

# Symptoms of anxiety and depression, and quality of life of patients with Crohn's disease

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**ABSTRACT – Background** – Crohn's disease is an idiopathic chronic inflammatory disease. It is classified as an inflammatory bowel disease. Crohn's disease can change patient quality of life, especially during flares. Crohn's disease has been associated with symptoms of anxiety and depression, because the clinical symptoms have a high impact on quality of life. **Objective** – To investigate the prevalence of symptoms of anxiety and depression in Brazilian patients diagnosed with Crohn's disease, as well as their quality of life. **Methods** – A total of 110 Brazilian patients aged 21-59 years, both genders, with Crohn's disease were included. The data were collected through questionnaires. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression symptoms. Quality of life was evaluated using the Inflammatory Bowel Disease Questionnaire. Data were analyzed by ANOVA, followed by the Duncan post-hoc test and the multiple linear regression test. **Results** – Of the total, 61.7% of participants reported symptoms of anxiety or depression or both. Regarding quality of life, the majority (43.6%) were classified as "regular" and the minority (3.6%) as "excellent". Multiple linear regression showed that worse quality of life correlated with greater presence of anxiety and depression symptoms (<0.001). **Conclusion** – Crohn's disease has considerable impact on quality of life and contributes to the appearance of anxiety and/or depression symptoms.

**HEADINGS** – Crohn disease. Quality of life. Anxiety. Depression.

## INTRODUCTION

Crohn's disease (CD) is an idiopathic chronic inflammatory disease. With ulcerative colitis (UC), it is classified as an inflammatory bowel disease (IBD)<sup>(1,2)</sup>. CD may affect any part of gastrointestinal system from mouth to anus. Typically, however, it affects the ileum and colon<sup>(2,3)</sup>. CD symptoms include abdominal pain, diarrhea, fecal incontinence, rectal bleeding, weight loss and fatigue. CD is characterized by periods of remission and recrudescence<sup>(2,4)</sup>.

The prevalence and incidence of the CD vary according to the geographical area studied. According to the World Gastroenterology Organization<sup>(5)</sup>, the prevalence of CD per 100,000 inhabitants in Europe, the Middle East, North America and Australia was 322, 29, 319, and 155, respectively; incidence per 100,000 inhabitants per year was 12.7, 5.0, 20.2, and 17.4 respectively. The highest rates of cases of CD were observed in Western and Northern Europe, as well as in North America. Moderate rates were recorded in the Middle East, Australia and New Zealand. The lowest rates were recorded in Africa, South America and Asia<sup>(4,6)</sup>.

The disease affects people of any age, but the diagnosis is made most consistently in the second or third decades<sup>(2,6)</sup>. There is some controversy regarding the prevalence of the disease, as some authors claimed it was equal for both genders, while others reported a predominance of males over females. Still others reported a female predominance<sup>(6,7)</sup>. Moreover, it was emphasized that the prevalence of CD appeared to be higher in urban areas than in rural areas, and higher in upper socioeconomic classes<sup>(5)</sup>.

As this disease develops in the gastrointestinal tract, the nutritional status of patients may be affected by reduction in food intake caused by gastrointestinal symptoms, malabsorption and

medical treatment. CD is usually also associated with nutritional deficiency that can range from mild to severe<sup>(8,9)</sup>.

CD can change quality of life, especially during flares, and may cause major changes in the physical, emotional and social lives of patients. CD has been associated with symptoms of anxiety and depression<sup>(10-12)</sup>.

There is evidence that the continuous psychological suffering can exacerbate disease activity and increase the risk of a flare<sup>(13-15)</sup>. The belief in the relevance of psychological factors in inflammatory bowel diseases is not new. The first time the concept was addressed was in the 1930s, when gastroenterologists and psychiatrists suggested that life events and emotional experiences probably correlated with flares of intestinal symptoms<sup>(16)</sup>. Although this association is now well accepted, some studies report that there remains controversy regarding the possible role of psychological factors in CD<sup>(10,14,17)</sup>.

Thus, the objective of this study was to investigate the prevalence of symptoms of anxiety and depression in Brazilian patients diagnosed with CD, as well as their quality of life.

## METHODS

### Survey area and population

This was a cross-sectional survey, with 110 adult subjects. The following criteria were considered for inclusion in the survey: residents of any region of Brazil; age 21-59 years; both genders; and diagnosis with CD by a medical professional. Then, from March to August 2016, the population was selected from private Facebook groups dedicated to individuals with IBD. The purpose of these groups is to discuss the progression of diseases, to obtain new

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information and to share particular histories. It should be noted that Facebook was the only social network selected because of the large number of participants with IBD and because of the ease of contacting participants. The subjects were invited individually to participate in the survey. Inclusion criteria were highlighted at the time of the invitation.

### Ethical aspects of the survey

This survey was approved by the Research Ethics Committee of the Federal University of Fronteira Sul (UFFS) by a Presentation Certificate for Ethics Assessment, number 51795915.9.0000.5564. Through a succinct description, all participants were informed regarding the objectives and procedures of the survey, and through online communication they provided consent.

### Anxiety and depression symptoms

The Hospital Anxiety and Depression Scale (HADS) was used to identify symptoms of anxiety and depression in patients with CD. The HADS was developed primarily to identify anxiety and depression symptoms in patients in non-psychiatric hospitals, and was later extended to non-hospitalized patients and individuals without a disease<sup>(18-20)</sup>. The HADS was translated into several languages, and was validated for Portuguese in 1995. It contains 14 items, divided into sub-scales of anxiety and depression. Each item can be scored from 0 to 3, with a maximum score of 21 points for each scale<sup>(20,21)</sup>. There are two cut-off points indicated for use in both subscales: HAD-anxiety (no anxiety – from 0 to 8; and higher or equal to 9 – with anxiety), and HAD-depression (without depression – between 0 and 8; and higher or similar to 9 – with depression)<sup>(22)</sup>.

### Quality of life

The quality of life of individuals with CD was evaluated using the Inflammatory Bowel Disease Questionnaire (IBDQ). The IBDQ was developed in 1988 in the United States, through extensive interviews with 54 patients with CD and 43 with UC. This instrument was translated into, and validated for Brazilian Portuguese. Currently, IBDQ contains 32 items, covering four domains: 1) intestinal symptoms, 2) systemic symptoms, 3) social aspects and, 4) emotional aspects. The response options are presented in the form of multiple choice, with seven alternatives: Score 1 – worst life quality to score 7 – best life quality<sup>(23)</sup>. The sum of all domains results in the total score, classifying quality of life:  $\leq 100$  points – low; 101 to 150 points – regular; 151 to 199 points – good; and  $\geq 200$  points – excellent. Some investigators concluded that IBDQ is a reliable measurement with good reproducibility, reflecting the major changes occurring in the health status of patients with IBD<sup>(23,24)</sup>.

### Sociodemographic data and health condition

Through participant reports, we obtained information regarding sociodemographic variables (age, gender and region of Brazil). Self-reporting was used as the criterion for obtaining information regarding disease activity period (remission or activity), as well as for anthropometric measurements (current weight and height). Current weight and height were used to determine the anthropometric profile of participants through the body mass index (BMI), for adults of both genders, proposed by the World Health Organization (2002)<sup>(25)</sup>. The anthropometric profile of the participants was classified as low weight, normal weight, overweight, and obese.

### Statistical analysis

Data were analyzed using Statistica software, version 8.0. First, we performed one-way variance analysis (ANOVA), followed by the Duncan post-hoc test in order to compare i) anthropometric profile vs. anxiety, depression and bowel symptoms and; ii) periods of disease vs bowel symptoms, systemic symptoms, social and emotional aspects. Subsequently, we used the multiple linear regression test to compare depression and anxiety vs bowel symptoms, systemic symptoms, social aspects, emotional aspects and their total sum.

## RESULTS

Patient characteristics: sociodemographic and health status

A total of 110 patients with CD were included in this survey. The sociodemographic characteristics of the sample are summarized in TABLE 1. More women (77.27%) participated in the survey. Regarding region, response to the survey was highest among patients living in the southeast (64.54%) of Brazil. There was no participation of patients living in the northern region. Based on the classification of the anthropometric profile by BMI<sup>(25)</sup>, the majority of the patients were classified as eutrophic. Of the total, 14.5% (n=16) presented underweight, 51% (n=56) normal weight, 24.5% (n=27) overweight and 10% (n=11) obese.

TABLE 1 Demographic characteristics of patients with Crohn's disease (n=110).

Variables	Numbers
Gender	
Male	25
Female	85
Region	
South	23
Southeast	71
Midwest	02
Northeast	14
Age	33±8.6
BMI (kg/m <sup>2</sup> )	23.8±5.12

BMI: body mass index. The results are expressed by mean ± standard deviation.

### Anxiety and/or depression symptoms and quality of life classification

Among the total, 61.7% (n=69) reported anxiety symptoms, depressive symptoms, or both. The diagnoses are shown in FIGURE 1A. Simultaneous report of symptoms of anxiety and depression occurred in the majority (40%). We analyzed the effect of CD on quality of life using the IBDQ. The average score in each of the domains and the total sum of these domains 50.9±12.3 for intestinal symptoms, 17.6±6 for systemic symptoms, 22.1±9 for social aspects, 48.3±15.6 for emotional aspects, and 139±37.5 for the total. The average score of the sum of all domains classified the sample's quality of life as regular. FIGURE 1B shows the result the quality of life classification of all individuals included in the survey. Thus, the life quality of the majority of patients (43.6%) was classified as "regular", and the minority (3.6%) had the quality of life classified as "excellent".

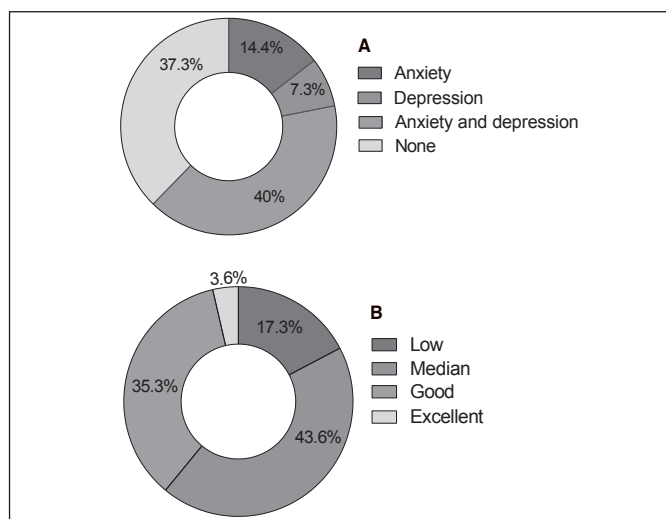


FIGURE 1. Diagnosis of symptoms of anxiety and/or depression (A); classification of quality of life (B) through the Inflammatory Bowel Disease Questionnaire (IBDQ) in patients with Crohn's Disease (CD).

### Classification of the anthropometric profile and intestinal symptoms associated with symptoms of anxiety and depression

Duncan's post-hoc test showed that the anthropometric profile interferes significantly only with depression symptoms (FIGURE 2B). Thus, the higher the BMI, the greater the number of depressive symptoms. That is, obese participants presented significantly

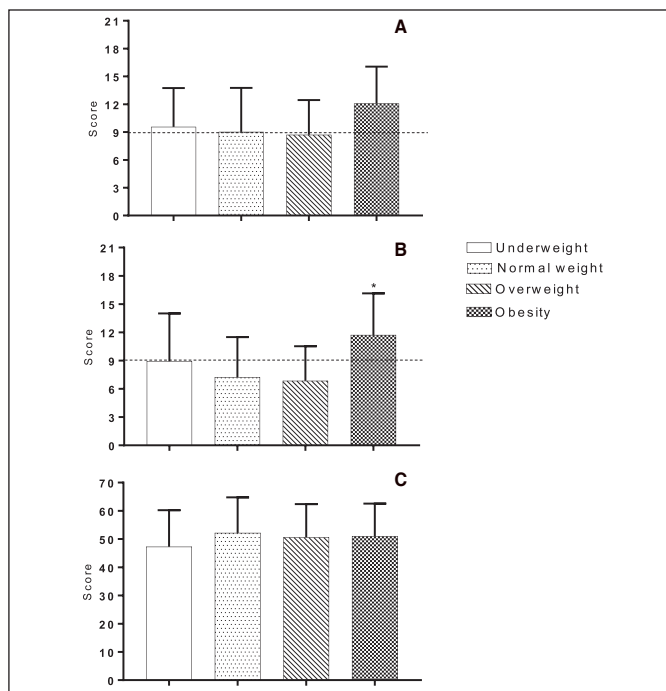


FIGURE 2. Classification of the anthropometric profile of patients with Crohn's disease (CD) versus A) anxiety symptom scores; B) depression symptom scores; C) intestinal symptom scores. \* Significantly different from underweight, normal weight and overweight ( $P<0.05$ ). The dashed line indicates that when it is equal to or greater than 9 there are symptoms of anxiety or depression.

more symptoms than did patients who are underweight, had normal weight or who were overweight. However, the relationship between the anthropometric profile versus anxiety symptoms and intestinal symptoms did not show a significant difference. That is, the anthropometric profile did not interfere with either symptom (FIGURE 2A, C). It is important to highlight that the symptoms of anxiety and depression were related to the classification of the anthropometric profile individually and not simultaneously, different from the result shown in FIGURE 1A.

### Periods of CD associated with IBDQ domains

In relation to CD periods, 55.5% (n=61) of the patients reported active disease and 44.5% (n=49) reported remission. It is important to note that 53.6% (n=37) and 46.4% (n=32) of the patients with active disease and those remission, respectively, presented anxiety and/or depression symptoms. It is also important to note that active CD disease significantly affected life quality of patients more than did CD remission (FIGURE 3). This was shown by an impairment in all domains, from intestinal and systemic symptoms to social and emotional aspects.

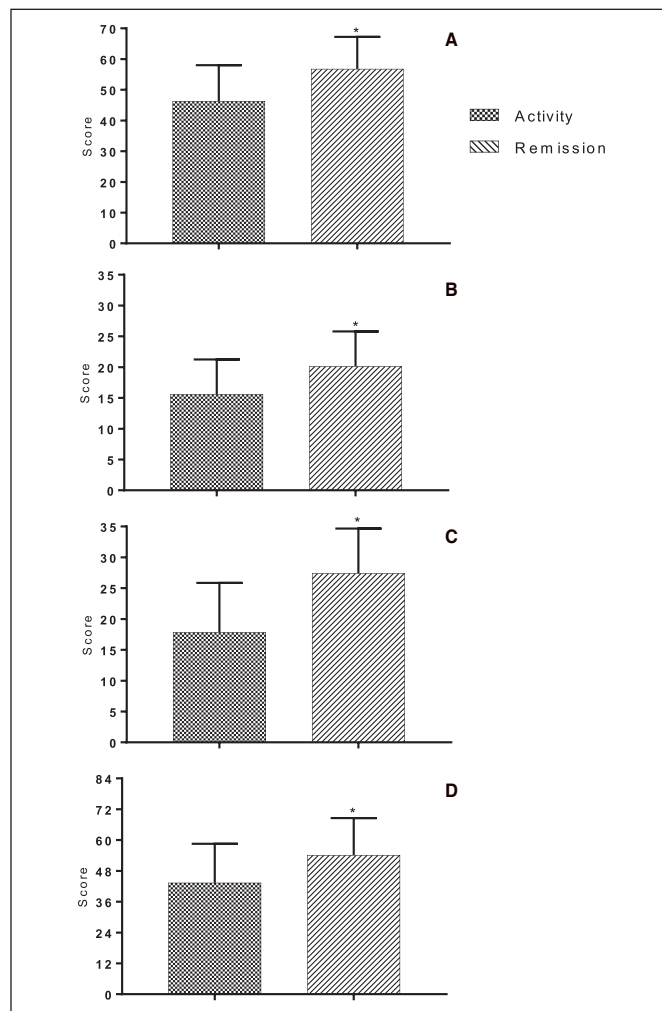


FIGURE 3. Association of Crohn's disease (CD) periods versus A) intestinal symptom scores; B) systemic symptom scores; C) social aspect scores and; D) emotional aspect scores. \* Significantly different from active disease ( $P<0.001$ ).

### Anxiety symptoms correlated to IBDQ domains

The correlation of anxiety symptoms with the IBDQ questionnaire responses is shown in TABLE 2. Anxiety symptoms were correlated with the four domains covered in the IBDQ, as well as with the total result of the four domains ( $P < 0.05$ , multiple linear regression test). In addition, it should be noted that the correlations resulted in negatives, because the higher anxiety score, the more anxiety symptoms were reported, with lower IBDQ scores recorded. Worse quality of life of patients with CD correlated with greater reporting of anxiety symptoms.

TABLE 2. Comparison of anxiety symptoms versus Inflammatory Bowel Disease Questionnaire (IBDQ) of patients with Crohn's disease.

IBDQ	R	P
Intestinal symptoms	- 0.448	<0.001
Systemic symptoms	- 0.513	<0.001
Social aspects	- 0.349	<0.001
Emotional aspects	- 0.666	<0.001
Total	- 0.591	<0.001

$P < 0.05$  is statistical significant.

### Depression symptoms correlated with IBDQ domains

The correlation of depression symptoms with the IBDQ questionnaire is displayed in TABLE 3. This comparison was similar to that of anxiety symptoms. Thus, from the multiple linear regression test, the correlations were shown to significant ( $P < 0.05$ ) and were negative: the higher the depression scores, the more symptoms reported, resulting in lower IBDQ scores. This suggests that the worse quality of life for CD patients correlated with greater reporting of depressive symptoms.

TABLE 3 Comparison of depression symptoms versus Inflammatory Bowel Disease Questionnaire (IBDQ) of patients with Crohn's disease.

IBDQ	R	P
Intestinal symptoms	- 0.241	<0.001
Systemic symptoms	- 0.538	<0.001
Social aspects	- 0.422	<0.001
Emotional aspects	- 0.632	<0.001
Total	- 0.530	<0.001

$P < 0.05$  is statistically significant.

## DISCUSSION

In general, the results obtained in the present survey demonstrated that patients with CD have a reduced in quality of life and more symptoms of anxiety and depression simultaneously. The female predominance with respect to adherence to survey participation is consistent with the literature, for CD and both IBD entities<sup>(12,17)</sup>. The average age ( $33 \pm 8.6$ ) was similar to the published literature as well, being  $32.7 \pm 11.4$ <sup>(12)</sup>,  $40.6 \pm 11.8$ <sup>(17)</sup>,  $37.2 \pm 11.9$ <sup>(26)</sup> e  $35.07 \pm 12.51$ <sup>(27)</sup>. Regarding region, the majority of the patients (64.54%) resided in the southeastern region of Brazil. Patients in the northern region did not participate in the survey.

With regard to reporting symptoms of anxiety and/or depression in this survey, we found a predominance of anxiety, followed by anxiety concomitantly with depression, and finally depression alone. If anxiety symptoms concomitant with those of depression

were disregarded, anxiety would be predominant. Other studies have also reported that anxiety symptoms were more prevalent compared to those of depression<sup>(27-29)</sup>. In a research of the French Association of Patients with IBD (n=1663), 12% of patients reported depression and 41% reported anxiety<sup>(30)</sup>. Our sample size was smaller (n=110), in which 7.3% of the patients reported symptoms of depression and 14.4% reported anxiety symptoms. When comparing these values to the present survey, we showed that the values were similar in the sense of including more patients with symptoms of anxiety than depression. In addition, when comparing the results of anxiety and/or depression diagnosis (61.7%) to other studies, similar values were found, as in a Brazilian study, performed with 50 patients affected by CD, where 58% were diagnosed with symptoms of anxiety and/or depression<sup>(17)</sup>.

Regarding the disease period, some authors describe that the symptoms of anxiety and depression were often identified when IBD was active<sup>(10,31)</sup>. In addition, there is evidence to suggest that frequent psychological suffering may exacerbate disease activity<sup>(13-15)</sup>. In the present survey, we found that symptoms of anxiety and/or depression are more associated with active disease (53.6%) than for disease in remission (46.4%). This was expected, since clinical manifestations are aggravated during flares. In other studies, the same was observed, but with different values. Andrews et al. (1987)<sup>(32)</sup>, reported that 66% and 37% of all patients presenting with the disease in activity and remission, respectively, had symptoms of anxiety and/or depression. Bennebroek et al.<sup>(33)</sup> found that 41.9% and 21.2% of the total number of patients with active disease and remission, respectively, manifested symptoms of depression and/or anxiety.

Through the IBDQ, we verified that CD had a significant impact on patient quality of life and daily activities. IBDQ is an important tool for health professionals to measure patient satisfaction and the effects of CD on quality of life. According to Alowais et al. (2016)<sup>(34)</sup> in a study conducted in Saudi Arabia, and De Boer et al. (1995)<sup>(35)</sup> in a study performed in Amsterdam, both in patients with IBD, the authors found that the average score of intestinal and systemic symptoms, social and emotional aspects, and the sum of these were lower than those found in the present survey. Pontes et al. (2004)<sup>(23)</sup> and Cohen et al. (2010)<sup>(36)</sup>, both in Brazil with IBD patients, found average score slightly higher than the one reported in the present study. Despite variations among the studies, all indicated poorer quality of life. These variations may be associated with cultural understanding of the disease, disease behavior, disease treatment response, environmental factors, social support and assistance from health professionals<sup>(34)</sup>.

Pallis et al. (2002)<sup>(37)</sup> and Cohen et al. (2010)<sup>(36)</sup> reported that disease activity significantly affected the quality of life of patients in all domains of symptoms. We also observed significant association between the disease period and the quality of life.

Guthrie et al. (2002)<sup>(38)</sup> described the importance of identifying and alleviating psychological distress in patients with IBD, because such suffering contributes to the loss of quality of life regardless of disease severity. Psychological factors including depressed mood and anxiety, if related to quality of life, may have a negative influence on the course of IBD. And as shown in the results of this survey, significantly worse quality of life correlated with the greater the number of symptoms of anxiety and depression.

The classification of the anthropometric profile of patients with CD in this survey ( $23.8 \pm 5.12$  kg/m<sup>2</sup>) was similar to that of patients evaluated by Aghdassi et al. (2007)<sup>(39)</sup> and Cohen et al. (2010)<sup>(36)</sup>, being  $23.05 \pm 0.45$  kg/m<sup>2</sup> and  $24.66 \pm 3.77$  kg/m<sup>2</sup>, respectively. We

reported eutrophy, that is, adequate weight. It should be noted that patients with IBD are more susceptible to protein-energy malnutrition that is primarily caused by reduced food intake, poor food absorption, increased gastrointestinal losses and increased nutritional requirements<sup>(36-40)</sup>. However, the fact that a little less than half of the survey patients reported disease in remission may have contributed to the adequate classification of the anthropometric profile, within the recommended limits. In addition, the present study found that obese patients had significantly more symptoms of depression than did underweight, eutrophic and overweight patients. The literature suggests that excess body weight is highly-associated with the appearance of anxiety and depression symptoms<sup>(41,42)</sup>. A recent study in Poland with patients with IBD also found significant results regarding overweight and higher levels of depressive symptoms<sup>(43)</sup>.

Finally, it is necessary to point some limitations of the present study. First, the fact that the research was performed in a virtual and impersonal manner, i) made it difficult to interpret questionnaire responses and to interact with the patients' responses; and ii) depended on the veracity of the subjects with respect to their answers. Another important point that may have influenced the results in this research is that the patients participating in groups of social networks destined to a certain disease tend to be the most naive and most susceptible to quackery.

## CONCLUSION

CD had a significant impact on the patient quality of life, especially when the symptoms are exacerbated. CD also contributed considerably to the appearance of symptoms of anxiety and depression. Therefore, it is important to emphasize the need for pharmacological and/or psychological treatment for individuals affected by CD with anxiety and/or depression, as well as to provide nutritional assistance to these patients, for maintenance and/or recovery of adequate weight, and for the reduction of gastrointestinal symptoms.

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## Authors' contribution

Tomazoni EI: developed the research design, collected data, participated in the statistical analysis, table elaboration and writing. Benvegnú DM: participated in the development of the research design, the statistical analysis and writing.

Tomazoni EI, Benvegnú DM. Sintomas de ansiedade e depressão, e a qualidade de vida de pacientes com doença de Crohn. *Arq Gastroenterol.* 2018;55(2):148-53.

**RESUMO – Contexto** – A doença de Crohn é uma doença inflamatória crônica, idiopática e classificada na categoria de “Doença Inflamatória Intestinal”. A doença de Crohn pode alterar a qualidade de vida dos pacientes, especialmente quando está em um período de exacerbação clínica dos sintomas. Nesse sentido, a doença de Crohn tem sido associada a sintomas de ansiedade e depressão, pois os sintomas clínicos têm um alto impacto na qualidade de vida. **Objetivo** – Investigar a prevalência de sintomas de ansiedade e depressão em pacientes brasileiros diagnosticados com doença de Crohn, bem como sua qualidade de vida. **Métodos** – Um total de 110 pacientes brasileiros, com idade entre 21-59 anos, de ambos os gêneros, com doença de Crohn foram incluídos no estudo. Os dados foram virtualmente coletados através de questionários. A *Hospital Anxiety and Depression Scale (HADS)* foi utilizada para diagnosticar os sintomas de ansiedade e depressão. A qualidade de vida foi avaliada utilizando o *Inflammatory Bowel Disease Questionnaire (IBDQ)*. Os dados foram analisados através do teste ANOVA, seguido do teste post-hoc Duncan e também do teste de regressão linear múltipla. **Resultados** – Do total de participantes, 61,7% foram diagnosticados com sintomas de ansiedade ou sintomas de depressão ou ambos os sintomas. Em relação à classificação de qualidade de vida, a maioria dos pacientes (43,6%) teve a classificação como “regular” e a minoria (3,6%) como “excelente”. Assim, o teste de regressão linear múltipla mostrou, significativamente, que quanto pior a qualidade de vida dos pacientes com doença de Crohn, maior a presença de sintomas de ansiedade e depressão (<0,001). **Conclusão** – A doença de Crohn tem um impacto considerável na qualidade de vida dos pacientes e também contribui para o surgimento dos sintomas de ansiedade e depressão.

**DESCRITORES** – Doença de Crohn. Qualidade de vida. Ansiedade. Depressão.

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