Mood swings in patients with Crohn's disease: incidence and associated factors

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Summary

Objective: To assess the incidence of mood swings (MS) and possible associated factors in patients with Crohn's disease (CD). **Methods:** Prospective longitudinal study of 50 patients (60% females; mean age 40.6 years) with a diagnosis of CD over a 16-month follow-up. Clinical activity was assessed by the CD activity index. Psychological status self-report tools (Beck Depression Inventory and the anxiety subscale of the Hospital Anxiety and Depression Scale) were used for mood disorder diagnosis. The tools were applied at baseline and at four-month intervals thereafter. **Results:** The inflammatory phenotype was the most common (86%); 36% had a previous history of surgery related to CD; 82% were in clinical remission at baseline. MS occurred in 58% of patients; 28% had progression of depression and/or anxiety symptoms from baseline normal mood, and 30% had baseline depressive and/or anxious mood normalized. In 38% of patients with MS, no change in the disease clinical activity could be found ($p = 0.015$), whereas 20% had a change in CD activity. Female gender and absence of previous surgery related to CD complications were associated with higher MS incidence ($p = 0.04$ for both). **Conclusion:** In this study, a high MS incidence (58%) was found in patients with CD. Female gender and absence of previous surgery from CD complications were associated with a higher MS incidence. Periodic psychological assessment could be useful to detect and approach MS in patients with CD.

Keywords: Croh's disease; mood swings; depression and anxiety; psychology.

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Introduction

Crohn's disease (CD) is a transmural inflammatory disease, incurable to date, that may affect the whole gastrointestinal tract, from the mouth to the anus. First described by Gunzburg and Oppenheimer in 1932, it is an immune-mediated disease characterized by a remitting-relapsing course[1]. As it a chronic disease, its impact on the quality of social, occupational, and family life may be significant[2-4].

In North America, the annual incidence of CD ranges from 2.2 to 14.3 cases per 100,000 people, with prevalence rates being 26 to 210 cases per 100,000 people[5,6]. Despite the lower CD incidence in South America and Asia, several studies have directed attention to the growing number of cases diagnosed worldwide[7]. In Brazil, one of the first studies reported was that by Gaburri et al., highlighting the growing numbers of individuals diagnosed with CD in the second half of the 20th century[8]. These data were later confirmed by Souza et al.[9].

CD etiology remains unknown. Inflammatory bowel diseases (IBDs) were once considered psychosomatic. Progress in biomedical understanding in the field of chronic illnesses has highlighted genetic, environmental, and molecular features in IBD pathogenesis[10]. On the other hand, the contributions of psychological factors on the disease course have been neglected[11].

The current understanding of IBD multifactorial causality focuses on a possible disease process modulation by emotional states, which might aggravate symptoms, cause relapses or, on the contrary, positively influence the previous situation[12-14]. In this new setting, environmental, food, immune, and infectious factors have been exhaustively investigated as possible causes for CD. Currently, one of the most accepted theories is the immune. However, a strong indication of the impact of emotions on intestinal diseases is observed both in CD and ulcerative colitis[15].

Recently, a number of reports have approached the occurrence of psychological disorders affecting patients with CD, as well as possible interactions[10,15]. Although this association is currently well-accepted, there has been little change and impact on the disease course and clinical practice[15,16]. There is much controversy, and there are few prospective and controlled studies on the possible role that psychological aspects play in eliciting and/or influencing clinical course of IBD.

The gastrointestinal tract is one of the most common sites affected by somatic symptoms precipitated by psychological factors. The fact that depression symptoms can have a direct influence on immune disorders associated with CD[17] and a negative effect on several chronic diseases is noted[18]. In addition, a great number of patients relate the occurrence of appetite loss, nausea, and diarrhea to an event generating anxiety[19].

Determining the occurrence of mood swings and their possible association with patients' and CD characteristics may allow for the implementation of specific therapies targeting an identified psychological disorder, thus contributing to a better overall approach, which may improve the quality of life. However, few studies are reported in Brazil regarding CD, despite the growing interest in the topic. To date, there are no prospective longitudinal studies in Brazil assessing the occurrence of mood swings in patients with CD, as well as possible factors associated with the disease.

Considering the importance of the topic, the current study aims to assess the incidence of mood swings in patients with CD, as well as the possible associated factors.

Methods

This is a prospective longitudinal study in which 55 patients with CD in regular follow-up at the outpatient IBD clinic of the Gastroenterology Department of the Universidade Federal de Juiz de Fora's (UFJF) Hospital were consecutively included in a psychological assessment of their mood status. The assessment was conducted from August 2009 to December 2010.

The study was approved by the UFJF's Ethics in Research Committee and all subjects signed an informed consent containing information about the study objective and methods. The patients were assured the right not to participate in the study; nonparticipation would not interfere with their treatment in the facility.

CD diagnosis was established by combining clinical, endoscopic, and radiologic data supplemented by the typical histological aspect in either mucous membrane biopsies or surgery resection specimens when available[20].

The following were considered exclusion criteria: (a) age < 18 years or > 65 years; (b) indication of hospital admission or immediate surgery resulting from CD complication; (c) fulminating disease; (d) presence of a stoma or short bowel syndrome; (e) current or previous diagnosis of psychosis; (f) pregnancy; (g) breastfeeding women; (h) lost to follow-up.

Demographics, such as gender, age, marital status, and education, were recorded at baseline. Medical history and clinical features related to CD were evaluated for: (a) CD location; (b) disease duration (in months); (c) clinical activity; (d) presence and site of fistulae; (e) medication use; (f) current history of alcohol intake and tobacco use; (g) prior surgery history if resulting from CD complication; (h) family history of depression. Alcohol intake was considered significant when higher than 60 grams/day in males and 40 grams/day in females.

The Vienna classification was used to assess the phenotype of patients with CD[21]. Disease activity was assessed through the Crohn's Disease Activity Index

(CDAI), which has been strictly developed and validated; a score < 150 points was considered "remitting disease" and a score ≥ 150 points was considered "disease activity"[22].

In the presence of fistulae, a drainage evaluation was routinely performed in order to grade them as either "open and actively draining" or "closed", as previously suggested[23].

The assessment of CD activity was conducted by a physician unaware of the patient's psychological status at the time of the application of questionnaires.

The psychological assessment was performed by a single professional (Flávia D'Agosto Vidal de Lima) at baseline and at four-month intervals thereafter over the 12 subsequent months. The patients were requested to complete the psychological status self-report, the Beck Depression Inventory (BDI), and the seven-item anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A), aiming to identify depression or anxiety symptoms, respectively. The HADS-A has been previously used in patients with IBD[24], showing good reliability and validity.

The BDI is a psychometric instrument of depression self-report widely used in several populations, translated into several languages, and validated in different countries, including Brazil[25]. The original scale contains 21 items including symptoms and attitudes, with their severity ranging from 0 to 3, aiming to identify the presence of depressive mood indicators, encompassing different symptom categories, such as: mood (sadness, loss of interest, crying, mood swings), vegetative or somatic (weight loss, loss of appetite, sleep loss, fatigue), cognitive (guilt, hopelessness, suicidal ideation), social (social isolation, self-consciousness), and motor (inhibition, excitement)[26]. Patients scoring > 20 were considered as having a depressive mood in accordance with the Brazilian BDI validation[25].

The HADS-A is a simple self-reported scale with 14 multiple choice questions containing two subscales for anxiety and depression. In two wide literature reviews, the HADS showed appropriate screening properties for separate dimensions of anxiety and depression[27]. Patients scoring > 8 at HADS-A were considered as having anxiety symptoms according to the national validation[28].

Patients exhibiting a change in their psychological status in at least one follow-up visit were considered as having mood swings. Patients with a diagnosis of mood swings were assigned to psychological treatment according to their indication.

At the psychological reassessment, CD's clinical activity was ascertained to establish any correlation between the two variables, as well as a temporal relationship. The comparison between groups, as well as a possible relationship between socio-demographic and clinical data and mood swings, was analyzed by using Student's *t*-test and the chi-squared test or the Mann-Whitney test as appropriate. The possible correlation between mood swings and CD clinical activity was assessed by *t*-tests for paired samples. A p-value < 0.05 was considered statistically significant. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) 14.0.

Results

Initially, 55 patients with CD were assessed. Two (3.7%) patients did not meet the inclusion criteria and were excluded from the initial interview. Fifty-three (96.3%) patients were, therefore, included (33 females and 20 males, mean age 40.6 ± 11.8 years, ranging from 18 to 65 years). Over follow-up, three (5.7%) patients were lost and consequently excluded from the study. Thus, a total of 50 subjects participated in the entire period of study.

Table 1 shows the main socioeconomic and clinical characteristics of the participants at baseline.

The mean CD duration was 78 months; most patients (86%) had the inflammatory phenotype of the disease, with 41 (82%) patients in clinical remission and 18 (36%) having already undergone some surgical procedure to treat CD complications.

As for the initial psychological assessment, 14 (28%) patients were observed to have baseline depressive mood; 28 (56%) had anxiety symptoms. Mood swings were found in 29 (58%) patients assessed throughout follow-up. Out of these, 14 (28%) subjects had progression of depression and/or anxiety symptoms compared with the baseline normal mood, while 15 (30%) had a mood normalization from baseline depressive and/or anxious mood during the follow-up.

Table 2 shows the association between mood swings and sociodemographic and clinical characteristics of patients with CD. Females and patients who had not undergone a previous surgery from CD complications were found to have a significantly higher incidence of mood swings (p = 0.04 for both). A trend for an association of alcohol intake and higher incidence of mood swings was found (p = 0.06), though the number of patients with an alcoholic intake in the sample was too low (n = 3) for a robust statistical analysis.

During follow-up, no correlation between mood swings and change in CD clinical activity was observed (p = 0.15). Thus, out of 29 (58%) patients with mood swings, 19 (38%) did not show any change in CD clinical activity, while 10 (20%) had a change in CD activity, with 5 (10%) showing a flare in a previously remitting disease and 5 (10%) having a remission in a previously active disease.

Table 1 – Clinical and sociodemographic features in Crohn's disease (n = 50)

Gender	
Female (n) (%)	32 (64)
Male (n) (%)	18 (36)
Age (years) (mean ± SD)	40.6 ± 11.8
Race	
White (n) (%)	43 (86)
Non-white (n) (%)	7 (14)
Marital status	
Married (n) (%)	29 (58)
Single/separated (n) (%)	21 (42)
Occupation	
Stable income (n) (%)	36 (72)
No fixed income (n) (%)	14 (28)
Education	
Elementary (n) (%)	23 (46)
High school and college (n) (%)	27 (54)
Smoking (n) (%)	4 (8)
Alcohol intake (n) (%)	3 (6)
Disease duration (months) (mean ± SD)	78.3 ± 58.7
History of depression in the family (n) (%)	23 (46)
Crohn's disease phenotype	
Inflammatory (n) (%)	43 (86)
Penetrating (n) (%)	4 (8)
Stenosing (n) (%)	3 (6)
Initial CDAI	
Remission (n) (%)	41 (82)
Clinical activity (n) (%)	9 (18)
Previous surgery (n) (%)	18 (36)
BDI	
Normal (n) (%)	36 (72)
Depressive mood (n) (%)	14 (28)
Initial HADS	
Normal (n) (%)	22 (44)
Anxiety (n) (%)	28 (56)

SD, standard deviation; CDAI, Crohn's Disease Activity Index; BDI, Beck depression inventory; HADS, Subscale of the Hospital Anxiety and Depression Scale.

Discussion

Sigmund Freud, in 1886, highlighted the role of psychological suffering in the genesis of organic alterations (e.g., diarrhea, constipation, abdominal pain, etc.), influenced by both conscious and unconscious factors[29]. Subsequently, with the advent of psychoanalysis, the unconscious origin of diseases, regression, and gains has been consolidated. However, only in the 1930s, with psychosomatic therapies based on the study of mind-body relationships and the importance of the emotional origin of organic diseases, IBDs were classified as a psychosomatic etiology, a status they held over many years[30]. In the 1950s, behaviorism was concerned with seeking scales and instruments for treatment evaluation, as well as specific diagnostic criteria, by dealing with methodology, reliability, and validity of diagnoses and studies[31].

Currently, the most accepted theory for IBD etiology is immune. However, the role of the emotions in the immune system is evident[15]. Stress might be defined as a breaking in the natural homeostasis in which the body's normal multisystem response to an insult is exceeded, which could trigger, enhance, or maintain the intestinal mucosa inflammation[32]. In addition to the importance of stress in the immune theory, Zozaya et al. pointed out the importance of a series of factors influencing the individual's behavior with respect to recovery in chronic illnesses, such as the individual's biological framework, genetics, and environmental and psychological factors[33]. Therefore, several studies have demonstrated the importance of psychological factors in the course of disease, as well as in the treatment response of several chronic diseases[34-37]. This has also been approached in several studies evaluating a correlation between stress and IBD activity. Despite conflicting results, many patients assign importance to psychological factors, particularly stress, as contributing to the disease onset and clinical course[18,38].

Despite several studies addressing psychological factors and their influence on the inflammatory bowel disease course, North et al.[14] highlighted various methodological limitations in these studies, such as retrospective design, short follow-up, and inclusion of patients having CD and ulcerative colitis (URC) in the same study, among other flaws[39-41]. In spite of the methodological improvement in subsequent studies, the results remain controversial[19].

Andrews et al. assessed 162 patients with IBD through the HADS and observed an overall prevalence of anxiety and/or depression in approximately 33% of patients. It was found that patients with a more severe illness presented a higher incidence of anxiety and/or depression symptoms than those clinically well

Table 2 – Relationship between clinical and sociodemographic features and mood swings in patients with Crohn's disease

Characteristics	Patients with mood swings (n = 29) n (%)	Patients without mood swings (n = 21) n (%)	p
Gender			0.04
Female – n (%)	22 (44)	10 (20)	
Male – n (%)	7 (14)	11 (22)	
Age (mean)	21	29	0.24
Marital status			0.21
Stable relationship, n (%)	19 (38)	10 (20)	
No steady partner, n (%)	10 (20)	11 (22)	
Race			0.38
White – n (%)	26 (52)	17 (34)	
Non-white – n (%)	3 (6)	4 (8)	
Fixed income			0.57
Yes – n (%)	20 (40)	16 (32)	
No – n (%)	9 (18)	5 (10)	
Education			0.90
Complete Elementary School (n)	14	9	
Complete High School (n)	12	10	
University (n)	3	2	
Smoking			0.74
Yes – n (%)	2 (4)	2 (4)	
No – n (%)	27 (54)	19 (38)	
Alcoholism			0.06
Yes – n (%)	3 (6)	0 (0)	
No – n (%)	26 (52)	21 (42)	
Disease duration (months)	29	21	0.75
Previous surgery resulting from CD			0.04
Yes – n (%)	7 (14)	11 (22)	
No – n (%)	22 (44)	10 (20)	
Corticosteroid use			0.15
Yes – n (%)	8 (16)	10 (20)	
No – n (%)	21 (42)	11 (22)	

CD, Crohn's disease.

(50% *versus* 8%, p = 0.01)[24]. Other studies have also documented a higher incidence of depression and/or anxiety symptoms in patients with IBD; this association, to date, appears to be more consistent in ulcerative colitis than in CD[40,42-44].

Goodhand et al. assessed, in a recently published cross-sectional study, 204 patients with IBD (103 with URC and 101 with CD) and 124 healthy individuals for the occurrence of depression or anxiety disorder by using the HADS. Depression and anxiety were twice as

frequent in patients with IBD than in the control group. The incidence of mild, moderate, and severe depression was 15%, 3%, and 1%, respectively. Anxiety occurred more frequently, with an incidence of mild anxiety in 25%, moderate anxiety in 29%, and severe anxiety in 4%. If, on one hand, the occurrence of mood disorders was associated with the disease activity in URC cases, the same did not occur in patients with CD, which supports the data found in this study's population[45].

This is the first Brazilian prospective longitudinal study assessing the incidence of mood swings in outpatients with CD, as well as the factors that might be associated with CD.

The present study clearly demonstrates a high incidence (58%) of mood swings in patients with CD compared with a healthy adult population. Andrade et al. assessed 1,464 individuals in the catchment area of the Clinics Hospital of the Medical School of the Universidade de São Paulo and observed that approximately 45% of the assessed population had some kind of mood disorder. Major depression was observed in 19% and 13% of females and males, respectively. Anxiety diagnosis was also more common in females, occurring in 16% of cases[46]. Similar data were also observed by the National Comorbidity Survey, a nationwide study assessing 8,098 adults, a probabilistic sample of the general American population[47].

Mood swings were practically bidirectional, that is, a similar percentage of patients (30%) had their IBD and HADS-A scores normalized from baseline depressive and/or anxious mood during follow-up, while another group (28%) developed depression or anxiety symptoms from a baseline normal mood over the study time. Thus, a periodic screening of the psychological status appears important to detect mood swings over the course of the disease, whether CD is active or not.

The incidence of mood swings (58%) observed in the present study is quite high compared with the prevalence of anxiety and depression (25% to 36%) in other studies also assessing CD patients[40,46,48]. The definition used in the present study to consider the presence of mood swings in CD (i.e., a mood swing was considered when patients had a change in their psychological status in at least one follow-up visit) perhaps warrants, at least partially, the high mood swing rate observed in this study. Also, as a result of the chronic condition experienced by these patients, a higher predisposition to psychological disorders in this population due to onerous conditions of life could be found. It is important to underline that the psychometric tests used in this study, such as BDI and HADS-A, are appropriate and widely validated methods to investigate depression and anxiety symptoms in clinical populations[10,18,42].

Interestingly, history of previous surgery was a protective factor for the occurrence of mood swings. A possible explanation for this observed association is that those patients may have had their fear decreased, as they had already undergone a surgical procedure promoting short- and medium-term symptomatic relief. Thus, the operated patients, following the elimination of physical symptoms that were worsening their health status, were also expected to show psychological improvement.

Regarding the high mood swing rate in females (44% of the patients), there is no scientific explanation justifying the fact; however, a number of studies indicate that women are more susceptible to psychological disorders[46,49-54], which may result from concerns about body image, effects of the disease on relationships and life, and other factors relating these symptoms to female hormones.

It is important to underline that, despite the low rate of significant alcohol intake observed in this study, these patients were prone to mood swings. This fact is not surprising, as the impact of alcohol abuse on the psyche is well known. Of note, during the systematic follow-up of the patients, they were instructed on the harm caused by alcohol abuse, which warrants the low alcohol intake in the study group.

Despite the high incidence of mood swings in the study sample, their correlation with a change in the disease activity could not be proved. The present study disagrees with the results obtained by Houssam et al., who observed higher anxiety and hopelessness levels associated with higher disease activity indices (also assessed by the CDAI)[55]. A higher disease reactivation likelihood following stressful events was also observed in other studies[56]. However, these studies were performed in patients with ulcerative colitis, which often has a different clinical course than CD.

However, a limitation in the current study should be reported. Although the patients analyzed attended the IBD clinic in this institution, the sample size calculation had to be based on their assiduity, considering the study's longitudinal design.

Conclusion

Based on the above considerations, the mood swing incidence over the follow-up was observed to be high (58%), comprising the majority of the study patients. The disorder was predominantly found in females and those not undergoing a surgical procedure resulting from CD. In spite of the significant incidence of mood swings in the

study group, no association between this incidence and a change in CD activity could be observed.

Periodic psychological assessment may be useful to detect and manage mood swings in patients with CD. Further studies seeking to make connections between psychological and organic features are necessary, in order to better know the patient and develop better therapeutic strategies to improve quality of life in these patients.

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