	HADS anxiety >7	OR	95% confidence interval	P	HADS anxiety >7	OR	95% confidence interval	P
	n (%)				n (%)			
Use of mesalazine								
Yes	26 (30.2)	0.72	0.36–1.4	0.375	18 (20.9)	0.6	0.28–1.2	0.190
No	22 (37.7)	1			18 (30.5)	1		
Use of steroids								
Yes	3 (42.9)	1.5	0.33–7.2	0.685	6 (50)	3.4	1.03–11.4	0.073
No	45 (32.6)	1			30 (22.6)	1		
Use of immunosuppressants								
Yes	14 (42.4)	1.6	0.76–3.7	0.195	10 (31.3)	1.5	0.64–3.6	0.341
No	34 (30.4)	1			26 (23)	1		
Use of biologics								
Yes	15 (34.1)	1.06	0.5–2.2	0.868	14 (30.4)	1.5	0.69–3.3	0.287
No	33 (32.7)	1			22 (22.2)	1		
Cohabitants during lockdown								
0–1	23 (41.8)	1.8	0.92–3.7	0.081	19 (34.5)	2.2	1.05–4.8	0.034
≥2	25 (27.8)				17 (18.9)	1		

CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; BMI, body mass index; MAD, mood and/or anxiety disorders; EIM, extra-intestinal manifestations.

ended. Factors associated with anxiety were mainly IBD activity and female sex, whereas factors associated with depression were more variable, with an important influence of IBD activity.

In an international public health emergency such as the COVID-19 pandemic, it is important to investigate the psychological impact on vulnerable populations such as patients with IBD.[6,7] Knowledge of this effect could lead to interventions to reduce the impact. Several studies have evaluated what the pandemic and the lockdown have meant in terms of mental health in the general population.[1–5] However, few studies have assessed mental health effects during and after lockdown in a pandemic among patients with specific chronic diseases that may leave them feeling more threatened and at higher risk.

Here we report symptoms of depression and anxiety in relation to pandemic COVID-19 lockdown in a population with IBD. The proportion with symptoms during lockdown was similar to proportions found immediately after the IBD diagnosis, another moment of special vulnerability. Although the proportion of patients with anxiety and depression during lockdown was high, it is similar to that found in the general population during this period and lower than reported from other surveys of patients with IBD.[6–9] The divergence can be explained by the fact that our interviews were targeted to specific individuals, which avoided biases involved with an open survey offered to anyone who would participate and who may have different motivations for doing so. Therefore, this choice avoided a selection bias that can affect studies relying on online web-based surveys made generally available. Another possible explanation is that our study was focused on a population with chronic disease confined to their homes, with the majority of people not going out to work during lockdown. This situation may have favored a sense of security in patients with IBD who would likely perceive that they have a higher risk of infection and worse evolution of COVID-19 disease, as some surveys have suggested.[10,19]

We found a significant decrease in symptoms of anxiety and depression after lockdown. This important finding suggests that the psychological consequences of lockdown among people with IBD might not be persistent, as has been shown in the general population and health workers after Wuhan eased its lockdown.[20]

In the general population, during a lockdown, women seem to have experienced more mental health difficulties than men, particularly in relation to anxiety and certain sleep disorders, such as insomnia.[3,4,21,22] In our study, female sex was a consistent risk factor for anxiety during and after lockdown. This finding is worth considering for patients with IBD. The differences between men and women in the development of depression symptoms seemed to have been minimal in our cohort, as previously described in the general population during lockdown.[3,22]

A factor more consistently associated with both anxiety and depression in this study was disease activity. We have shown an important relationship between IBD activity and anxiety and depression during the COVID-19 pandemic. This effect of disease activity on anxiety and depression has been extensively described in IBD before this outbreak.[7,23] The existence of IBD activity in the context of a lockdown together with a blockade of the health system could be important in the development of symptoms of mental health conditions.[10,19] The effect of disease

Table 3 Univariate analysis of risk factors for the presence of significant symptoms of depression during and after lockdown.

	During				After			
	HADS depression >7 n (%)	OR	95% confidence interval	P	HADS depression >7 n (%)	OR	95% confidence interval	P
Sex								
Men	11 (13.9)	1			9 (11.4)	1		
Women	20 (30.3)	2.6	1.1–6.13	0.017	13 (19.7)	1.9	0.75–4.7	0.165
Age								
<40 years	10 (14.9)	1			8 (9)	1		
≥40 years	21 (26.9)	2.1	0.9–4.8	0.079	16 (20.5)	2.6	0.96–7.1	0.053
Disease type								
CD	19 (26.4)	1.8	0.81–4.1	0.144	15 (20.8)	2.4	0.9–6.5	0.059
UC	12 (16.4)	1			7 (9.6)	1		
BMI								
<30	25 (20)	1			19 (15.2)	1		
≥30	6 (30)	1.7	0.59–4.9	0.377	3 (15)	0.98	0.26–3.6	1
Current smoker								
Yes	4 (18.2)	0.79	0.24–2.5	0.786	1 (4.5)	0.23	0.02–1.8	0.189
No	27 (22)	1			21 (17.1)	1		
Regular alcohol use								
Yes	10 (25.6)	1.3	0.58–3.3	0.448	9 (23.1)	2.1	0.83–5.5	0.108
No	21 (19.8)	1			13 (12.3)	1		
Marital status								
Married/partner	20 (18.7)	1			18 (16.8)	1		
Divorced/single/widowed	11 (28.9)	1.7	0.75–4.1	0.185	4 (10.5)	0.58	0.18–1.8	0.353
Education								
Low level	24 (24.7)	1.9	0.76–4.8	0.160	18 (18.6)	2.5	0.79–7.8	0.106
High level	7 (14.6)	1			4 (8.3)	1		
Active employee								
Yes	8 (15.4)	0.55	0.22–1.3	0.188	7 (9.9)	0.43	0.16–1.1	0.081
No	23 (24.7)	1			15 (20.3)	1		
Comorbidity								
Yes	22 (31.9)	3.4	1.4–8.2	0.003	14 (20.3)	2.1	0.84–5.5	0.102
No	9 (11.8)	1			8 (10.5)	1		
Previous history of MAD								
Yes	8 (53.3)	5.3	1.7–16.1	0.004	7 (46.7)	6.7	2.1–21.1	0.002
No	23 (17.7)	1			15 (11.5)	1		
Active IBD								
Yes	14 (48.3)	5.4	2.2–13.2	<0.001	11 (61.1)	16.5	5.3–51.3	<0.001
No	17 (14.7)	1			11 (8.7)			
EIM								
Yes	6 (26.1)	1.3	0.48–3.8	0.582	5 (21.7)	1.7	0.56–5.2	0.348
No	25 (20.5)	1			17 (13.9)			
IBD-related surgical history								
Yes	3 (30)	1.6	0.39–6.7	0.446	3 (30)	2.6	0.62–11	0.178
No	28 (20.7)	1			19 (14.1)			
Use of mesalazine								
Yes	16 (18.6)	0.67	0.3–1.4	0.325	11 (12.8)	0.64	0.25–1.5	0.334
No	15 (25.4)	1			11 (18.6)	1		

Table 3 (*Continued*)

	During				After			
	HADS depression >7 *n* (%)	OR	95% confidence interval	*P*	HADS depression >7 *n* (%)	OR	95% confidence interval	*P*
Use of steroids								
Yes	2 (28.6)	1.5	0.27–8.1	0.642	7 (58.3)	11	3.1–39.1	<0.001
No	9 (21.0)	1			15 (11.3)	1		
Use of immunosuppressants								
Yes	9 (27.3)	1.5	0.62–3.7	0.347	5 (15.6)	1.04	0.35–3	1
No	22 (19.6)	1			17 (15)	1		
Use of biologics								
Yes	14 (31.8)	2.3	1.01–5.2	0.043	10 (21.7)	2	0.79–5	0.133
No	17 (16.8)	1			12 (12.1)	1		
Cohabitants during lockdown								
0–1	18 (32.7)	2.8	1.2–6.5	0.009	14 (25.5)	3.5	1.3–9	0.007
≥2	13 (14.4)	1			8 (8.9)			

CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; BMI, body mass index; MAD, mood and/or anxiety disorders; EIM, extra-intestinal manifestations.

Table 4 Risk factors independently associated with the presence of significant symptoms of anxiety and depression, during and after lockdown.

	Anxiety during lockdown			Anxiety after lockdown		
	Adjusted OR	95% confidence interval	*P*	Adjusted OR	95% confidence interval	*P*
Sex: female	2	1.2–5.4	0.012	2.5	1.01–6.3	0.047
Disease type: CD				3.3	1.3–8.5	0.010
Previous history of MAD				2.9	0.8–10.7	0.099
Active IBD	4.3	1.8–10.4	0.001	4.1	1.2–13.7	0.019
Cohabitants during lockdown, 0-1				1.9	0.79–4.7	0.148

	Depression during lockdown			Depression after lockdown		
	Adjusted OR	95% confidence interval	*P*	Adjusted OR	95% confidence interval	*P*
Sex: female	2	0.79–5.5	0.134			
Comorbidity	3.3	1.1–9.8	0.024			
Previous history of MAD	0.98	0.21–45	0.98	6.3	1.6–24.9	0.008
Active IBD	6	1.9–18.1	0.001	7.5	2.1–26.8	0.002
Use of steroids				6.4	1.4–29	0.015
Use of biologics	2.9	1.1–7.6	0.031			
Cohabitants during lockdown, 0-1	3.1	1.2–8.2	0.017	2.2	0.71–6.9	0.170

CD, Crohn's disease; UC, ulcerative colitis; IBD, inflammatory bowel disease; BMI, body mass index; MAD, mood and/or anxiety disorders; EIM, extra-intestinal manifestations.

activity persisted after lockdown, emphasizing an important role for this factor in the presence of mental health symptoms.

Factors independently associated with depression during lockdown were more variable and included comorbidity, use of biologics, and living alone or with only one person during lockdown. Patients may have not been able to gain proper care from the health system because of the lockdown or have had a lack of social support in this context. High-quality social connections with friends and family members are associated with a reduced likelihood of depression, and being under a stay-at-home order has been previously associated with greater health anxiety, financial worry, and loneliness.[22,24] However, after lockdown, factors associated with depression were those commonly found in IBD, such as disease activity or previous MAD, showing that the situation quickly resolved for many participants once lockdown ended.

A potential limitation of the study is that the assessment was made through phone interviews. This method of contact could have led participants to give answers that they thought might be socially desired rather than reflecting their true feelings, especially in the case of men, who often find it harder to express feelings they perceive as weakness.[25] However, disease activity using these phone questionnaires has been validated in the context of IBD.[26,27] Moreover, our sample is not fully representative of the whole population of patients with IBD because they all had a recent diagnosis and were closely followed up in specific IBD units. Strengths of our study are that it did not rely on a general online survey made available to the target population. Instead, each patient with a recent diagnosis was personally contacted, allowing us to avoid the selection bias of including only those who were motivated to respond.

In summary, our findings indicated that in an IBD population in highly stressful situations, such as an international public health emergency and lockdown, vulnerability to mental health conditions should be especially considered, particularly in women and in patients with active disease.

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Author contributions

Conception and design: LS, PB, CvH and MTRC Development of methodology: LS, PB, AG, JC, RL, MFG, MA,RJ, and MTRC. Acquisition of data: LS and PB Analysis and interpretation of data: LS, PZ, and CvH. Writing, review and/or revision of the manuscript: all authors. Study supervision: RJ and PZ.

Conflicts of interest

Laura Sempere declares that there is no conflict of interest.

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References

1. Ren X, Huang W, Pan H, Huang T, Wang X, Ma Y. Mental health during the Covid-19 outbreak in China: a meta-analysis. Psychiatr Q. 2020;91:1033–45, http://dx.doi.org/10.1007/s11126-020-09796-5.

2. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. Brain Behav Immun. 2020;89:531–42, http://dx.doi.org/10.1016/j.bbi.2020.05.048.

3. Gualano MR, Lo Moro G, Voglino G, Bert F, Siliquini R. Effects of COVID-19 lockdown on mental health and sleep disturbances in Italy. Int J Environ Res Public Health. 2020;17:1–13, http://dx.doi.org/10.3390/ijerph17134779.

4. Planchuelo-gómez Á, Odriozola-gonzález P, Jesús M, Luis-garcía De R. Longitudinal evaluation of the psychological impact of the COVID-19 crisis in Spain. J Affect Disord. 2020;277:842–9.

5. Qian M, Wu Q, Wu P, Hou Z, Liang Y, Cowling BJ, et al. Anxiety levels, precautionary behaviours and public perceptions during the early phase of the COVID-19 outbreak in China: a population-based cross-sectional survey. BMJ Open. 2020;10:1–10, http://dx.doi.org/10.1136/bmjopen-2020-040910.

6. Graff LA, Walker JR, Bernstein CN. Depression and anxiety in iflammatory bowel disease: a review of comorbidity and management. Inflamm Bowel Dis. 2009;15:1105–18, http://dx.doi.org/10.1002/ibd.20873.

7. Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients with Inflammatory Bowel Disease: a systematic review. J Psychosom Res. 2016;87:70–80, http://dx.doi.org/10.1016/j.jpsychores.2016.06.001.

8. Al Sulais E, Mosli M, Alameel T. The psychological impact of COVID-19 pandemic on physicians in Saudi Arabia: a cross-sectional study. Saudi J Gastroenterol. 2020;26:249–55, http://dx.doi.org/10.4103/sjg.SJG_174_20.

9. Trindade IA, Ferreira NB. COVID-19 pandemic's effects on disease and psychological outcomes of people with inflammatory bowel disease in Portugal: a preliminary research. Inflamm Bowel Dis. 2020, http://dx.doi.org/10.1093/ibd/izaa261.

10. Zingone F, Siniscalchi M, Savarino EV, Barberio B, Cingolani L, DÍncà R, et al. Perception of the COVID-19 pandemic among patients with inflammatory bowel disease in the time of telemedicine: cross-sectional questionnaire study. J Med Internet Res. 2020;22, http://dx.doi.org/10.2196/19574, e19574.p9.

11. Maaser C, Sturm A, Vavricka SR, Kucharzik T, Fiorino G, Annese V, et al. ECCO-ESGAR guideline for diagnostic assessment in IBD Part 1: initial diagnosis, monitoring of known IBD, detection of complications. J Crohn's Colitis. 2019;13:144–64, http://dx.doi.org/10.1093/ecco-jcc/jjy113.

12. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. Int J Environ Res Public Health. 2020;17, http://dx.doi.org/10.3390/ijerph17051729, 1729.p25.

13. Stern AF. The hospital anxiety and depression scale. Occup Med (Chic Ill). 2014;64:393–4, http://dx.doi.org/10.1093/occmed/kqu024.

14. Evertsz' FB, Hoeks CCMQ, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, et al. Development of the

patient harvey bradshaw index and a comparison with a clinician-based harvey bradshaw index assessment of Crohn's disease activity. J Clin Gastroenterol. 2013;47:850–6, http://dx.doi.org/10.1097/MCG.0b013e31828b2196.

15. Walmsley RS, Ayres RCS, Pounder RE, Allan RN. A simple clinical colitis activity index. Gut. 1998;43:29–32, http://dx.doi.org/10.1136/gut.43.1.29.

16. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, Brant SR, et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19SupplA, http://dx.doi.org/10.1155/2005/269076.

17. Harbord M, Annese V, Vavricka SR, Allez M, Barreiro-de Acosta M, Boberg KM, et al. The first european evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. J Crohn's Colitis. 2016;10:239–54, http://dx.doi.org/10.1093/ecco-jcc/jjv213.

18. Bernstein CN, Zhang L, Lix LM, Graff LA, Walker JR, Fisk JD, et al. The validity and reliability of screening measures for depression and anxiety disorders in inflammatory bowel disease. Inflamm Bowel Dis. 2018;24:1867–75, http://dx.doi.org/10.1093/ibd/izy068.

19. D'Amico F, Rahier J, Leone S, Peyrin-Biroulet L, Danese S. Views of patients with inflammatory bowel disease on the COVID-19 pandemic: a global survey. Lancet Gastroenterol Hepatol. 2020;5:631–2, http://dx.doi.org/10.1016/S2468-1253(20)30131-X.

20. Lu P, Li X, Lu L, Zhang Y. The psychological states of people after Wuhan eased the lockdown. PLOS ONE. 2020;15:1–12, http://dx.doi.org/10.1371/journal.pone.0241173.

21. Bigalke JA, Greenlund IM, Carter JR. Sex differences in self-report anxiety and sleep quality during COVID-19 stay-at-home orders. Biol Sex Differ. 2020;11:1–11, http://dx.doi.org/10.1186/s13293-020-00333-4.

22. Tull MT, Edmonds KA, Scamaldo KM, Richmond JR, Rose JP, Gratz KL. Psychological outcomes associated with stay-at-home orders and the perceived impact of COVID-19 on daily life. Psychiatry Res. 2020;289, http://dx.doi.org/10.1016/j.psychres.2020.113098, 113098.p6.

23. Nahon S, Lahmek P, Durance C, Olympie A, Lesgourgues B, Colombel JF, et al. Risk factors of anxiety and depression in inflammatory bowel disease. Inflamm Bowel Dis. 2012;18:2086–91, http://dx.doi.org/10.1002/ibd.22888.

24. Werner-Seidler A, Afzali MH, Chapman C, Sunderland M, Slade T. The relationship between social support networks and depression in the 2007 National Survey of Mental Health and Wellbeing. Soc Psychiatry Psychiatr Epidemiol. 2017;52:1463–73, http://dx.doi.org/10.1007/s00127-017-1440-7.

25. Deng Y, Chang L, Yang M, Huo M, Zhou R. Gender differences in emotional response: inconsistency between experience and expressivity. PLOS ONE. 2016;11:1–12, http://dx.doi.org/10.1371/journal.pone.0158666.

26. Echarri A, Vera I, Ollero V, Arajol C, Riestra S, Robledo P, et al. The Harvey-Bradshaw index adapted to a mobile application compared with in-clinic assessment: the MediCrohn study. Telemed e-Health. 2020;26:80–8, http://dx.doi.org/10.1089/tmj.2018.0264.

27. Higgins PDR, Schwartz M, Mapili J, Zimmermann EM. Is endoscopy necessary for the measurement of disease activity in ulcerative colitis? Am J Gastroenterol. 2005;100:355–61, http://dx.doi.org/10.1111/j.1572-0241.2005.40641.x.