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ORIGINAL ARTICLE

Study of personality and anxiety in children and adolescents with inflammatory bowel disease

Estudio de personalidad y ansiedad en niños y adolescentes con enfermedad inflamatoria intestinal

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What do we know about the subject matter of this study?

Certain personality traits are common in patients with inflammatory bowel disease. There is no evidence that a particular personality type may predispose to developing this condition.

What does this study contribute to what is already known?

This study supports the hypothesis that children and adolescents with inflammatory bowel disease present common personality traits and lower anxiety levels than the average population.

Abstract

Objective: to analyze the presence of common personality traits and anxiety states in children and adolescents with inflammatory bowel disease (IBD). **Patients and Method:** Longitudinal, prospective, and analytical study by applying the questionnaires Children's Personality Questionnaire, High School Personality Questionnaire, State-Trait Anxiety Inventory for Children, and State-Trait Anxiety Inventory for patients with IBD aged between 9 and 18 years seen at reference IBD units in Aragon, Spain. The participants excluded were those with active disease, defined as a score ≥ 10 on the Pediatric Crohn's Disease Activity Index (PCDAI Score) or ≥ 10 on the Pediatric Ulcerative Colitis Activity Index (PUCAI Score). **Results:** Twenty-six patients participated (73% male). 61.5% presented Crohn's disease (CD) and 38.5% ulcerative colitis (UC). No patient presented active disease. The personality profile as a group was characterized by being open, emotionally stable, calm, sober, sensible, enterprising, impressionable, dependent, serene, perfectionist, and relaxed. 50% of the CD patients were enterprising versus no UC patients ($p < 0.05$). There were no statistically significant differences when comparing the remaining personality factors based on IBD

Keywords:
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type, age, or sex. Patients with CD tended to be calmer (p = 0.0511) and patients with UC more introverted (p = 0.0549). The sample presented a state anxiety level (A/E) -1.1 ± 0.8 SD compared with the population average. The level of anxiety as a feature (A/R) was -0.6 ± 1 SD. Males had significantly lower levels than females in the case of A/E (p < 0.05). **Conclusions:** The presence of common personality traits in the pediatric population with IBD stands out but there was no greater anxiety than in the reference population.

Introduction

In recent years, there has been an interest in knowing whether there is a characteristic personality profile in people with inflammatory bowel disease (IBD). Although few studies relate personality to IBD, several personality traits have been studied. Certain personality traits such as alexithymia, neuroticism, and perfectionism are frequent in these patients. However, there is no evidence that any particular personality type predisposes to the development of IBD[1-10].

On the other hand, there is controversy about the comorbidity of certain psychological disorders such as anxiety and depression in patients with IBD. Some authors find no association between these disorders and IBD, while others point out that they are more frequent than in the general population[1,11]. Although most of the studies that have evaluated the prevalence of anxiety and depression in IBD have been carried out in the adult population, these disorders have also been described in children and adolescents with IBD. According to a study conducted in 79 IBD patients aged 9 to 17 years, 39% of the participants had symptoms compatible with high levels of anxiety[12]. In this study, the IMPACT-III questionnaire that assesses aspects of quality of life in patients with IBD was used to establish which patients were in remission. 63% of the participants met the criteria for disease activity. However, as in adults, the prevalence rates of anxiety and depression are highly variable in the pediatric IBD population.

The objective of this study is to evaluate the presence of certain common personality traits as well as the presence of anxiety states in the population of children and adolescents with IBD in our sphere.

Patients and Method

Longitudinal, prospective, analytical study conducted between December 2017 and June 2018. We included those patients with IBD, either ulcerative colitis (UC) or Crohn's disease (CD), aged between 9 and 18 years who were being monitored in IBD reference units in Aragon, Spain, and excluded those with active disease, defined as a score ≥ 10 on the Pediatric Crohn's Disease Activity Index (PCDAI Score) or ≥ 10 on the Pediatric Ulcerative Colitis Activity Index (PUCAI Score).

Those patients who met the inclusion criteria received by ordinary mail an informative document describing the objective of the study. All those who agreed to collaborate were given two validated questionnaires, one on anxiety and the other on personality, during a single visit at the *Hospital Infantil Miguel Servet* under the supervision of the same pediatric psychologist. The information document provided the telephone number for contacting the psychologist to arrange the visit. Those patients who did not contact the psychologist after receiving the information document received a telephone call informing them of the study. There were no losses in the sample due to not having achieved telephone communication. On the day the patients completed the questionnaires and before participation, we requested informed consent.

From the clinical records, the following variables were collected: sex, age at diagnosis, time of disease evolution, type of IBD, disease activity index (PCDAI and PUCAI Score) at the time of the psychological evaluation, current pharmacological treatment, number of drugs used so far, and complications related to the disease.

40 patients met the inclusion criteria. Of these, 14 patients were not included (11 patients refused to participate, 2 patients did not attend the appointment arranged with the psychologist, and 1 patient attended the appointment but refused to complete the questionnaires), resulting in a study population of 26 patients (figure 1).

The personality questionnaire used was the Children's Personality Questionnaire (CPQ) for patients aged between 8 and 12 years and the High School Personality Questionnaire (HSPQ) for patients between 12 and 18 years of age. Both questionnaires are composed of 140 multiple-choice questions and assess 13 personality traits and a scale of mental ability or intelligence. These 14 scales or first-order factors allow obtaining 4 second-order factors or more general dimensions in the personality structure.

In both the CPQ and the HSPQ, each scale or factor is directly scored. The direct scores are transformed into universally significant values called DECA. This transformation is carried out by comparing these scores with the ones obtained from a representative sample of the study's general population subjects. The DECA are distributed on a 10-point scale equidistant in typical units. Thus, DECA 5 and 6 are mean values, 4 and 7 show a small deviation (in one and the other deviation, respectively), 2, 3, 8 and 9 indicate a large deviation, and 1 and 10 are extreme values. All these positions are considered relative to the specific population on which the typing was performed[13,14].

The anxiety questionnaire used was the State-Trait Anxiety Inventory for Children (STAIC) for patients aged between 9 and 15 years and the State-Trait Anxiety Inventory (STAI) for patients aged 16 years and older. These questionnaires assess two independent concepts of anxiety: anxiety as a current state (A/S) and anxiety as a trait (A/T). They consist of 40 items, 20 items assigned to each of the A/S and A/T subscales. After obtaining the A/S and A/T scores, they are compared with the scores obtained from a representative sample of the population. From the direct scores, percentile and DECA scores are obtained[15-17].

A descriptive analysis of the sample was performed which determinate the measures of central tendency and dispersion (mean ± standard deviation) as well as the minimum and maximum values. Regarding the study of the personality factors, the percentage of patients who had a high score on each factor was calculated. For this purpose, the DECA was calculated for each first-order factor. DECA 1 to 3 and 8 to 10 were considered significant for each personality factor. Based on the DECA of the first-order factors, the scores of the second-order factors were obtained. A comparative study was carried out between the personality factors according to sex, age, and type of disease using contingency tables analyzed with Fisher's exact test. As for the study of the anxiety state, percentile scores were obtained from the direct scores and the results were expressed as mean ± standard deviation. The data collected were analyzed using the IBM® SPSS® Statistics software. The threshold of statistical significance was set for a value of $p \leq 0.05$.

This research project was presented and approved by the Research Ethics Committee of the Community of Aragon (CEICA).

Results

26 patients participated in the study. 73.1% were male and 26.9% were female. The mean age was 14.7 years ± 2.33 SD (range 10-18.8). Regarding the type of IBD, 61.5% had CD and 38.5% had UC. The mean age of patients with CD was 14.72 years ± 2.3 SD (range 10-18.8) and the mean age of patients with UC was 14.8 years ± 2.1 SD (range 12.2-18.3). The mean age at disease diagnosis was 10.9 years ± 2.5 SD (range 5-14.6) and the time of disease evolution was 3.5 years ± 2.1 SD (range 0.1-8). None of the patients had active disease at the time of evaluation.

As for the complications caused by the disease, the following were observed in different patients: bowel resection due to stenosis, surgical intervention due to perianal Crohn's disease, pancytopenia due to azathioprine, and herpetic esophagitis.

At the time of the psychological evaluation, all patients were receiving some pharmacological treatment. Most were being treated with azathioprine (42.3%) and/or mesalazine (34.6%). 76.9% of the patients were receiving a single drug while 23% (6 patients) were receiving combined treatment with two or three drugs. One patient was on treatment with adalimumab, mesalazine, and azathioprine, 2 patients with mesalazine and azathioprine, 2 patients with methotrexate and ustekinumab, and one patient with adalimumab and azathioprine. 9 patients (34.6%) received treatment with biologic drugs (5 patients received adalimumab, 2 patients ustekinumab, one patient infliximab, and one patient vedolizumab).

The CPQ questionnaire was applied to 2 patients (age 8 and 12 years) and the HSPQ to 24 patients (age between 12 and 18 years), subsequently, all patients were analyzed as a whole according to the first- and second-order factors of the HSPQ. The personality

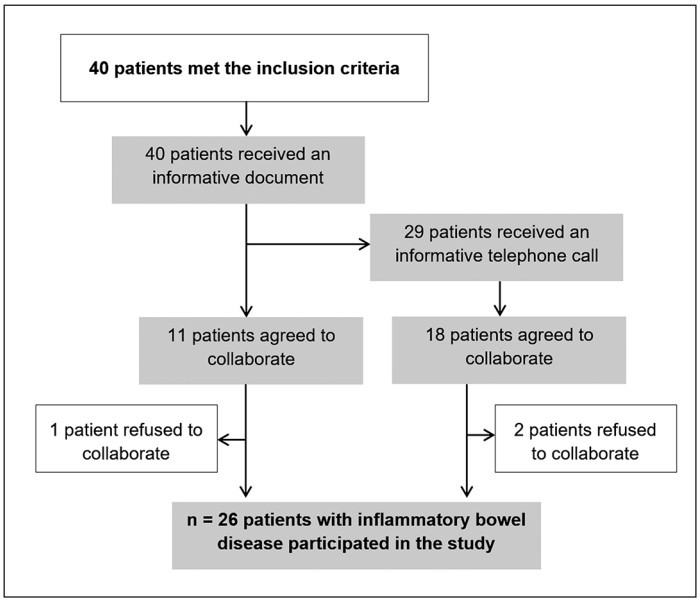

Figure 1. Diagram of patients included in the study.

profile of all patients was characterized as open, emotionally stable, calm, temperate, sensible, enterprising, impressionable, dependent, peaceful, perfectionist, and relaxed (table 1). In contrast, no patient scored in excitability (understood as impatient, demanding, hyperactive, or uninhibited) or in tough-mindedness (understood as little sympathy for the needs of others or rejection of illusions). Likewise, no patient was poorly integrated (a person who follows her/his own needs). 50% of CD patients (n = 8) were enterprising, while no UC patients scored on this factor. This difference was statistically significant (p = 0.0095).

There were no statistically significant differences when comparing the other first-order personality factors according to the type of IBD, sex, or age (table 2).

Regarding the second-order factors, the sample was characterized by low adjustment or anxiety (the subject scoring in this area usually finds life rewarding and succeeds in accomplishing what she/he believes to be important), introversion (tendency to be reserved, self-sufficient, inhibited), calm (adaptable, submissive, temperate, cautious, impressionable, not very expressive), and dependence (passive, group-driven). No patient scored on excitability or independence (table 3). Patients with CD had more adjustment and more calmness than patients with UC (50% and 62.5% vs. 20% and 20% respectively, p = 0.0511). On the other hand, patients with UC were more introverted than those with CD (40% vs. 6.3%, p = 0.0549). Although these differences did not reach significance, there was a statistical trend. There were no statistically significant differences when comparing the second-order factors according to sex or age (table 3).

Concerning the state anxiety, the STAIC questionnaire was applied to 16 patients and the STAI questionnaire to 10 patients, according to age. The whole sample of patients presented a state anxiety level (A/S) -1.1 ± 0.8 SD compared with the mean of the general standardized population. The level of anxiety as a trait (A/T) of the whole sample of patients was -0.6 ± 1 SD compare with the mean of the general standardized population. Comparing by age group, both A/S and A/T were lower in children than in adolescents (table 4). However, no statistically significant differences were found according to age. Patients with CD, both children and adolescents, had lower levels of A/S and A/T than children and adolescents with UC. This difference was less present in children in the case of A/T (table 4). However, there were no statistically significant differences when comparing A/S and A/T according to the type of IBD. Males, regardless of age, had lower levels of A/S and A/T than females (table 4). In this case, a statistically significant difference was observed for A/S (p = 0.0331) with higher anxiety scores in female patients.

Table 1. HSPQ Questionnaire. Total results in first-order personality factors

Scale	High score (positive) n (%)	Low score (negative) n (%)
Sociability	7 (26.9)	4 (15.4)
Ego-strength	10 (38.5)	2 (7.7)
Excitability	0 (0)	8 (30.8)
Dominance	4 (15.4)	4 (15.4)
Enthusiasm	3 (11.5)	7 (26.9)
Conscientiousness	6 (23.1)	3 (11.5)
Venturesome	8 (30.8)	1 (3.8)
Sensitivity	10 (38.5)	0 (0)
Individualism	4 (15.4)	2 (7.7)
Apprehensiveness	1 (3.8)	10 (38.5)
Self sufficiency	3 (11.5)	3 (11.5)
Will power	7 (26.9)	0 (0)
Tension	1 (3.8)	9 (34.6)

*HSPQ: High School Personality Questionnaire.

Discussion

The study included patients with IBD of different sex, age, socioeconomic level, race, cultural level, and area of residence (rural and urban). Despite the great heterogeneity of the sample, we found a series of common personality traits. The personality profile of the patients, as a group, was characterized by being open, emotionally stable, calm, temperate, sensible, enterprising, impressionable, dependent, peaceful, perfectionist, and relaxed. It is striking that despite being common traits in the population, none of the patients scored in excitability, tough-mindedness, or lack of perfectionism. Half of the patients with CD were enterprising as opposed to none of the patients with UC, considering this difference statistically significant.

The enterprising personality trait is defined as a socially daring person, not inhibited or shy. Regarding the second-order factors according to the type of disease, we observed a statistical trend in the factors calmness and introversion. Patients with CD tend to be calmer and patients with UC tend to be more introverted. These findings contrast with those of a 2016 study which included 108 adult IBD patients that showed greater extroversion in UC patients. However, as occurs in our study, this difference was not statistically significant[18]. In this study, it was found that patients with CD present greater control of negative emotions

Table 2. HSPQ Questionnaire. First-order personality factors

Scale	High score (positive) n (%)		Low score (negative) n (%)	
	CD n = 16	UC n = 10	CD n = 16	UC n = 10
Sociability	3 (18.75)	4 (40)	3 (18.75)	1 (10)
Ego-strength	8 (50)	2 (20)	0 (0)	2 (20)
Excitability	0 (0)	0 (0)	6 (37.5)	2 (20)
Dominance	2 (12.5)	2 (20)	1 (6.25)	3 (30)
Enthusiasm	1 (6.25)	2 (20)	5 (31.25)	2 (20)
Conscientiousness	4 (25)	2 (20)	2 (12.5)	1 (10)
Venturesome	8 (50)	0 (0)	0 (0)	1 (10)
Sensitivity	4 (25)	6 (60)	0 (0)	0 (0)
Individualism	2 (12.5)	2 (20)	2 (12.5)	0 (0)
Apprehensiveness	0 (0)	1 (10)	7 (43.75)	3 (30)
Self sufficiency	1 (6.25)	2 (20)	3 (18.75)	0 (0)
Will power	4 (25)	3 (30)	0 (0)	0 (0)
Tension	0 (0)	1 (10)	6 (37.5)	3 (30)

Scale	High score (positive) n (%)		Low score (negative) n (%)	
	Children n = 16	Adolescents n = 10	Children n = 16	Adolescents n = 10
Sociability	6 (37.5)	1 (10)	2 (12.5)	2 (20)
Ego-strength	6 (37.5)	4 (40)	1 (6.25)	1 (10)
Excitability	0 (0)	0 (0)	5 (31.25)	3 (30)
Dominance	1 (6.25)	3 (30)	2 (12.5)	2 (20)
Enthusiasm	2 (12.5)	1 (10)	4 (25)	3 (30)
Conscientiousness	4 (25)	2 (20)	2 (12.5)	1 (10)
Venturesome	5 (31.25)	3 (30)	0 (0)	1 (10)
Sensitivity	5 (31.25)	5 (50)	0 (0)	0 (0)
Individualism	2 (12.5)	2 (20)	2 (12.5)	0 (0)
Apprehensiveness	0 (0)	1 (10)	6 (37.5)	4 (40)
Self sufficiency	2 (12.5)	2 (20)	3 (18.75)	0 (0)
Will power	4 (25)	3 (30)	0 (0)	0 (0)
Tension	1 (6.25)	0 (0)	7 (43.75)	2 (20)

Scale	High score (positive) n (%)		Low score (negative) n (%)	
	Male n = 19	Female n = 7	Male n = 19	Female n = 7
Sociability	7 (36.8)	0 (0)	3 (15.8)	1 (14.3)
Ego-strength	8 (42.1)	2 (28.6)	1 (5.3)	1 (14.3)
Excitability	0 (0)	0 (0)	7 (36.8)	1 (14.3)
Dominance	3 (15.8)	1 (14.3)	3 (15.8)	1 (14.3)
Enthusiasm	3 (15.8)	0 (0)	5 (26.3)	2 (28.6)
Conscientiousness	5 (26.3)	1 (14.3)	2 (10.5)	1 (14.3)
Venturesome	6 (31.6)	2 (28.6)	0 (0)	1 (14.3)
Sensitivity	8 (42.1)	2 (28.6)	0 (0)	0 (0)
Individualism	2 (10.5)	2 (28.6)	2 (10.5)	0 (0)
Apprehensiveness	0 (0)	1 (14.3)	9 (47.4)	1 (14.3)
Self sufficiency	1 (5.3)	2 (28.6)	3 (15.8)	0 (0)
Will power	5 (26.3)	2 (28.6)	0 (0)	0 (0)
Tension	1 (5.3)	0 (0)	6 (31.6)	3 (42.8)

*HSPQ: High School Personality Questionnaire; IBD: inflammatory bowel disease; CD: Crohn's disease; UC: ulcerative colitis.

Table 3. HSPQ Questionnaire. Second-order personality factors

Scale	High score (positive) n (%)	Low score (negative) n (%)
Anxiety	2 (7.7)	10 (38.5)
Extroversion	4 (15.4)	5 (19.2)
Excitability	0 (0)	12 (46.1)
Independence	0 (0)	2 (7.7)

Scale	High score (positive) n (%)		Low score (negative) n (%)	
	CD n = 16	UC n = 10	CD n = 16	UC n = 10
Anxiety	1 (6.25)	1 (10)	8 (50)	2 (20)
Extroversion	4 (25)	0 (0)	1 (6.25)	4 (40)
Excitability	0 (0)	0 (0)	10 (62.5)	2 (20)
Independence	0 (0)	0 (0)	1 (6.25)	1 (10)

Scale	High score (positive) n (%)		Low score (negative) n (%)	
	Children n = 16	Adolescents n = 10	Children n = 16	Adolescents n = 10
Anxiety	0 (0)	2 (20)	7 (43.75)	3 (30)
Extroversion	4 (25)	0 (0)	3 (18.75)	2 (20)
Excitability	0 (0)	0 (0)	8 (50)	4 (40)
Independence	0 (0)	0 (0)	1 (6.25)	1 (10)

Scale.	High score (positive) n (%)		Low score (negative) n (%)	
	Male n = 19	Female n = 7	Male n = 19	Female n = 7
Anxiety	1 (5.3)	1 (14.3)	7 (36.8)	3 (42.8)
Extroversion	4 (21)	0 (0)	2 (10.5)	3 (42.8)
Excitability	0 (0)	0 (0)	3 (15.8)	2 (28.6)
Independence	0 (0)	0 (0)	1 (5.3)	1 (14.3)

*HSPQ: High School Personality Questionnaire; IBD: inflammatory bowel disease; CD: Crohn's disease; UC: ulcerative colitis.

compared with patients with UC. In our sample, we observed that patients with IBD tend to be emotionally stable, especially patients with CD, which would be in line with the results obtained in such a study.

Other studies have shown that most of the patients with IBD are uncomfortable in the presence of others. According to Haller et al, people with IBD generally remain "closed" in their environment and have a small support network consisting mainly of their close family[18,19]. As Haller concludes, most of our patients limit their relationships to a narrower circle of trust although in general, they tend to be open and participative.

Similar to what has been described in other studies[1,4,6,10], our sample significantly scored in perfectionism. The perfectionist attitude can have a negative impact since the evolution of the disease is beyond their control, which can generate stress, favoring a vicious circle that worsens the control of the disease.

As previously described, the prevalence of anxiety symptoms and anxiety disorders in IBD is highly variable among different studies, presenting a higher prevalence of anxiety during periods of disease activity[1,20-22]. It is striking that the presence of anxiety symptoms in pediatric patients with IBD is lower than in other groups of pediatric patients with other chronic diseases. In the case of diabetes and asthma, the prevalence rates of anxiety range between 27% and 33% respectively versus 16.4% in IBD[23-25].

Table 4. STAIC and STAI Questionnaire

Scale	STAIC n = 16	STAI n = 10	Total n = 26
	Age ($\bar{x}$ ± SD) 13.1 ± 1.4	Age ($\bar{x}$ ± SD) 17.3 ± 0.9	Age ($\bar{x}$ ± SD) 14.7 ± 2.4
State anxiety ($\bar{x}$ ± SD)	-1.1 ± 0.8	-1 ± 0.7	-1.1 ± 0.8
Trait anxiety ($\bar{x}$ ± SD)	-0.7 ± 0.6	-0.5 ± 1.5	-0.6 ± 1

Scale	CD n = 16			UC n = 10		
	STAIC n = 10	STAI n = 6	Total n = 16	STAIC n = 6	STAI n = 4	Total n = 10
State anxiety ($\bar{x}$ ± SD)	-1.3 ± 0.7	-1.2 ± 0.7	-1.3 ± 0.7	-0.8 ± 1	-0.7 ± 0.6	-0.8 ± 0.8
Trait anxiety ($\bar{x}$ ± SD)	-0.7 ± 0.6	-0.7 ± 1.5	-0.7 ± 1	-0.7 ± 0.4	-0.1 ± 1.7	-0.4 ± 1

Scale	Female			Male		
	STAIC n = 3	STAI n = 4	Total n = 7	STAIC n = 13	STAI n = 6	Total n = 19
State anxiety ($\bar{x}$ ± SD)	-0 ± 1.4	-0.9 ± 0.9	-0.5 ± 1.1	-1.4 ± 0.4	-1.1 ± 0.6	-1.2 ± 0.5
Trait anxiety ($\bar{x}$ ± SD)	-0.2 ± 0.3	-0.1 ± 2	-0.2 ± 1.1	-0.8 ± 0.5	-0.7 ± 1.3	-0.8 ± 0.9

*STAIC: State-Trait Anxiety Inventory for Children; STAI: State-Trait Anxiety Inventory; CD: Crohn's disease; UC: ulcerative colitis

This same trend has been observed in adults with IBD, who present a higher prevalence of anxiety compared with the general population but lower compared with patients with other chronic diseases[26]. In addition, pediatric patients with IBD have shown to have lower rates of anxiety than adults with IBD[1,23,27,28]. These differences may be due to the longer time of disease progression in adults along with the presence of more complications derived from the disease.

Despite this, one of the main reasons for the large variability in the prevalence of anxiety disorders and anxiety symptoms in IBD patients is the absence of a single rating scale. A systematic review published in 2016 which included 66 studies, used 16 scales (5 for anxiety and depression, 6 for depression, and 5 for anxiety), yet only 2 were validated in individuals with IBD[22,26,29].

In our sample, we observed that as a group, patients with IBD presented lower levels of state anxiety compared with the mean of the Spanish population with which the questionnaire was validated, showing similar levels of anxiety as a trait to the mean of the standardized population. This stands out because, although all the patients were in the remission phase of the disease, many of them were in a period of school exams or even a situation of school bullying was reported, which could be related to a higher state of anxiety.

In contrast to our work, there are studies carried out in pediatric populations with IBD which reached high levels of anxiety symptoms. This would be the case of an Irish study carried out in 79 patients with IBD with a similar age range to our study. However, this work presents some methodological differences that could justify such differences. On the one hand, the Spence Children's Anxiety Scale (SCAS) was used to assess anxiety symptoms instead of the STAI and, on the other hand, the percentage of patients with active disease was not specified during the evaluation, and the questionnaires were filled by the patients at home and sent to the researchers instead of under the supervision of an expert psychologist[12].

In our sample, patients with CD presented lower levels of anxiety compared with patients with UC, especially in the case of anxiety as a current state, without reaching statistical significance. This contrasts with what has been published in other studies in which anxiety symptoms are more frequent in patients with CD[22,29]. Regarding sex differences, males presented significantly lower levels of anxiety as a current state than females. This result is in line with the findings of previous studies in patients with IBD which reported higher rates of anxiety in the female sex[20,21].

This study has some limitations. One of them would be related to the characteristics of the patients finally included in the study, since participation in the study was conditioned by the availability or desire of the patients to participate, which could lead to a selection bias. Initially, the project was expected to include a minimum of 40 patients who met the inclusion and

exclusion criteria. In the end, the total number of patients was reduced to 26, with only 65% of participation.

In conclusion, in this heterogeneous series of children and adolescents with IBD, we detected the presence of a common personality trait characterized by being open, emotionally stable, calm, temperate, sensible, enterprising, impressionable, dependent, peaceful, perfectionist, and relaxed. There was no greater anxiety in pediatric patients with IBD than in the reference population.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

Authors state that no economic support has been associated with the present study.

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