The Influence of the Inflammatory Bowel Diseases on the Perceived Stress and Quality of Life in a Sample of the South-Western Romanian Population

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ABSTRACT: Background: Inflammatory bowel diseases (IBD) represent a category of chronic diseases of gastrointestinal tract with a long-term evolution which includes flares and periods of remission. The aim of the study is to identify and quantify the relationship between IBD status, perceived stress, coping mechanisms, and patients QOL. Methods: Cross-sectional study on two samples consisting of 70 IBD patients monitored in the Gastroenterology Department of the Emergency Clinical County Hospital Craiova, Romania, respectively 70 healthy volunteers. Collected data include socio-demographic details, personal and familial medical history, clinical status, presumed risk factors, perceived stress (Perceived Stress Scale-PSS), coping strategies (COPE questionnaire) and Health-Related Quality of Life (HRQOL-SF-36 scale). Results: Perceived stress was considerably higher on IBD subjects (p<0.0001). The assessment of HRQOL has shown that patients had the best perception over their physical and emotional domains of SF-36 (p<0.0001), while the most often coping mechanisms used are those from the problem-focused category. Conclusions: There is a significant relationship between increased activity of IBD and higher level of stress, that led to the development of problem-focused coping strategies. We did not find a strong correlation between lower HRQOL levels and the items considered as potential risk factors.

KEYWORDS: IBD, quality of life, perceived stress, coping mechanisms, risk factors.

Background
In the category of Inflammatory bowel diseases (IBD) are included Crohn’s disease (CD), ulcerative colitis (UC), and indeterminate colitis, which represent chronic diseases of gastrointestinal tract that have a long-term course, characterized by flares and periods of remission, with two peaks of onset (a larger one between 15 to 30 years, respectively a smaller one between 50 to 70 years) [1,2].

Their etiology is supposed to be the outcome of a complex combination of genetic, environmental and psychological vulnerabilities, that may lead to an aberrant response of the immune system to intestinal microbiome, inside the intestinal wall [2-4].

The incidence and prevalence of IBD are continuously increasing worldwide, but there were recorded different values depending on geographical region, population, gen-der distribution, or industrial development of each country [3,5].

In Europe were recorded 2.2 million of IBD patients, with a prevalence rate of 505/100,000 for UC, respectively 322/100,000 for CD, the biggest rate of incidence in North-Western countries, and a very important socio-economic burden [5-8], while the epidemiological data for Romania have shown prevalence rates of 2.42/100,000 for UC and 1.51/100,000 for CD [9].

The IBD produce symptoms that affect in a very serious way the daily life of patients, including gastrointestinal pain and bleeding, severe diarrhea, reduced appetite and important loss of weight, malnutrition, fever and fatigue, as well as possible extraintestinal complications like arthritis, skin lesions and eye inflammation, all of them reflected in reduced quality of life (QoL).

These symptoms may be accompanied by psychological issues, due to disease awareness which implies feelings of incurability or possible negative evolution to worsened stages that require surgery or to malignant diseases, the burden of a lifetime treatment, disruption of life-goals, professional and familial absenteeism, loss of energy and self-esteem, fear, social stigma and isolation.

One of the most important outcomes of these negative factors is psychological stress, a
problem that needs the development of coping mechanisms in order to be solved [10-12].

The perceived stress as an individual response to difficulties is influenced by each person’s evaluations and appraisals of the stressors, thus, leading to the development and use of the coping strategies [13].

Stress was defined as “a process in which environmental demands tax or exceed the adaptive capacity of an organism, resulting in psychological and biological changes that may place persons at risk for disease” [14] or as any threat to an organism’s homeostasis, that at the same time has the important role of keeping in equilibrium the psychological and physiological balance [15].

The relationship between gastrointestinal disturbances and changes of the psychological status was mentioned for the first time in the 1930s, when it was observed that intense emotions involved exacerbation of bowel symptoms [16].

Initially IBD were considered psychosomatic diseases, lately they were viewed as organic diseases [17] while currently it is stated that psychological disturbances can augment IBD severity [18,19], in-creasing the risk of flare-ups [20,21].

Recent evidences showed that psychological issues are present both during the flares and during the period of clinical remission [22-24].

Studies on animal model have shown that stress may rise up the jejunum and colonic mucosal permeability, by altering the bacteria-host interactions [25,26].

The presumed mechanism behind this process is the dysfunction of the cholinergic system and of the mucosal mast cells [27,28].

Also, the stress-induced catecholamine secretion leads to higher levels of bacterial adhesion to mucosa [29].

There were added increased fluid secretion and immune factors the action of which resulted in increased colonic motility and defecation [17,30-33].

The clinical course of IBD can be indirectly influenced by stress, due to tendency to unhealthy behaviors like smoking, inappropriate diet, poor adherence to drug therapy, and having frequent flares as direct outcome [34-36].

As a consequence of this unfavorable course of IBD, some physical symptoms and psychological conditions like loss of bowel control, soiling, fatigue, body image issues, sexual-life issues, social alienation, dependency to care from others, disrupted professional career may lead to a lower self-esteem, feelings of uselessness or stigmatization in this group of patients [37-39].

Coping strategies are considered to be the specific efforts, behavioral and psychological, that any individual employs to master, tolerate, reduce, or minimize stressful events [40] and they were categorized mostly as either emotion focused (maladaptive) or problem focused strategies (adaptive) [13].

Many studies emphasized that in the case of IBD patients, the most used coping strategies are those passive [39,41] or escape-avoidance strategies, only few of them using problem focused coping mechanisms [42,43].

The in-appropriate coping strategies in IBD could lead to negative outcomes as distress, maladaptive behavior and poor adjustment [44,45].

The problem-focused coping strategies that aim to alter or eliminate the source of stress were proved to be more often used by the IBD patients who perceived their illness as understandable and controllable [45], while emotion-focused coping that aims to reduce the emotional distress was mostly met in patients who are denying the reality of the intestinal disease [46].

Maladaptive coping strategies have been found to be strongly associated with worsened daily professional and leisure activities or social functioning in patients with IBD [47,48], and especially with lower QoL [49].

The positive relationship between engagement coping strategies and QoL was revealed by studies where the increased use of this kind of psychological response mechanisms were associated with higher QoL [50-52].

In IBD, QoL is affected by coping strategies mentioned above, but also by other factors such as disruption of daily living, negative impact of the illness on the education and professional career of patients, social isolation due to stigma, lack of interpersonal functioning, and the disability induced by disease [53].

Patients confronted with the active disease have poorer QoL compared to those who have a quiescent disease [18,54-57].

The aim of our study was to identify and quantify the possible relationships between IBD status, the level of perceived stress, the categories of coping mechanisms used by affected individuals, respectively the way in which all of these are influencing the patients QoL.
Materials and Methods

In the period between January 2019 and June 2020, a cross-sectional study was conducted on two samples consisting of 70 patients (inpatients and outpatients) over 16 years-old, diagnosed, at least six months before the current assessment, with one of the two forms of IBD (UC, respectively CD), respectively 70 volunteers (medical students from the University of Medicine and Pharmacy of Craiova, and medical trainees from the Emergency Clinical County Hospital Craiova).

The control group was designed to consist of individuals who were not exposed to any high-level stressor, without medical conditions, aged between the limits of the biggest peak of onset of IBD [1].

The recruited individuals were under the medical supervision in the Gastroenterology Department of the Emergency Clinical County Hospital Craiova, Romania.

The study sample consisted of patients who were diagnosed only by a gastroenterologist through endoscopic exams and/or histopathological evaluation, in the above-mentioned hospital setting or in another gastroenterology clinic.

The exclusion criteria were represented by the positive history for any kind of mental illnesses or psychopharmacological treatment/psychotherapy, pregnancy, the lack of complete medical history of the patient from the first diagnosis to the moment of current assessment, and patients who did not accept to participate or who were unable to understand and sign the informed consent after they received the detailed explanations about the research to be carried out.

The recruited individuals could only participate once in the research and they were not included again if they presented to the hospital setting, where the study was done more than once during the recruitment period.

For the study purposes information was collected directly from the subjects, through a self-administered questionnaire, and included the socio-demographic details (age, gender, occupational and marital status, living environment, level of education), respectively personal and familial medical history.

The questionnaire was filled in the same day with the gastroenterological evaluation.

These data were confronted with the information collected from the medical records of each patient, for confirming the accuracy of the data obtained through questionnaires.

The assessment of the clinical status was done only by a gastroenterologist, and was based on the evidences regarding medical history and the outcomes of the current consultation.

The collected data referred to the IBD type (CD/UC), time elapsed from the onset of the disease (first diagnosis), the possible extraintestinal manifestations (type and severity), current and/or previous treatment for intestinal disease, surgical history, other comorbidities and their treatment, as well as family history for IBD.

The studied pathology was classified in our research according to the Montreal Classification [58], while at the moment of evaluation the disease activity was measured using Crohn’s Disease Activity Index (CDAI) [59] for CD, and Partial Mayo Score (pMayo) [60] for UC.

pMayo was used in order to categorize the patients as being in remission (score of 0-2) or in an active stage of the disease (score of ≥3).

Also, the active disease scores were divided into mild disease (pMayo of 3 or 4) and moderate/severe disease (pMayo ≥5).

In order to have a complete view of each subject, the questionnaire included items about the presumed risk factors for an unfavorable course of IBD such as fetal or maternal trauma at delivery, alcohol consumption, smoking, psychological trauma within family.

Patients’ subjective perception of stress was reported in our study on the 14-items version of the Perceived Stress Scale (PSS) [61].

The PSS is the most used instrument for measuring the individual perception of stress.

Its 14 items include life stressful situations and it measures the way in which individuals give response to them, as well as the level of unpredictability, loss of self-control and overloading respondents find in their lives.

Each item scores from 0 to 5, and higher scores indicate greater perceived stress [62].

Coping strategies of each recruited individual in our study have been measured and categorized using the COPE questionnaire, a 53-item index of coping comprising of 14 scales for active coping, planning, suppressing competing activities, restraint coping, seeking support for instrumental reasons, seeking social support for emotional reasons, positive reinterpretation and growth, acceptance, turning to religion, focusing on and venting emotion, denial, behavioral disengagement, mental disengagement, and a single item measure of alcohol-drug disengagement [63].
The reason behind using this inventory was that the COPE is designed for a variety of situations, most of which were associated with the effects of IBD symptoms [47].

Health-Related Quality of Life (HRQOL) was evaluated using one of the most used questionnaires in medical research and practices, the SF-36, which allows the IBD re-searcher a complete view on the functional status, well-being, and general perception of health [64].

The SF-36 has 36 items covering the following eight domains: physical functioning (10 items), role limitations due to physical problems (role physical, 4 items), social functioning (2 items), bodily pain (2 items), mental health (5 items), role limitations due to emotional problems (role emotional, 3 items), vitality (4 items), general health perceptions (5 items), and 1 item related to general health (transitional health) [65].

For the control group, the same questionnaires related to the socio-demographic data were used, respectively level of stress and HRQOL.

We have considered that since the subjects included in the control sample are healthy, the clinical data and COPE questionnaire were not relevant for the purposes of this study.

The whole procedure of the research was presented to each recruited subject by the research assistant who also was responsible to collect the filled questionnaire, and to verify if all fields have been completed.

After this check, the questionnaires with missing data were returned to the subjects in order to be completely filled.

This measure assured a zero drop-out rate.

All collected data were digitally recorded in an anonymized and secured electronic database consisting of Microsoft Excel folders.

The present study was reviewed and approved by the Ethics committees of the Emergency Clinical County Hospital Craiova and of the University of Medicine and Pharmacy of Craiova and were in line with the Helsinki Declaration.

Statistical Analysis

Statistical analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), together with the XLSTAT add-on for MS Excel (Addinsoft SARL, Paris, France) and IBM SPSS Statistics 20.0 (IBM Corporation, Armonk, NY, USA) for processing the data.

Descriptive data were described as mean±standard deviation (SD) for quantitative variables and proportions for qualitative ones.

Because the study involved a numerical comparison between 2 groups of patients that didn’t have a normal (gaussian) distribution, the nonparametric Mann-Whitney test was primarily used, instead of the Student t test, to detect significant differences between the values in the compared data series.

We used the Chi square test ($\chi^2$) to assess the differences between the study group and the control group over the other qualitative variables analyzed in this study.

Analysis of covariance (ANCOVA) was used to estimate the impact of some items considered as predictor values over questionnaire scales.

Results

According to the socio-demographic data, the study sample was characterized by a predominance of female gender (62.86%), most of the subjects being involved in a formal or informal couple relationship (72.85%), and urban residence for the majority of them (67.14%).

There were highly statistically significant differences (Chi square $p<0.001$) between study sample’s characteristics and the control sample ones for almost all items, excepting gen-der distribution (Table 1).
Table 1. Socio-demographic data of the studied population.

| Category             | Study sample | Control  | p      |
|----------------------|--------------|----------|--------|
| Age                  | 38.03±12.61  | 25.94±5.28 | <0.0001|
| Gender               | Female       | 44 (62.86%) | 41 (58.57%) | 0.6036 |
|                      | Male         | 26 (37.14%) | 29 (41.43%) |
|                      | Married      | 39 (55.71%) | 17 (24.29%) |
|                      | Couple       | 12 (17.14%) | 17 (24.29%) |
|                      | Divorced     | 6 (8.57%)   | 5 (7.14%)   |
|                      | Single       | 13 (18.57%) | 31 (44.29%) |
| Marital status       | Rural        | 23 (32.86%) | 5 (7.14%)   |
|                      | General school| 9 (12.86%) | 0 (0.00%)   |
|                      | Highschool   | 27 (38.57%) | 32 (45.71%) |
|                      | Post-secondary school | 8 (11.43%) | 0 (0.00%) |
|                      | Higher education | 26 (37.14%) | 38 (54.29%) |
|                      | Employed     | 44 (62.86%) | 38 (54.29%) |
| Residence            | Urban        | 47 (67.14%) | 65 (92.85%) |
|                      | Rural        | 23 (32.86%) | 5 (7.14%)   |
| Education            | General school| 9 (12.86%) | 0 (0.00%)   |
|                      | Highschool   | 27 (38.57%) | 32 (45.71%) |
|                      | Post-secondary school | 8 (11.43%) | 0 (0.00%) |
|                      | Higher education | 26 (37.14%) | 38 (54.29%) |
|                      | Employed     | 44 (62.86%) | 38 (54.29%) |
| Professional status  | Student      | 6 (8.57%)   | 32 (45.71%) |
|                      | Retired      | 12 (17.14%) | 0 (0.00%)   |
|                      | Unemployed   | 8 (11.43%)  | 0 (0.00%)   |

The research methodology we have followed included collecting data about personal and familial history of physical and psychological trauma, and about the adoption of the risk behaviors such as smoking and alcohol consumption, respectively. Thus, we found significant differences between the two samples related only to maternal psychotrauma, with a higher rate for the study sample, and the risk behaviors, with lower rates for the study sample, while the other items, trauma at birth and family psychotrauma, showed a slightly dominance in the study sample, but without statistical significance (Table 2).

We believe that lower rates for the risk behaviors in the study sample are due to the onset of the IBD, with the subsequent medical treatment and physicians' recommendations for reducing risky behaviors.

Table 2. Trauma and risk behaviors in the studied population.

| Category               | Study sample | Control  | p      |
|------------------------|--------------|----------|--------|
| Trauma at birth        | No           | 58 (82.86%) | 61 (87.14%) | 0.478 |
|                        | Yes          | 12 (17.14%) | 9 (12.86%) |
| Maternal psychotrauma  | No           | 45 (64.29%) | 56 (80.00%) | 0.038 |
|                        | Yes          | 25 (35.71%) | 14 (20.00%) |
| Family psychotrauma    | No           | 37 (52.86%) | 40 (57.14%) | 0.610 |
|                        | Yes          | 33 (47.14%) | 30 (42.86%) |
| Smoking                | No           | 55 (78.57%) | 35 (50.00%) | 0.0004 |
|                        | Yes          | 15 (21.43%) | 35 (50.00%) |
| Alcohol consumption    | No           | 2 (2.86%)   | 6 (8.57%)   | 0.610 |
|                        | Weekly       | 9 (12.86%)  | 14 (20.00%) |
|                        | Monthly      | 2 (2.86%)   | 8 (11.43%)  |
|                        | Occasional   | 19 (27.14%) | 28 (40.00%) |
|                        | Almost never/Never | 38 (54.29%) | 14 (20.00%) |

We have studied from the clinical point of view only the study sample. The predominant form of IBD within the diagnosed subjects was UC (84.29%), with half of the patients being in a remission stage of the disease at the moment of evaluation (51.43%), and almost a third of them with mild activity (30.00%).

According to the Montreal classification of inflammatory bowel disease it was noted that for patients with CD the A2 group of Age at diagnosis (11.43%) was predominant, respectively non-stricturing, non-penetrating behavior (B1 type-10.00%) and colonic location (8.57%).

None of these patients presented associated perianal disease. For UC, the most prominent disease extent was E1 (42.86%).

All these aspects were completed by a lack of a positive family history for this kind of pathology (97.14%).
The IBD was not a reason for a surgical intervention, only three patients underwent this procedure in the past, while corticosteroid therapy was used in half of the subjects (52.86%).

Since data from literature [66,67] emphasized the importance of the anemia in the disease’s evolution, in the process of its management and the patient’s quality of life, we also collected data regarding the hemoglobin level in our study sample.

As above-mentioned, the IBD activity was moderate or severe in 13 patients, and according to the laboratory’s results, anemia was also noticed in 11 subjects (Table 3).

**Table 3. Clinical data of the study sample.**

| Category                        | Study sample |
|--------------------------------|--------------|
| Diagnosis                       | CD 11 (15.71%)|
|                                | UC 59 (84.29%)|
| Montreal Age at diagnosis       | A2=8 (11.43%)|
|                                | A3=3 (4.29%)|
| Montreal Location               | L1=2 (2.86%)|
|                                | L2=6 (8.57%)|
| Montreal Behavior               | B1=7 (10.00%)|
|                                | B2=1 (1.43%)|
|                                | B3=3 (4.29%)|
| Montreal classification for CD  | L2=6 (8.57%)|
|                                | L3=3 (4.29%)|
|                                | B1=7 (10.00%)|
|                                | B2=1 (1.43%)|
|                                | B3=3 (4.29%)|
| Montreal classification of extent of UC | Montel Extent |
|                                | E2=12 (17.14%)|
|                                | E3=17 (24.29%)|
| CDAI                           | Remission 7 (10.00%)|
|                                | Mild activity 1 (1.43%)|
|                                | Moderate activity 8 (11.43%)|
|                                | Severe or very severe activity 2 (2.86%)|
|                                | Remission 29 (41.43%)|
|                                | Mild activity 40 (57.14%)|
|                                | Moderate activity 2 (2.86%)|
|                                | Severe or very severe activity 1 (1.43%)|
| pMayo                          | No 68 (97.14%)|
|                                | Yes 2 (2.86%)|
| Family history for IBD         | No 67 (95.71%)|
|                                | Yes 3 (4.29%)|
| Surgical history               | No 67 (95.71%)|
|                                | Yes 3 (4.29%)|
| Corticosteroids                | No 33 (47.14%)|
|                                | Yes 37 (52.86%)|
|                                | Mild (Hb=10-12g/dl) 2 (2.86%)|
|                                | Moderate (Hb=8-10g/dl) 8 (11.43%)|
|                                | Severe (Hb=<8g/dl) 1 (1.43%)|
|                                | Absent 59 (84.29%)|

The scores of the PSS, related to the perceived impact of life stressful situations, were compared between the two samples.

As scoring instructions of PSS provided, there were three categories of perceived stress (low, moderate and severe), for our study sample, the most frequent being the moderate one (65.71%), while for the control sample the low perceived stress being the characteristic one (64.29%).

This difference was statistically highly significant (p<0.0001), a similar situation being recorded also for the mean scores of the PSS (p<0.0001) (Table 4).

**Table 4. Perceived stress levels.**

| Category   | Study Sample | Control | p     |
|------------|--------------|---------|-------|
| PSS level  | Low 1 (1.43%)| 45 (64.29%)| <0.0001|
|            | Moderate 46 (65.71%)| 15 (21.43%)| <0.0001|
|            | Severe 23 (32.86%)| 10 (14.29%)| <0.0001|
| PSS Mean Scores | 32’20±5’99 | 17’83±10’39 | <0.0001 |
The assessment of the HRQOL through the SF-36 questionnaire, where the higher scores represent better mental and physical health, have shown the worse subjects’ perception on the general health (average score of 39.86±19.19), as well as on the bodily pain (44.54±30.21), respectively role physical (49.29±47.20) domains.

On the other hand, for the control sample, the most affected domain as reported by the recruited individuals was the role (69.52±41.21).

However, this domain was the only one out of the eight covered by the SF-36 where a statistically significant difference between the two studied samples could not be found (Table 5).

**Table 5. Health-related quality of life domains.**

| SF 36 Domains Scores | Study sample | Control | p   |
|----------------------|--------------|---------|-----|
| Physical             | 65.29±23.76  | 100.00±0.00 | <0.0001 |
| Role physical        | 49.29±47.20  | 100.00±0.00 | <0.0001 |
| Role emotional       | 59.52±46.76  | 69.52±41.21 | 0.1727  |
| Energy               | 52.71±20.28  | 89.64±13.11 | <0.0001 |
| Emotional            | 63.89±17.36  | 90.06±12.70 | <0.0001 |
| Social               | 59.46±35.38  | 93.04±8.68  | <0.0001 |
| Pain                 | 44.54±30.21  | 98.71±3.37  | <0.0001 |
| General              | 39.86±19.19  | 98.57±5.84  | <0.0001 |

Given the highly significant differences between the PSS and the SF-36 mean scores, both showing a worse outcome for the study group, while past trauma and risk behaviors are not more present, leads to the conclusion that the stress level and lower perceived quality of life are due to the onset of the ICD, and are not ICD’s cause.

We have considered that, for the patients included in the study sample, the level of HRQOL could be influenced by disease-related factors, such as clinical, therapeutic or psychological elements, and, accordingly we performed an ANCOVA in order to estimate the values for the SF-36 scales using as predictors the following factors: disease extent (Montreal classification for UC), corticosteroid therapy, the duration in years since the diagnosis was established, and the presence of maternal psychotrauma in the patients’ history, as the only type of trauma significantly more present in the study group (Table 6).

**Table 6. The predictive value of the health-related quality of life domains over clinical factors.**

| Goodness of fit statistic (Variable): | Physical | Role physical | Role emotional | Energy | Emotiona l | Social | Pain | General |
|--------------------------------------|----------|---------------|----------------|--------|------------|--------|------|---------|
| R²                                   | 0.041    | 0.052         | 0.067          | 0.079  | 0.068      | 0.028  | 0.036| 0.061   |
| p                                    | 0.808    | 0.716         | 0.580          | 0.481  | 0.574      | 0.908  | 0.852| 0.638   |

| Standardized coefficients (Variable): | Physical | Role physical | Role emotional | Energy | Emotiona l | Social | Pain | General |
|--------------------------------------|----------|---------------|----------------|--------|------------|--------|------|---------|
| Years of evolution                   | 0.109    | 0.076         | 0.060          | 0.047  | -0.129     | -0.107 | -0.056| 0.037   |
| Disease extent (UC)-E1               | 0.055    | 0.195         | 0.330          | 0.312  | 0.213      | 0.153  | 0.127| -0.008  |
| Disease extent (UC)-E2               | 0.117    | 0.007         | 0.121          | 0.190  | 0.240      | 0.094  | 0.062| 0.053   |
| Disease extent (UC)-E3               | 0.000    | 0.000         | 0.000          | 0.000  | 0.000      | 0.000  | 0.000| 0.000   |
| Corticosteroid therapy (No)          | 0.029    | -0.039        | -0.110         | -0.112 | -0.083     | -0.032 | 0.055| -0.140  |
| Corticosteroid therapy (Yes)         | 0.000    | 0.000         | 0.000          | 0.000  | 0.000      | 0.000  | 0.000| 0.000   |
| Maternal psychotrauma (No)           | 0.092    | -0.183        | -0.144         | -0.261 | -0.166     | -0.099 | 0.091| -0.194  |
| Maternal psychotrauma (Yes)          | 0.000    | 0.000         | 0.000          | 0.000  | 0.000      | 0.000  | 0.000| 0.000   |

| p for Model parameters (Variable):   | Physical | Role physical | Role emotional | Energy | Emotiona l | Social | Pain | General |
|--------------------------------------|----------|---------------|----------------|--------|------------|--------|------|---------|
| Years of evolution                   | 0.425    | 0.575         | 0.655          | 0.726  | 0.340      | 0.438  | 0.681| 0.782   |
| Disease extent (UC)-E1               | 0.766    | 0.291         | 0.074          | 0.089  | 0.245      | 0.412  | 0.493| 0.966   |
| Disease extent (UC)-E2               | 0.486    | 0.965         | 0.468          | 0.251  | 0.152      | 0.579  | 0.713| 0.750   |
| Disease extent (UC)-E3               | 0.844    | 0.788         | 0.452          | 0.440  | 0.566      | 0.828  | 0.711| 0.339   |
| Corticosteroid therapy (No)          | 0.539    | 0.220         | 0.330          | 0.079  | 0.261      | 0.510  | 0.543| 0.192   |
| Corticosteroid therapy (Yes)         | 0.000    | 0.000         | 0.000          | 0.000  | 0.000      | 0.000  | 0.000| 0.000   |

10.12685/CHSJ.48.01.01
The following model equations were obtained by ANCOVA:

- Physical = 56.95334 + 0.53316 * Years of evolution + 2.54859 * Disease extent (UC) E1 + 6.78220 * Disease extent (UC) E2 + 1.34364 * Corticosteroid therapy (No) + 4.29166 * Maternal psychotrauma (No);
- Role physical = 49.78278 + 0.74518 * Years of evolution + 18.11293 * Disease extent (UC) E1 + 0.85427 * Disease extent (UC) E2 - 2.54859 * Disease extent (UC) E1 + 8.41427 * Disease extent (UC) E2 - 2.31339 * Disease extent (UC) E1 - 10.51066 * Disease extent (UC) E2 - 4.47701 * Disease extent (UC) E1 - 9.47278 * Disease extent (UC) E2 - 8.41427 * Disease extent (UC) E1 - 4.67827 * Disease extent (UC) E2 - 3.31503 * Corticosteroid therapy (No) + 5.55095 * Maternal psychotrauma (No);
- Emotional = 64.95932 - 0.46036 * Years of evolution + 7.24518 * Disease extent (UC) E1 + 13.91143 * Disease extent (UC) E2 - 10.16317 * Corticosteroid therapy (No) - 5.68672 * Maternal psychotrauma (No);
- Energy = 51.68151 + 0.19717 * Years of evolution + 12.50660 * Disease extent (UC) E1 + 9.47278 * Disease extent (UC) E2 - 4.47701 * Disease extent (UC) E1 + 0.85427 * Disease extent (UC) E2 - 3.65960 * Disease extent (UC) E1 - 2.46458 * Disease extent (UC) E2 - 5.24170 * Corticosteroid therapy (No) - 7.29938 * Maternal psychotrauma (No);
- Social = 62.06254 - 0.80847 * Years of evolution + 11.00962 * Disease extent (UC) E1 + 8.41427 * Disease extent (UC) E2 - 3.31503 * Corticosteroid therapy (No) - 7.17655 * Maternal psychotrauma (No);
- General = 45.46897 + 0.14689 * Years of evolution - 2.85805 * Disease extent (UC) E1 - 4.67827 * Disease extent (UC) E2 + 3.31503 * Corticosteroid therapy (No) + 5.55095 * Maternal psychotrauma (No);
- Pain = 35.69495 - 0.35877 * Years of evolution + 7.71331 * Disease extent (UC) E1 + 6.78220 * Disease extent (UC) E2 + 1.34364 * Corticosteroid therapy (No) - 7.17655 * Maternal psychotrauma (No);
- Alcohol = 42.48716 - 0.88106 * Years of evolution - 2.85805 * Disease extent (UC) E1 + 1.34364 * Corticosteroid therapy (No) + 5.55095 * Maternal psychotrauma (No);
- Substance = 40.88716 - 0.88106 * Years of evolution - 2.85805 * Disease extent (UC) E1 + 1.34364 * Corticosteroid therapy (No) + 5.55095 * Maternal psychotrauma (No);

Unfortunately, the model equations did not provide a sufficient goodness of fit (p>0.05 for all models), and none of the independent variables used as estimates held a significant influence over the SF-36 scales (Table 6).

The coping strategies as evaluated by the COPE questionnaire were grouped, according to the scoring methodology, in the following categories: problem-focused coping mechanisms, emotion-focused coping mechanisms, maladaptive coping mechanisms, respectively alcohol/substance use.

For our study sample, the behavioral and psychological strategies that individuals are using to minimize the stressful effects of the IBD were mostly focused on the problems represented by the disease (average COPE-score of 2.85±0.56), in a different way that the one mentioned by previous studies [10,41].

The maladaptive mechanisms, including also the use of psychoactive substances and alcohol, were the latest in terms of favorite instruments used for individual adjustment to the psychological stress (Table 7).

### Table 7. Coping strategies as evaluated by the COPE questionnaire.

| Coping mechanisms | COPE 1 | COPE 2 | COPE 3 | COPE 4 | COPE 5 | COPE 6 | COPE 7 |
|-------------------|--------|--------|--------|--------|--------|--------|--------|
| Problem-focused (average) | 3.12±0.71 | 3.24±0.76 | 2.84±0.77 | 1.93±1.44 | 3.12±0.67 | 2.65±0.79 | 3.10±0.67 |
| Emotion-focused (average) | 3.13±0.79 | 2.04±0.61 | 2.27±0.81 | 2.70±1.00 | 2.54±0.73 | 2.03±0.49 | 1'1'±0.40 |
| Maladaptive coping | 14.24±2.78 (2.85±0.56) | 13.61±2.46 (2.72±0.49) | 6.84±1.62 (2.28±0.54) | |

### Discussion

The purpose of this cross-sectional study was to identify the possible correlations between the clinical variables and psychological ones in patients with IBD.

More than that, we have followed the subjective level of disease impact and stress perception over the patient’s quality of life and its relationship with the biological aspects.

As previous studies have shown, the IBD course and symptoms are often influenced by psychological conditions [68], even if there is not yet very consistent scientific evidence in support of this hypothesis [69].

Regarding the socio-demographic characteristics of our study sample, we could consider that only the age of the subjects fits into the literature-mentioned coordinates, as long as we had patients with average age of 38.03±12.61 years, similar to the epidemiological data [1].

It was interesting to find out that, in terms of psycho-traumatic events noticed in the personal history of the patients, the trauma associated with the experiencing or witnessing of a violent
or dangerous events within their family is directly correlated with the development of IBD [70,71].

More than that, according to the previously published researches, childhood trauma and physical abuse are associated with the onset of UC, respectively higher IBD incidence [72-74].

Despite this evidence, for our study sample, the history of any kind of trauma (obstetrical, maternal or family) was not significantly associated with the other evaluated items (p>0.05).

Risk behaviors such as smoking and/or alcohol consumption are associated with IBD, in one case as protective factors (smoking for UC [75] and moderate alcohol intake for IBD [76,77]), and at the other as risk factors [75,78].

We found out highly significant differences between the study sample and the control group, regarding these two lifestyle factors (p<0.001), in terms of predominance for both smoking and alcohol consumption within control subjects.

This lack of association between development of IBD and the risk behaviors is consistent with the results of previous studies that showed no association between alcohol and IBD [79,80].

At the same time, we did not find any significant correlation between alcohol/substance consumption, used as coping mechanism, and the other items measured in our research.

Some other clinical characteristics that were present in our patients, such as use of corticosteroids or anemia, were not significantly correlated with the impact of IBDs on the HRQOL or perceived stress level.

These findings are opposites to the literature, which maintained that anemia associated with IBD has a serious impact on patients’ QOL [65], while corticosteroid therapy has also important effects especially on the individuals diagnosed with IBD psychological status [81].

Research on the pathophysiological mechanisms of IBD have lately emphasized that psychological stress is directly correlated with intestinal disease, being revealed extensive evidence that showed a reciprocal influence between IBD and this psychological condition [82].

The long-term evolution of stress, from the period of childhood to adult life, seems to be the source of an earlier onset of IBD [83], that could lead to severe complications represented by the psychiatric diseases [84,85].

Despite of this evidence, for our study sample, we could not identify any significant correlation between severity of perceived stress and the duration of IBD evolution (p>0.05).

Previous studies underlined that the higher levels of perceived stress are associated with increased disease activity in subjects with IBD [24].

Moreover, the perceived stress is mirroring the impact of the IBD meaning of threat, over the individual in the context of poor coping mechanisms.

Our results on measuring the perceived stress levels through PSS did show a direct highly significant correlation between PSS scores and IBD activity, as measured by CDAI/Mayo scores (p<0.00001).

Thus, our findings are consistent with previously published studies on this topic, which showed that higher levels of perceived stress were associated with a greater likelihood of increased activity of IBD [34,86,87].

The influence existing between level of stress and the development of coping mechanisms is considered an intrinsically one, or better said a cause-effect type relationship.

As it was mentioned above, the IBD is strictly connected to distress and other psychological issues, which are affecting even the natural history of these chronic intestinal conditions [33,88,89].

In this context, it was showed that the coping mechanisms which patients with IBD are adopting may vary from passive and escape-avoidance strategies [90] to active, optimistic and self-reliant ones [42].

The patients from our study sample had used a predominant problem-focused coping mechanism that is mentioned by other studies to be significantly positive correlated the increased disease severity, while similar to our results was not strongly associated with emotion-focused coping [91].

Based on these results, we could consider that the psychological impact of the intestinal disease is more important as the severity of symptoms is increasing, and the most prominent way to cope with it seems to be the active involvement in the solving of the problem (p<0.05).

More than that, there were found evidences that problem-focused coping mechanism could lead to an increased quality of life as perceived by the affected individuals through a reduction in the level of distress induced by IBD [52,90].
Another aspect directly influenced by the IBD symptoms severity and, even more importantly, by the level of psychological distress is the quality of life, facts mentioned by numerous previous studies [38,92].

For our patients, the subjective perception over the HRQOL had maximum levels for physical (65.29±23.76), respectively emotional (63.89±17.36) domains as assessed by SF-36 while for the control group the best scores were recorded for both physical and role physical domains (100.00±0.00) (Table 5).

Many longitudinal studies underlined that HRQOL of the IBD patients have a positive trajectory over time, being worse in the period consecutively to the diagnosis moment, with a later significant improvement [48,93,94].

Our cross-sectional study could not prove a significant correlation between the duration of the disease and the HRQOL, probably due to variability of the time-interval between diagnosis and evaluation moment (5.30±4.72 years).

Even if other studies noticed that the disease severity, respectively level of distress are determinants of the quality of life, facts mentioned by our study sample we could not find significant correlations between HRQOL scores and these factors [47].

Conclusions

Our study has revealed significant aspects related to the impact of IBD at the individual level in terms of perceived stress and affected quality of life.

The increased activity of the disease represents a determinant of the higher level of stress, which our patients have dealt with by using problem-focused coping mechanisms.

Even if the patients QOL was lower compared to the control, the items considered as potential factors that are deter-mining the reducing of QOL in IBD patients were not statistically significant.

Conflict of interests

None to declare.

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