


Factors Related To Anxiety And Depression In Patients With Inflammatory Bowel Disease: Influence Of Emotions On Intestinal Diseases

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1 INTRODUCTION

The two clinical forms of inflammatory bowel disease (IBD), Crohn's disease (CD) and ulcerative colitis (UC), are chronic intestinal disorders that are idiopathic in nature, unpredictable and incurable, and

ABSTRACT

Crohn's disease and ulcerative colitis are Inflammatory Bowel Diseases (IBD) characterized by periods of activity and remission, sometimes with major functional impairment, and thus may be associated with psychological symptoms and stigmatization of patients. The purpose of this study was to identify the main factors associated with anxiety and depression in patients with (IBD). The psychological aspect was analyzed using two globally validated questionnaires - the Patient Health Questionnaire (PHQ-9) and the General Anxiety Disorder questionnaire (GAD-7) - in addition to a sociodemographic questionnaire, which were applied to three groups, each composed by 100 individuals, the first for outpatients diagnosed with IBD, the second for outpatients without IBD diagnosis and the third for healthy individuals. IBD patients had a higher frequency of positive indicators for anxiety (55%) and depression (42%) compared to the other groups ($p < 0.05$), in addition, individuals in the IBD group also had more intense degrees of anxiety and depression than the other groups ($p < 0.05$). The main factors related to the higher prevalence of anxiety and depression were lower frequency of steady job, higher frequency of social class E, as well as having self-perception of unhealthy ($p < 0.05$). Those who were diagnosed with IBD with less than two years of symptoms had less depression and most who have anxiety and depression do not use anxiolytics and antidepressants.

Keywords: Crohn's disease, Ulcerative colitis, Depression, Anxiety, Prevalence.

require long-term treatment. Although there are clear differences between these diseases, there are common aspects, one of which is the high likelihood of compromising mental health, possibly due to the chronic and progressive nature, contributing negatively to quality of life (De Boer, et al., 2016).

The psychological aspects of IBD patients have been studied since the 1930s to the present day, making the relationship between bowel and psychological manifestations undeniable (Bonaz & Bernstein, 2013).

People with IBD live with unpleasant symptoms such as diarrhea, abdominal pain, possible complications such as stenosis and fistulas that may result in hospitalizations and surgical procedures. These symptoms, combined with the uncertainty of their course, foster exacerbated worries, so these fears can entail emotional compromise and culminate in the most common psychiatric disorders in IBD: anxiety and depression (Enns, et al., 2018).

The importance of these disorders is also described by epidemiology, which shows expressive numbers. The prevalence of depressive symptoms in IBD ranges from 9.3% to 68%, while in anxiety it ranges from 22.5% to 80% (Byrne, et al., 2017). Furthermore, compared to the general population, individuals with IBD are two to four times more likely to develop lifetime depressive disorders and three to five times more likely to develop anxiety disorders. As a result, combined with the lack of psychological therapy, there are organic changes in various physiological systems. Such changes are described by immunoneuroendocrinology (Bottaccioli, Bottaccioli & Minelli, 2019), which explains that emotions directly interfere with the endocrine, immune and nervous systems so that they interact bidirectionally with the enteric system, which consequently negatively affects the course of IBD by worsening symptoms.

As some examples, Mittermaier, et al. (2004) observed a higher number of seizures in depressed patients. Gradus, et al. (2010) reported in a study between 1981 and 2006 that there were a higher number of suicide cases in IBD patients than in the general population. Byrne, et al. (2017) stated that depressive and anxiety disorders are associated with higher morbidity and mortality in people with chronic medical conditions.

Thus, for a psychological intervention, a thorough study of these patients is necessary in order to obtain a diagnosis of such emotional disturbances. From this, it will be possible to establish effective therapeutic measures to avoid the mentioned complications. Furthermore, although there is a lot of research showing the relationship between IBD with anxiety and depression (Bonaz & Bernstein, 2013; Enns, et al., 2018; Byrne, et al. (2017); Bottaccioli, Bottaccioli & Minelli, 2019; Mittermaier, et al., 2004; Gradus, et al. 2010), there is a lack of information about which specific aspects of IBD are most associated with these disorders. This is essential to identify in practice which patients would be more prone to these disorders, which could facilitate their prevention and treatment. Thus, the aim of the present study was to identify the main factors associated with anxiety and depression in patients with IBD

2 METHOD

2.1 PARTICIPANTS

The research was a cross-sectional, descriptive study involving the application of questionnaires to three different groups. The first, called the IBD group, consisted of 100 adult patients seen at the coloproctology outpatient clinics of two tertiary referral IBD hospitals who were literate and over 18 years of age. The second group, called the outpatient control group, consisted of 100 patients followed up in the coloproctology outpatient clinics of the same hospitals, but for other diseases, without IBD, literate, and over 18 years of age. The third was a group of visitors to an urban park where outdoor activities are practiced, the Park-Control group, consisting of 100 adult patients who reported to be healthy, without IBD, literate, and over 18 years of age.

2.2 MATERIAL

The instruments for data collection were the General Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9), a sociodemographic questionnaire, and another questionnaire applied exclusively to the IBD group. Specifying them, the GAD-7 is an instrument for the assessment, diagnosis, and monitoring of generalized anxiety disorder (usually called just anxiety), composed of seven items, arranged on a four-point scale: 0 (none of that symptom once in a two-week period) and 3 (almost every day of that symptom in a two-week period); therefore, its score ranges from 0 to 21. A positive indicator is considered equal to or greater than 10. Thus, the lower the sum number (closer to 0), the lower the positive indicator for the disorder, and the closer to the maximum sum, the greater the intensity of the pathology. It was published by Spitzer, Kroenke, Williams & Lowe (2006) and validated by Kroenke, Spitzer, Williams, Monahan & Lowe (2007), according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders - DSM-IV. The literature already cited identified sensitivity of 89% and specificity of 82% (Bergerot, Mitchell, Ashing & Kim, 2017).

The PHQ-9 is used to assess, diagnose, and monitor the presence or absence of major depressive disorder (commonly referred to as depression) (Martin, Rief, Klaiberg & Braehler, 2006). The tool was developed according to DSM-IV criteria and allows for the diagnosis and tracking of depression levels. It is composed of nine items arranged on a scale identical to the GAD-7, with the same functioning as its sum and its score ranging from 0 to 27. The questionnaires that assess the presence of depression in patients with IBD have been validated by a specific study that demonstrated that The PHQ-9 has higher sensitivity (95%) when compared to other equally validated questionnaires (Starcevic & Portman, 2013).

These questionnaires were prepared according to the DSM-IV. Although there is an update of this manual, the DSM-V, there has been no significant change in the diagnostic criteria for anxiety and depression that would compromise their use (Starcevic & Portman, 2013; Bernstein, et al., 2018). Both the PHQ-9 and the GAD-7 are copyrighted questionnaires, owned by the company Pfizer. However, this company grants free permission to copy and reproduce them.

The sociodemographic questionnaire was prepared by the authors, addressing issues related to age, gender, marital status, education, housing situation, economic situation, smoking, having or not having health insurance, and concomitant diseases.

In the last questionnaire, exclusively for the IBD group, there were four questions related to the time of IBD diagnosis, IBD surgery and hospitalizations, and psychological care.

2.3 PROCEDURE

The approach to patients in the IBD group was performed after an educational lecture on "Quality of Life and IBD", previously planned by the authors, and questionnaires were administered in the coloproctology outpatient clinics. For the control group of outpatients, the approach was also carried out in coloproctology outpatient clinics while the patients were waiting for their appointments for diseases other than IBD. For the control-park group, the approach was performed on people who were within the aforementioned urban park.

For the three groups, the same procedures for data collection were performed: after reading and signing the Informed Consent Form (ICF), the participants received the GAD-7, PHQ-9, and the sociodemographic survey questionnaires. They were instructed about the purpose of the project and the operation of the self-administered questionnaires. The questionnaires were filled out individually, confidentially, without the need for identification, and placed in a frosted folder immediately after being returned to the researchers.

At the end, all research participants were instructed with information about places where psychological health services were provided and ways to obtain them through the public health system via an informational pamphlet.

2.4 DATA ANALYSIS

As for data treatment, the comparison between age and different groups was performed by the Analysis of Variance Test (ANOVA), followed by the post-test for comparison of means (Tukey). The evaluation of the association of categorical variables, both sociodemographic and IBD-related, with different groups of patients or with different diagnoses of IBD or with signs of anxiety and depression, was performed by the chi-square test, with Bonferroni correction when necessary. The other results of this study were presented as descriptive statistics or tables. The statistical analysis was performed in the statistical program SPSS, version 23.0, considering a significance level of 5%.

3 RESULTS

The sociodemographic characteristics of individuals in the three groups studied are shown in Table 1, and it can be seen that the groups are similar in terms of gender, ethnicity, and smoking distribution ($p>0.05$). There was lower mean age in the Control-park group ($p<0.001$), more divorced individuals in the DII group ($p=0.010$), more individuals with stable employment in the Control-park group ($p=0.014$), and individuals from lower social classes in the DII group ($p<0.001$).

TABLE 1. Sociodemographic characteristics of the studied individuals according to group.

Variables	Groups			p-value
	DII	Ambulatory control	Control-park	
Genre				
Female	54,0 (54)	51,0 (51)	40,0 (40)	0,114
Male	46,0 (46)	49,0 (49)	60,0 (60)	
Average age				
	44,77±16,82a	49,49±14,38a	36,69±13,93b	<0,001
Age group (years)				
18-25	14,0 (14)ab	7,0 (07)b	23,0 (23)a	<0,001
26-36	26,0 (26)a	12,0 (12)b	35,0 (35)a	
37-59	37,0 (37)ab	53,0 (53)a	34,0 (34)b	
≥60	23,0 (23)a	28,0 (28)a	8,0 (08)b	
Ethnicity				
Whites	44,0 (44)	44,0 (44)	28,0 (28)	0,054
Grizzlies	44,0 (44)	49,0 (49)	53,0 (53)	
Blacks	11,0 (11)	6,0 (06)	16,0 (16)	
Yellow	0,0 (00)	1,0 (01)	3,0 (03)	
Indians	1,0 (01)	0,0 (00)	0,0 (00)	
Marital status				
Single	37,0 (37)a	22,0 (22)a	36,0 (36)a	0,010
Married	54,0 (54)a	58,0 (58)a	51,0 (51)a	
Divorced	3,0 (03)b	16,0 (16)a	12,0 (12)a	
Widower	6,0 (06)a	4,0 (04)a	1,0 (01)a	

Smoking				
Yes	12,0 (12)	13,0 (13)	11,0 (11)	0,910
No	88,0 (88)	87,0 (87)	89,0 (89)	
Job/occupation				
Employee	53,0 (53)b	62,0 (62)ab	76,0 (76)a	0,014
Unemployed	29,0 (29)a	22,0 (22)a	17,0 (17)a	
Retired	18,0 (18)a	16,0 (16)a	7,0 (07)a	
Social Class				
A	3,0 (03)a	1,0 (01)a	0,0 (00)a	<0,001
B	4,0 (04)a	5,0 (05)a	5,0 (05)a	
C	21,0 (21)b	23,0 (23)b	44,0 (44)a	
D	26,0 (26)b	44,0 (44)a	41,0 (41)ab	
E	46,0 (46)a	27,0 (27)b	10,0 (10)c	

Results are presented as mean \pm standard deviation of the mean (age) or relative frequency (absolute frequency). P value in one-way ANOVA test or chi-square test. Different letters in the row indicate significant difference between groups (Tukey's post-test or chi-square test as Bonferroni correction, $p < 0.05$).

Regarding the results of the PHQ-9 questionnaire, the IBD group obtained 42.0% of positive indicators for depression, significantly higher than the control-park group (13.0%) ($p=0.001$), but with no statistically significant difference when compared to the control-ambulatory group (31.0%). Thus, it is possible to observe that individuals with IBD had a higher prevalence of depression. In addition, when evaluating stratified by severity, it seems that there were no patients with severe form of depression in the control-ambulatory group, unlike the other groups ($p=0.001$) (Table 2).

TABLE 2. Prevalence of depression among the groups studied according to the PHQ-9 questionnaire.

Depression	Group			p-value
	DII	Ambulatory control	Control-park	
Negative (≤ 10)	58,0 (58)b	69,0 (69)b	87,0 (87)a	0,001
Positive (> 10)	42,0 (42)a	31,0 (31)a	13,0 (13)b	
Moderate (10-14)	19,0 (19)a	14,0 (14)a	8,0 (08)a	
Moderately severe (15-19)	9,0 (09)a	7,0 (07)a	4,0 (04)a	
Severe (≥ 20)	14,0 (14)a	10,0 (10)a	1,0 (01)b	

Results are presented as mean \pm standard deviation of the mean (age) or relative frequency (absolute frequency). P value in one-way ANOVA test or chi-square test. Different letters in the row indicate significant difference between groups (Tukey's post-test or chi-square test as Bonferroni correction, $p < 0.05$).

Similar values were also found for anxiety, with a prevalence of 55.0% when compared to the control-ambulatory group (38.0%) ($p < 0.05$) and control-park group (20.0%) ($p < 0.001$). In addition, there were also fewer individuals with severe anxiety in the control-park group compared to the other groups ($p < 0.001$) (Table 3).

TABLE 3. Prevalence of anxiety among the groups studied according to the GAD-7 questionnaire.

Anxiety	Group			p-value
	DII	Ambulatory control	Control-park	
Negative (≤ 10)	45,0 (45)b	62,0 (62)b	80,0 (80)a	$< 0,001$
Positive (> 10)	55,0 (55)a	38,0 (38)a	20,0 (20)b	
Moderate (10-14)	19,0 (19)a	17,0 (17)a	12,0 (12)a	
Severe (≥ 15)	36,0 (36)a	21,0 (21)a	8,0 (08)b	

Results are presented as mean \pm standard deviation of the mean (age) or relative frequency (absolute frequency). P value in one-way ANOVA test or chi-square test. Different letters in the row indicate significant difference between groups (Tukey's post-test or chi-square test as Bonferroni correction, $p < 0.05$).

To identify possible factors that could directly influence the emergence of anxiety or depression, the information collected was crossed with groups of individuals. Regarding age, there was no general difference between the groups, and the only significant observation was in the analysis of anxiety in the control-ambulatory group, in which 85.7% of the elderly were negative and 14.3% positive ($p = 0.005$).

Comparing only individuals with positive criteria for depression (PHQ-9 \geq 10) and occupation/employment, it was observed that the IBD group had a smaller number of people with stable employment (4.8%) than the other groups (19.4% for the control-ambulatory group and 46.2% for the control-park group) (p<0.001) (table 4).

TABLE 4. Frequency of individuals with PHQ-9 \geq 10 in relation to occupation.

Occupation	Group			p-value
	DII	Ambulatory control		
Internship	0,0 (00)a	0,0 (00)a	15,4 (02)a	<0,001
Stable Employment	4,8 (02)b	19,4 (06)ab	46,2 (06)a	
Autonomous	40,5 (17)a	32,3 (10)a	23,1 (03)a	
Retired	16,7 (07)a	12,9 (04)a	0,0 (00)a	
Unemployed	38,1 (16)a	35,5 (11)a	15,4 (02)a	

Data are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test, with Bonferroni correction, p <0.05).

In the population with positivity for anxiety, seen in Table 5, the same occurred in the comparison with occupation, where the IBD group had 10.9% of people with stable employment, the control-ambulatory group 26.3%, and the control-park group 45% (p = 0.005).

TABLE 5. Frequency of individuals with GAD-7 \geq 10 in relation to occupation.

Occupation	Group			p-value
	DII	Ambulatory control		
Internship	0,0 (00)a	0,0 (00)a	10,0 (02)a	0,005
Stable Employment	10,9 (06)b	26,3 (10)ab	45,0 (09)a	
Autonomous	38,2 (21)a	34,2 (13)a	15,0 (03)a	
Retired	16,4 (09)a	10,5 (04)a	5,0 (01)a	
Unemployed	34,5 (19)a	28,9 (11)a	25,0 (05)a	

Data are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test, with Bonferroni correction, p <0.05).

The influence of social class on the presence or absence of anxiety and depression among the groups was also analyzed. In the comparison of each class (A to E) between the groups, there was no difference regarding anxiety ($p = 0.293$) and depression ($p = 0.644$). It was also assessed in a grouped manner, i.e., classes A + B versus classes C + D + E, resulting in no difference for anxiety ($p = 0.493$) or depression ($p = 0.342$). Most individuals were from lower social classes. Regarding anxiety, when comparing A + B versus C + D + E classes, 5.5% x 94.5% were obtained in the group with IBD, 2.6% x 97.4% in the control-ambulatory group, and 0% x 100% in the control-park group. Regarding depression, 4.8% x 95.2% in the IBD group, 0% x 100% in the walker-control group and the control-park group.

Another analysis performed refers to the questioning about the self-perception of being healthy or not. When doing a simple analysis of the answers according to the groups, naturally those in the control-park group had a higher rate (93%) of "yes" answers, compared to 62% in the IBD group and 72% in the control-ambulatory group ($p < 0.001$) (Table 6).

TABLE 6: Comparison between the groups regarding the self-report of being healthy or not.

Self-reported healthy	Group			p-value
	DII	Ambulatory control	Control-park	
No	38,0 (38)a	22,0 (22)b	7,0 (07)c	<0,001
Yes	62,0 (62)c	78,0 (78)b	93,0 (93)a	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

However, the most important analysis was the one in which only the responses of the IBD group were compared with depression and anxiety. As for anxiety, of those who declared themselves healthy, 56.5% were negative for anxiety versus 24.2% with severe anxiety ($p = 0.004$). In the group that declared themselves unhealthy the opposite occurred, 55.3% had severe anxiety and only 26.3% negative for anxiety ($p = 0.004$) (Table 7).

TABLE 7. Frequency of self-reported healthy persons belonging to the IBD group in relation to the severity grade of GAD-7.

Self-reported healthy	GAD-7 Severity Grade			p-value
	Negative (<10)	Moderate (10-14)	Severe (≥15)	
Yes	56,5 (35)a	19,4 (12)b	24,2 (15)b	0,004
No	26,3 (10)b	18,4 (07)a	55,3 (21)a	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

Analogous percentages were found for the indicator of positive depression, as shown in Table 8. It is observed that of the self-reported healthy individuals in the IBD group, 75.8% were negative for depression, while 1.6% had severe depression ($p < 0.001$). In those declared unhealthy, only 28.9% were negative for depression, while 34.2% had severe depression ($p < 0.001$) (Table 8).

TABLE 8. Frequency of self-reported healthy persons belonging to the IBD group in relation to the degree of severity of the PHQ-9.

Self-reported healthy	PHQ-9 degree of severity				p-value
	Negative (<10)	Moderate (10-14)	Moderately severe (15-19)	Severe (≥20)	
Yes	75,8 (47)a	14,5 (09)a	8,1 (05)a	1,6 (01)b	<0,001
No	28,9 (11)b	26,3 (10)a	10,5 (04)a	34,2 (13)a	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

When asked about the presence or absence of comorbidities, 9% of the IBD group answered "yes", 19% of the control-ambulatory group and 6% of the control-park group ($p = 0.010$) (Table 9).

TABLE 9: Presence of comorbidities in the studied individuals according to the group.

Comorbidities	DII	Ambulatory control	Control-park	p-value
No	91.0 (91)ab	81,0 (81)b	94,0 (94)a	0,010
Yes	9.0 (9)ab	19,0 (19)a	6,0 (6)b	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

When analyzing the specific questionnaire for the IBD group, where information related to the disease and possible correlation with the presence of anxiety and depression were investigated, there was

no difference initially between CD and UC in terms of anxiety and depression. In the assessment of anxiety, comparing CD x UC, 46.6% x 40.7% were negative, had moderate anxiety 17.8% x 22.2% and severe anxiety 35.6% x 37% ($p = 0.834$). In assessing depression, 57.5% x 59.3% were negative and 42.5% x 40.7% were positive ($p = 0.942$). When stratifying the degree of severity of depression, there was no difference ($p = 0.124$).

It was observed that there was a difference only regarding the need for surgery, where the patients with CD were more operated on than the patients with UC ($p = 0.019$). The other aspects: time of diagnosis, need for hospitalization due to illness, psychological care or not, and use of anxiolytic/ antidepressant drugs showed no significant difference ($p > 0.05$) (Table 10). When these same factors were compared with the presence or absence of anxiety and depression, it was observed that there was less depression in those with less than two years of diagnosis ($p = 0.036$), most of the anxious did not use anxiolytics ($p = 0.022$), most of the depressed did not use antidepressants ($p = 0.010$), and there were no significant differences regarding hospitalization for the disease ($p = 0.942$), previous surgeries because of the disease ($p = 0.932$), and whether or not they received psychological care ($p = 0.463$) (Table 11).

TABLE 10. Association between complications and disease progression according to disease type in subjects in the IBD group.

Variable	Crohn's Disease	Ulcerative colitis	p-value
Time to diagnosis			
< 2 years	12,3 (09)	11,1 (03)	0,872
2-5 years	34,2 (25)	29,6 (08)	
> 5 years	53,4 (39)	59,3 (16)	
Have you been hospitalized for IBD?			
Yes	74,0 (54)	70,4 (19)	0,915
No	26,0 (19)	29,6 (08)	
Previous surgery due to IBD?			
Yes	42,5 (31)a	14,8 (04)b	0,019
No	57,5 (42)b	85,2 (23)a	
Do you receive/receive psychological assistance?			
Yes	13,7 (10)	25,9 (07)	0,252
No	86,3 (63)	74,1 (20)	
Do you use anxiolytic/antidepressant?			
Yes	28,8 (21)	25,9 (07)	0,976
No	71,2 (52)	74,1 (20)	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

TABLE 11. Association between complications and disease progression and presence or absence of anxiety/depression in patients in the IBD group.

Variable	Anxiety		p-value	Depression		p-value
	Positive	Negative		Positive	Negative	
Time to diagnosis						
< 2 years	9,1 (05)	15,6 (07)	0,433	2,4 (01)a	19,0 (11)b	0,036
2-5 years	23,6 (13)	28,9 (13)		26,2 (11)a	25,9 (15)a	
> 5 years	67,3 (37)	55,6 (25)		71,4 (30)a	55,2 (32)a	
Have you been hospitalized due to IBD?						
Yes	76,4 (42)	68,9 (31)	0,541	73,8 (31)	72,4 (42)	0,942
No	23,6 (13)	31,1 (14)		26,2 (11)	27,6 (16)	
Previous surgery due to IBD?						
Yes	38,2 (21)	31,1 (14)	0,598	35,7 (15)	34,5 (20)	0,932

No	61,8 (34)	68,9 (31)		64,3 (27)	65,5 (38)	
Do you receive/receive psychological assistance?						
Yes	20,0 (11)	13,3 (06)	0,538	21,4 (09)	13,8 (08)	0,463
No	80,0 (44)	86,7 (39)		78,6 (33)	86,2 (50)	
Do you use anxiolytic/antidepressant?						
Yes	38,2 (21)a	15,6 (07)b	0,022	42,9 (18)a	17,2 (10)b	0,010
No	61,8 (34)b	84,4 (38)a		57,1 (24)b	82,8 (48)a	

Results are presented as relative frequency (absolute frequency). P value in chi-square test. Different letters in the row indicate significant difference between the groups (chi-square test as Bonferroni correction, $p < 0.05$).

4 DISCUSSION

The starting point for the analysis of possible factors related to the higher prevalence of anxiety and depression in people with IBD than in the general population was the realization that this disproportion actually exists. As can be seen from the results, the individuals in the IBD group actually had more anxiety and depression than those in the control-ambulatory group, supposedly healthy people. Although the control-ambulatory group showed similar results from the GAD-7 and PHQ-9 questionnaires as the IBD group, demonstrating that IBD may not be the underlying cause of such disorders, it may actually be the simple presence of a chronic illness, which is a topic for further analysis that goes beyond the main purpose of this research. The fact is that the results presented here are in agreement with the literature in that there are more individuals with anxiety and depression with IBD than healthy people. A similar pattern has been found in the literature in showing that 9.3% to 68% of IBD patients have depressive disorders, while the world population average is 11.1% (Byrne, et al., 2017; Roberts, et al., 2018; Yongwen, et al., 2018); Addolorato, Capristo, Stefanini & Gasbarrini, 1997). This directly proportional relationship between IBD and psychiatric disorders occurs for two main reasons: the symptomatological nature of the disease, causing psychosocial distress, and intrinsic and bidirectional communication between the brain and the gut (Bonaz & Bernstein, 2013; Martin-Subero, Anderson, Kanchanatawan, Berk & Maes, 2016).

It is also observed that IBD predisposes and aggravates psychiatric disorders, especially mood and anxiety disorders, which also influence the course of the disease so as to aggravate it, generating a vicious cycle (Byrne, et al., 2017; Kiebles, Doerfler, & Keefer, 2010; Arantes et al., 2017). Several publications have also shown that anxiety and depression can be associated with chronic diseases other than just IBD, such as asthma, diabetes, and arthritis, perhaps because they also cause some degree of stress and discomfort in the long term (Lewis, et al., 2019; Nakagawa, et al., 2017). So much so that in the present research, in addition to the control-park group showing lower prevalence of anxiety and depression, when the data were stratified, it was observed that this group also showed a lower proportion of severe forms of the diseases. The group of people who make up the control-park group is characterized by performing some physical

activity, even if light and sporadic, which can be an effective means in the prevention and treatment of anxiety and depression disorders (Rebar, et al., 2015).

There was great homogeneity between the groups, which makes the following analysis of factors that may be related to anxiety and depression more adequate. In the control-park group, there were younger individuals and a greater number of singles, but this was expected because they were frequenters of an outdoor park. There was also a larger contingent of employees in this group, probably due to their age. These small differences between the groups, which in our view do not hinder the analysis, have also been noted in other publications that have compared healthy people and people with IBD (Kochar, et al., 2018; Rubin, et al., 2017).

Among those with positive criteria for anxiety, the DII group had fewer individuals with stable employment (10.9%) compared to the control-park group (45.0%). A large difference was also observed in terms of depression, where only 4.8% of patients in the DII group had stable employment compared to 46.2% in the control-park group. It is worth questioning whether the presence of anxiety and/or depression may be a cause or consequence of the lower employability in the DII group. Enns, et al. (2018) demonstrated that anxiety and depression impact work functionality and absenteeism, which may contribute to individuals having fewer permanent jobs. De Boer, et al. (2016) also reported in a study dedicated exclusively to assessing the difficulties presented by IBD patients in performing their work activities due to the effects of the disease, proving that, similar to the situation observed here, a large number of individuals with IBD did not have stable work, depended on receiving a pension, these individuals had great difficulty maintaining employment, resulting in low quality of life.

It is possible that the issue of employment is directly related to social class, since in the DII group 46% of the individuals belonged to social class E, against 27% in the control-ambulatory group and only 10% in the control-park group. However, when social classes were crossed with positivity for anxiety and depression, there was no statistical significance for this factor, showing that being employed, that is, having an occupation that gives more meaning to life, allows the individual to feel useful, which may mean more than just getting paid. Several authors have shown high rates of occupational and financial instability in patients with IBD, which may be related to the functional impairment generated by both the disease and the associated psychiatric disorders (Kim, et al., 2013; Williams, Budavari, Olden & Jones, 2005); Kessler, Ormel, Demler & Stang, 2003).

From an emotional point of view, self-perception of being healthy may have a much more positive effect on quality of life than information about disease activity scores. If an individual has criteria for moderately active IBD but is perceived to be healthy, this may in theory favor his quality of life, whereas another who has disease in remission but recognizes himself as a sick person may have a worse quality of life (Naftali, et al., 2019). Diener, Lucas & Scollon (2006) state that happiness is recognized from the overlap of positive experiences over negative ones, and considered as the main component of a healthy life. Therefore, the IBD patient who has more negative experiences than the population without the pathology

has a lower self-perception of being healthy, as was found in the present study, where both anxiety and depression were observed. It was found that patients in the IBD group had less self-perception of being healthy than individuals in the control-park group. It should be noted, however, that this factor is little researched, and it would be important to develop more research looking into emotional factors and how individuals' thoughts may influence psychiatric conditions specifically in IBD.

There was no statistically significant difference between the IBD and control group regarding the presence of comorbidities, however, an important fact to be highlighted is that there were more comorbidities in the control group, which may justify why this group has anxiety and depression at the same levels as patients with IBD, i.e., the fact of having a chronic disease would affect the emotional state, regardless of being IBD or not. This is an aspect little researched in the literature, as already pointed out, since much of the research compares people with IBD and healthy individuals, and in our opinion there should be further research on the subject.

When higher levels of anxiety and depression are observed in individuals with IBD, it is natural that numerous questions arise, such as whether or not there is a difference between CD and UC, if any specific aspect of IBD directly influences the emotional part, such as surgeries and hospitalizations. Thus, it was initially investigated whether there was a difference between the two forms of IBD, but this was not found to be the case, nor was there a difference in the severity of the disorders. Although many may be under the impression that UC is a more benign disease than CD, evidence shows that this is not always true, and UC can progress quite seriously and compromise patients' quality of life (Souza & Fiocchi, 2016). Thus, both would have a similar possibility of affecting patients emotionally and, therefore, would have similar prevalence of anxiety and depression, as already demonstrated by other authors (Arantes, et al., 2017; Lewis, et al., 2019; Kochar, et al., 2018). In the present study, patients with CD and UC were fairly homogeneous in terms of time from symptom onset to diagnosis, need for hospitalization for the disease, receiving or not receiving psychological care, and taking anxiolytic/ antidepressant medications, differing only in terms of having undergone surgery as a result of IBD, where there was a higher number in those with CD. The literature confirms that CD does indeed progress more toward surgical treatment over the years than UC, so that these data are in agreement with other studies (Frolkiset al., 2013; Bemelman & S-ECCO collaborators, 2018).

Lower prevalence of depression was observed among individuals with IBD diagnosed with less than two years of symptoms, which can be justified by the fact that they were probably treated in a timely manner, because when performed within the so-called "window of opportunity" there is a higher chance that the treatment will promote sustained remission (Berg, Colombel & Ungaro, 2019) and consequently provide a better quality of life. Thus, it was indeed expected that this result would be obtained, however, the same was not the case with regard to anxiety. It was also verified that most of those who presented positive scores for anxiety and depression did not use medication for these disorders, which can be explained by the difficulty of access to professionals who could indicate this treatment, since all patients

were from the public health system and, as already presented, belonging mainly to the lower social class. Naturally, in case of anxiety and / or depression and impossibility of treatment, the tendency is that such disorders remain active, as in fact it was found. Having had surgery or hospitalization as a result of the disease, receiving or not receiving specialized care did not influence the results.

Thus, it can be seen in the present research that people with IBD have a higher prevalence of anxiety and depression than healthy individuals, but no difference when compared to those with other chronic diseases. The main factors identified as causing or related to the emergence of such psychiatric disorders were the self-perception of being unhealthy and the lower rate of stable employment. Individuals with IBD diagnosed less than two years after symptom onset had less depression than those who took longer to be diagnosed, and finally, the majority of those with anxiety or depression do not use medications for these disorders. Although the data survey was conducted in two different hospitals and a park, all were from the same city, which can be characterized as a single study center, this being the main weakness of the research. One can also add the fact that inflammatory disease activity was not verified in the IBD group, in order to better characterize the influence of active disease on the prevalence of anxiety and depression, but neither was the activity of comorbidities verified in the control-ambulatory group. The justification for the fact that this evaluation was not carried out is to give more veracity to the information that was collected by means of a questionnaire, in order to provide the individuals with a greater degree of confidence regarding confidentiality so that they could adequately answer the intimate questions. The results found here are not a final point on the subject, but an addition of information regarding the importance of valuing the emotional aspects of patients with IBD, acting in the prevention, diagnosis, and adequate treatment.

REFERENCES

- De Boer, A. G., Evertsz, F. B., Stokkers, P. C., Bockting, C. L., Sanderman, R., Hommes, D. W., ..., Frings-Dresen, M. H. W. (2016). Employment status, difficulties at work and quality of life in inflammatory bowel disease patients. *Eur J Gastroenterol Hepatol*, 28, 1130–1136. doi: 10.1097/MEG.0000000000000685
- Bonaz, B. L. & Bernstein, C. N. (2013). Brain-gut interactions in inflammatory bowel disease. *Gastroenterology*, 144, 36-49. doi: 10.1053/j.gastro.2012.10.003
- Enns, M. W., Bernstein, C. N., Kroeker, K., Graff, L., Walker, J. R., Lix, L. M., ..., Marrie, R. A. (2018). The association of fatigue, pain, depression and anxiety with work and activity impairment in immune mediated inflammatory diseases. *PLoS one*, 13, e0198975. doi: 10.1371/journal.pone.0198975
- Byrne, G., Rosenfeld, G., Leung, Y., Qian, H., Raudzus, J., Nunez, C., & Bressler, B. (2017). Prevalence of anxiety and depression in patients with inflammatory bowel disease. *Can J Gastroenterol Hepatol*, 2017:6496727. doi: 10.1155/2017/6496727
- Bottaccioli, A. G., Bottaccioli, F., & Minelli, A. (2019). Stress and the psyche–brain–immune network in psychiatric diseases based on psychoneuroendocrineimmunology: a concise review. *Ann N Y Acad Sci*, 1437, 31-42. doi: 10.1111/nyas.13728
- Mittermaier, C., DeJaco, C., Waldhoer, T., Oefflerbauer-Ernst, A., Miehsler, W., Beier, M., ..., Moser, G. (2004). Impact of depressive mood on relapse in patients with inflammatory bowel disease: a prospective 18-month follow-up study. *Psychosom Med*, 66, 79–84. doi: 10.1097/01.psy.0000106907.24881.f2
- Gradus, J. L., Qin, P., Lincoln, A.K., Miller, M., Lawler, E., Sørensen, H. T., & Lash, T. T. (2010). Inflammatory bowel disease and completed suicide in Danish adults. *Inflamm Bowel Dis*, 16, 2158-2161. doi: 10.1002/ibd.21298
- Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Lowe, B. (2006). A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Arch Intern Med*, 166, 1092–1097. doi: 10.1001/archinte.166.10.1092
- Kroenke, K., Spitzer, R. L., Williams, J. B. W., Monahan, P. O., & Lowe, B. (2007). Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*, 146, 317-325. doi: 10.7326/0003-4819-146-5-200703060-00004
- Bergerot, C. D., Mitchell, H. R., Ashing, K. T., & Kim, Y. (2017). A prospective study of changes in anxiety, depression, and problems in living during chemotherapy treatments: effects of age and gender. *Support Care Cancer*, 25, 1897-1904. doi: 10.1007/s00520-017-3596-9
- Martin, A., Rief, W., Klaiberg, A., & Braehler, E. (2006). Validity of the brief patient health questionnaire mood scale (PHQ-9) in the general population. *Gen Hosp Psychiatry*, 28, 71-77. doi: 10.1016/j.genhosppsych.2005.07.003
- Starcevic, V., & Portman, M. E. (2013). The status quo as a good outcome: how the DSM-5 diagnostic criteria for generalized anxiety disorder remained unchanged from the DSM-IV criteria. *Aust N Z J Psychiatry*, 47, 995-997. doi: 10.1177/0004867413503719
- Bernstein, C. N., Zhang, L., Lix, L. M., Graff, L. A., Walker, J. R., Fisk, J. D., ..., Marrie, R. A. (2018). The Validity and Reliability of Screening Measures for Depression and Anxiety Disorders in Inflammatory Bowel Disease. *Inflamm Bowel Dis*, 24,1867-1875. doi: 10.1093/ibd/izy068

Roberts, T., Esponda, G. M., Krupchanka, D., Shidhaye, R., Patel, V., Rathod, S. (2018). Factors Associated With Health Service Utilisation for Common Mental Disorders: A Systematic Review. *BMC Psychiatry*, 18, 262. doi: 10.1186/s12888-018-1837-1

Yongwen, J., Chauhan, U., Armstrong, D., Marshall, J., Tse, F., Moayyedi, P., ..., Halder, S. (2018). A Comparison of the Prevalence of Anxiety and Depression Between Uncomplicated and Complex IBD Patient Groups. *Gastroenterol Nurse*, 41, 427-435. doi: 10.1097/SGA.0000000000000338

Addolorato, G., Capristo, E., Stefanini, G. F., & Gasbarrini, G. (1997). Inflammatory Bowel Disease: A Study of the Association Between Anxiety and Depression, Physical Morbidity, and Nutritional Status. *Scand J Gastroenterol Nurs*, 32, 1013-1021. doi: 10.3109/00365529709011218

Martin-Subero, M., Anderson, G., Kanchanatawan, B., Berk, M., & Maes, M. (2016). Comorbidity Between Depression and Inflammatory Bowel Disease Explained by Immune-Inflammatory, Oxidative, and Nitrosative Stress; Tryptophan Catabolite; And Gut-Brain Pathways. *NS Spectr*, 21, 184-98. doi: 10.1017/S1092852915000449

Kiebles, J. L., Doerfler, B., & Keefer, L. (2010). Preliminary Evidence Supporting a Framework of Psychological Adjustment to Inflammatory Bowel Disease. *Inflamm Bowel Dis*, 16, 1685-95. doi: 10.1002/ibd.21215

Arantes, J. A. V., Santos, C. H. M., Delfino, B. M., Silva, B. A., Souza, R. M. M., Souza, T. M. M., ..., Cruz, S. B. G. (2017). Epidemiological profile and clinical characteristics of patients with intestinal inflammatory disease. *J Coloproctol*, 37, 273-278. doi: 10.1016/j.jcol.2017.06.004

Lewis, K., Marrie, R. A., Bernstein, C. N., Graff, L. A., Patten, S. B., Sareen, J., ..., Bolton, J. M. (2019). The Prevalence and Risk Factors of Undiagnosed Depression and Anxiety Disorders Among Patients With Inflammatory Bowel Disease. *Inflamm Bowel Dis*, 25, 1674-1680. doi: 10.1093/ibd/izz045

Nakagawa, R., Yamaguchi, S., Kimura, S., Sadamasu, A., Yamamoto, Y., Sato, Y., ..., Ohtori, S. (2017). Association of Anxiety and Depression With Pain and Quality of Life in Patients With Chronic Foot and Ankle Diseases. *Foot Ankle Int*, 38, 1192-1198. doi: 10.1177/1071100717723133

Rebar, A. L., Stanton, R., Geard, D., Short, C., Duncan, M. J., & Vandelanotte, C. (2015). A Meta-Meta-Analysis of the Effect of Physical Activity on Depression and Anxiety in Non-Clinical Adult Populations. *Health Psychol Rev*, 9, 366-378. doi: 10.1080/17437199.2015.1022901

Kochar, B., Barnes, E. L., Long, M. D., Cushing, K. C., Galanko, J., Martin, C. F., ..., Sandler, R. S. (2018). Depression Is Associated With More Aggressive Inflammatory Bowel Disease. *Am J Gastroenterol*, 113, 80-85. doi: 10.1038/ajg.2017.423

Rubin, D. T., Feld, L. D., Goepfing, S. R., Margolese, J., Rosh, J., Rubin, M., ..., Wingate, L. (2017). The Crohn's and Colitis Foundation of America Survey of Inflammatory Bowel Disease Patient Health Care Access. *Inflamm Bowel Dis*, 23, 224-232. doi: 10.1097/MIB.0000000000000994

Kim, E. S., Cho, K. B., Park, K. S., Jang, B. I., Kim, K. O., Jeon, S. W., ..., Yang, C. H. (2013). Predictive Factors of Impaired Quality of Life in Korean Patients With Inactive Inflammatory Bowel Disease: Association With Functional Gastrointestinal Disorders and Mood Disorders. *J Clin Gastroenterol*, 47, e38-e44. doi: 10.1097/MCG.0b013e318266fff5

Williams, M., Budavari, A., Olden, K. W., & Jones, M. P. (2005). Psychosocial Assessment of Functional Gastrointestinal Disorders in Clinical Practice. *J Clin Gastroenterol*, 39, 847-857. doi: 10.1097/01.mcg.0000180637.82011.bb

Kessler, R. C., Ormel, J., Demler, O., & Stang, P. E. (2003). Comorbid Mental Disorders Account for the Role Impairment of Commonly Occurring Chronic Physical Disorders: Results From the National Comorbidity Survey. *J Occup Environ Med*, 45, 1257-1266. doi: 10.1097/01.jom.0000100000.70011.bb

Naftali, T., Eindor-Abarbanel, A., Ruhimovich, N., Shitrit, A. B. G., Sklerovsky-Benjaminov, F., Laish, I., ..., Broide, E. (2019). Sense of Coherence in People With and Without Inflammatory Bowel Diseases - Is There a Difference?. *J Gastrointestin Liver Dis*, 28, 29-32. doi: 10.15403/jgld.2014.1121.281.coh

Diener, E., Lucas, R. E., & Scollon, C. E. (2006). Beyond the Hedonic Treadmill: Revising the Adaptation Theory of Well-Being. *Am Psychol*, 61, 305-314. doi: 10.1037/0003-066X.61.4.305

Souza, H. S. P., & Fiocchi, C. (2016). Immunopathogenesis of IBD: Current State of the Art. *Nat Rev Gastroenterol Hepatol*, 13, 13-27. doi: 10.1038/nrgastro.2015.186

Frolkis, A. D., Dykeman, J., Negrón, M. E., Debruyn, J., Jette, N., Fiest, K. M., ..., Kaplan, G. G. (2013). Risk of Surgery for Inflammatory Bowel Diseases Has Decreased Over Time: A Systematic Review and Meta-Analysis of Population-Based Studies. *Gastroenterology*, 145, 996-1006. doi: 10.1053/j.gastro.2013.07.041

Bemelman, W. A., & S-ECCO collaborators. (2018). Evolving Role of IBD Surgery. *J Crohn's Colitis*, 12, 1005–1007. doi: 10.1093/ecco-jcc/jjy056

Berg, D. R., Colombel, J. F., & Ungaro, R. (2019). The Role of Early Biologic Therapy in Inflammatory Bowel Disease. *Inflamm Bowel Dis*, 25, 1896-1905. doi: 10.1093/ibd/izz059