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*Otilia GAVRILESCU, Cătălina MIHAI, Dana Teodora ANTON - PADURARU,
Stefana MOISA, Anamaria CIUBARA, Cristina CIJEVSCHI-PRELIPCEAN*

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Impact of Inflammatory Bowel Diseases on Quality of Life

Otilia GAVRILESCU¹, Cătălina MIHAI², Dana Teodora ANTON - PADURARU³,
Stefana MOISA⁴, Anamaria CIUBARA⁵, Cristina CIJEVSCHI-PRELIPCEAN⁶

Abstract

This study aims to assess the impact of inflammatory bowel diseases (IBD): ulcerative colitis (UC) and Crohn's disease (CD) on the patients' quality of life (QoL) and to identify the significant changes in QoL depending on the developmental particularities of IBD and the epidemiological parameters. A prospective study was conducted over a period of 36 months (October 2011 – October 2014) at the Institute of Gastroenterology and Hepatology, Iasi. The study was conducted on 254 patients diagnosed with IBD, 187 patients with UC and 67 patients with CD. The quality of life was assessed using the questionnaire IBDQ-32 (Inflammatory Bowel Disease Questionnaire), which is one of the most widely used questionnaires in QoL assessment. The total IBDQ score was slightly more reduced in the patients with UC compared to the patients with CD. Of the 4 subscales of the IBDQ score, the scores highlighting the emotional and social component were significantly more reduced in the patients with UC, while the scores for the bowel symptoms were significantly more reduced in the patients with CD. In both the patients with UC and with CD, the correlations between the UCDAI, respectively CDAI score and the IBDQ score were indirect, highlighting reduced values of IBDQ in patients with a severe activity of the disease. The severe flare of the disease had a negative impact on the patients' QoL. The present

¹ University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Gastroenterology, Iasi, ROMANIA. E-mail: otilianedelciuc@yahoo.com

² University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Gastroenterology, Iasi, ROMANIA. E-mail: catalinamihai@yahoo.com

³ University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Paediatrics, Iasi, ROMANIA. E-mail: antondana66@yahoo.com

⁴ University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Paediatrics, Iasi, ROMANIA. E-mail: stephaniemed@yahoo.com

⁵ University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Psychiatry, Iasi, ROMANIA. E-mail: anamburlea@yahoo.com (corresponding author)

⁶ University of Medicine and Pharmacy "Grigore.T.Popa" Iasi, Faculty of Medicine, Department of Gastroenterology, Iasi, ROMANIA. E-mail: cristinacijevschi@yahoo.com

study confirms the fact that the activity of the disease is the factor likely to have the highest impact on QoL in IBD patients.

Keywords: inflammatory bowel diseases, ulcerative colitis, Crohn's disease, quality of life.

Introduction

Inflammatory bowel diseases (IBD), represented by the two entities – ulcerative colitis (UC) and Crohn's disease (CD) are chronic diseases, with a relapsing course, marked by diseases flare, followed by periods of remission, sometimes even with total remission of the disease. Although they are chronic disorders, likely to trigger important morbidities, IBD do not influence general mortality significantly. Despite its ongoing development, the treatment of these disorders was especially oriented towards the disease flare. Thus, less interest was shown to the chronic aspects involved in IBD, such as: the psycho-social burden of chronic disorders, the quality of life (QoL) and its specific psychological comorbidities, limitation of social life, professional and emotional activities (Andrews *et al.*, 2010). However, over the last period, there has been growing awareness on the chronic nature of IBD and its underlying psycho-social implications, aspects that had been previously less known, or even ignored by the medical system (Andrews *et al.*, 2010). Although the incidence peak of IBD is comprised within the 20 to 40 years bracket (Agostini *et al.*, 2014), most patients outlive this time frame, despite the significant comorbidities associated. Life expectancy in patients with UC is the same as in the case of the general population; for the patients with CD, a slightly increased mortality was reported (Travis, 1997). The psycho-social impact of chronic diseases is always difficult to assess, especially due to the multifactorial nature of the psychological and social interactions, where a patient's disease is just one of the important variables (Pizzi *et al.*, 2006). More than 20 years ago, it was proven that IBD was likely to impact the QoL (Casellas *et al.*, 2000). Since then, various instruments approved for QoL assessment have been used, including questionnaires specific to certain diseases. Studies have pointed to the fact that an improvement in the patients QoL is inversely proportional to the activity of the disease (Casellas *et al.*, 2000, Lix *et al.*, 2008). Consequently, irrespective of the type of treatment – medical or surgical – remission contributes to improving QoL. Disease remission seems to increase the QoL score in all fields, not just in the field of abdominal symptoms, but also in systemic, social symptoms, or the physical and emotional function. However, the QoL score is still more reduced in the patients with IBD in remission, compared to the general population (Mikocka-Walus *et al.*, 2008). As far as sexual dysfunction is concerned, there is a limited number of studies on this subject. Nevertheless, surveys have shown that sexual

dysfunction is rather frequently met in patients with IBD (75% - women, 44% - men) (Moody *et al.*, 1993; Timmer *et al.*, 2007). Another interesting finding points to the fact that depression constitutes the most important factor causing sexual problems in case of both sexes. The fear of sexual rejection is more frequently met in women with IBD (Basson, 1998), while reluctance in approaching this subject was often met in both men and women (Dubinsky, 2007; Sorensen *et al.*, 1987). The present study aims to assess the impact of IBD (UC, CD) on the patients' QoL and to identify the significant changes in QoL depending on the developmental particularities of IBD and the epidemiological parameters.

Material and method

A prospective study was conducted over a period of 36 months (October 2011 – October 2014) at the Institute of Gastroenterology and Hepatology, Iai. The study was conducted on 254 patients diagnosed with IBD, 187 patients with UC and 67 patients with CD. The UC or CD diagnosis was supported by complete hematological, biochemical tests, endoscopic and imagistic examinations, as well as histopathology confirmation. The activity of the disease was quantified by means of the UCDAI/ CDAI score.

The quality of life was assessed using the questionnaire IBDQ-32 (Inflammatory Bowel Disease Questionnaire), which is one of the most widely used questionnaires in QoL assessment. The questionnaire contains 32 questions grouped into four fields: bowel symptoms (diarrhea, abdominal pain, rectal bleeding, and urgency), systemic symptoms (fatigue, sleep disorders), emotional functions (depression, irritability, anger) and social functions (absenteeism, affected social status, sexual activity). The answers were marked on a scale from 1 (the worst) to 7 (the best). The total score ranged between 32 and 224. The lowest the score, the most affected the QoL.

Statistical analysis

The data was centralised in the SPSS 18.0 database and processed with the adequate statistical functions. In the statistical analysis, both descriptive and analytical methods were used: the ANOVA test, the t-Student test, the c^2 test, or the Pearson (r) correlation coefficient.

Ethical aspects

All patients enrolled in the study signed an informed consent, which explained details about the purpose of the study, its methodology, the risks and benefits involved in the study, as well as information regarding the confidentiality of the results.

Results

The demographic structure of the study sample is given in *Table 1*. In statistical terms, there were no significant differences in the demographic parameters between patients with UC and CD (*Table 2*). Most patients with UC and CD came from the rural environment and were married. The sex distribution was approximately equal in the sample of patients with CD, while in the sample of patients with UC, the number of male patients prevailed (58%). The average age was 45.59 years old in the patients with UC and 43.57 in the patients with CD. The non-smoking status was preponderant in both groups (61% - UC, 52.2 % - CD).

Table 1. *Demographics*

	UC 187 patients	CD 67 patients
Sex	M - 110 patients (58.8%) F - 77 patients (41.2%)	M - 33 patients (49.3%) F - 34 patients (50.7%)
Age	45.59±14.92 (extremes 18-76 years old)	43.57±15.58 (extremes 19-82 years old)
Background	urban 125 patients (66.8%) rural - 62 patients (43.2%)	urban - 52 patients (77.6%) rural - 15 patients (22.4%)
Marital status	married 150 (80.2%); single 37 (19.8%)	married 49 (73.1%) single 18 (26.9%)
Smoker/ non-smoker	smoker - 73 patients (39%) non-smoker - 114 patients (61%)	smoker: 32 patients (47.8%) non-smoker: 35 patients (52.2%)

Table 2. *Structure of samples based on demographics*

Characteristics	UC Group (n=187)	CD Group (n=67)	Statistical differences (p)
Male, n (%)	110 (58.8%)	33 (49.3%)	0.226
Average age (min-max)	45.59±14.92 (18-76)	43.57±15.58 (19-82)	0.800
Urban environment, n (%)	125 (66.8%)	52 (77.6%)	0.136
Married, n (%)	150 (80.2%)	49 (73.1%)	0.301
Smoker, n (%)	73 (39.0%)	32 (47.8%)	0.271

Most patients with UC presented mild and moderate forms of disease; only 16.5% were in remission and 22.5% of the patients had severe forms of the disease. Compared with UC, severe forms of CD were found in a smaller percentage (6% of cases); most patients with CD presented moderate forms of the disease (Table 3).

Table 3. Structure of samples based on disease activity

Disease activity	UC 187 patients		CD 67 patients	
	n	%	n	%
Remission	31	16,5	17	25,4
Mild	57	30,5	20	29,8
Moderate	57	30,5	26	38,8
Severe	42	22,5	4	6,0

The total IBDQ score was slightly more reduced in the patients with UC compared to the patients with CD. Of the 4 subscales of the IBDQ score, the scores highlighting the emotional and social component were significantly more reduced in the patients with UC, while the scores for the bowel symptoms were significantly more reduced in the patients with CD (Table 4).

Table 4. IBDQ score – UC vs. CD

IBDQ Score	UC Group (n=187) Average score± SD(extreme)	CD Group (n=67) Average score ± SD(extreme)	P values for F _{ANOVA} test
Total score	134.74±32.52 (66-200)	138.82±31.84 (70-200)	0.376
Bowel symptoms	33.68±8.15 (15-51)	29.78±7.81 (14-46)	0.001
Systemic symptoms	33.77±8.26 (17-52)	32.39±8.01 (16-50)	0.239
Emotional functions	33.02±9.36 (11-54)	37.85±9.07 (16-58)	0.001
Social functions	34.45±8.77 (17-55)	38.42±7.99 (22-53)	0.001

In both the patients with UC and with CD, the correlations between the UCDAI, respectively CDAI score and the IBDQ score were indirect, highlighting reduced values of IBDQ in patients with a severe activity of the disease (Figure 1). The severe flare of the disease had a negative impact on the patients' QoL.

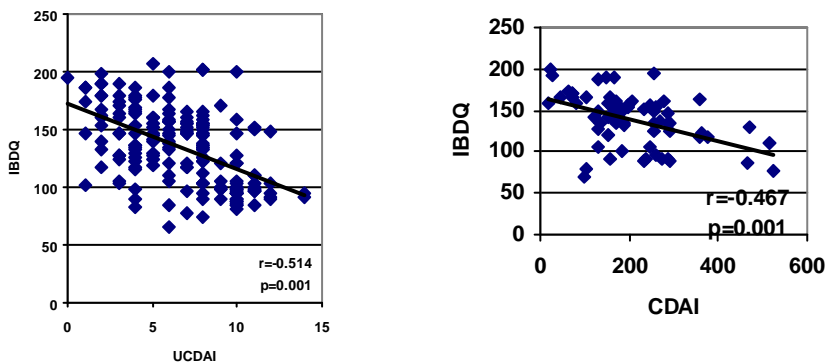


Figure 1. Correlation of the IBDQ scores with the UC/ CD activity

The age of the patients with UC was in low direct correlation with the IBDQ score; slightly higher IBDQ values were noticed in older patients, but no statistically significant differences were highlighted ($r = +0.109$; $R = 0.0118$; $p = 0.138$) (Figure 2).

Similarly, the age of the patients with CD did not correlate with the IBDQ score ($r = +0.002$; $R = 0.000006$; $p = 0.987$), (Figure 2). The lowest IBDQ score was recorded in a single patient aged under 20 years old (87), and the highest score was recorded in a single patient aged over 80 years old (158).

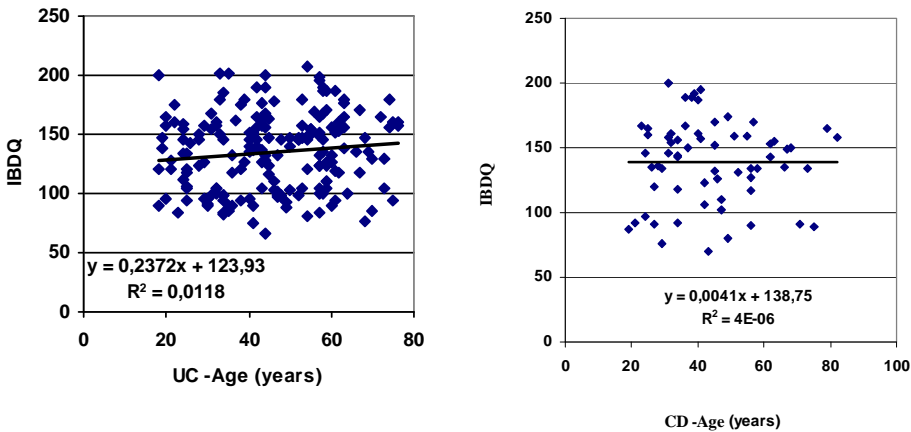


Figure 2. Correlation of the IBDQ score with age

In the patients with UC, the IBDQ score presented values ranging from 66 to 207; the extreme values were recorded in the male patients where the group average was 136.97 ± 34.68 , slightly higher compared to the one recorded in the female group, with an average of 131.56 ± 29.08 ($p = 0.264$), (Figure 3). In the patients with CD, both the average IBDQ score and its subgroups were slightly higher in the female patients with CD ($p > 0.05$), (Figure 4).

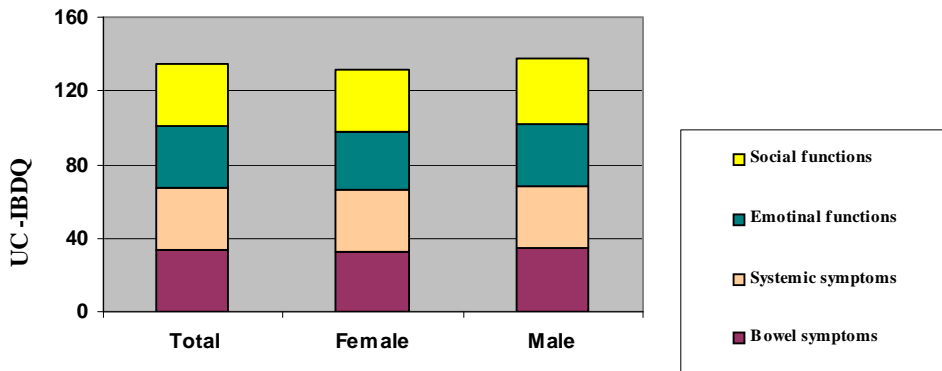


Figure 3. IBDQ score by gender, in patients with UC

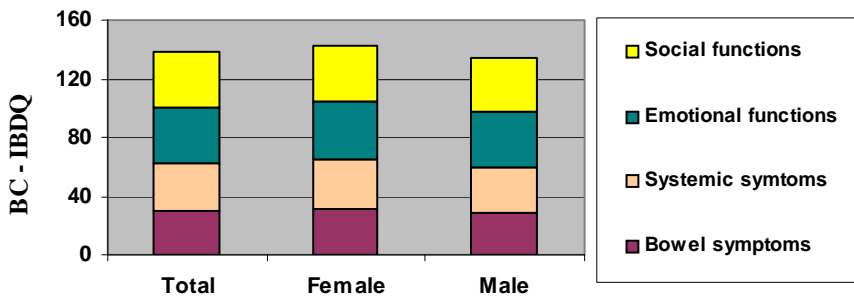


Figure 4. IBDQ score by gender, in patients with CD

In both groups, the average IBDQ score did not present significant differences between the average values recorded in smokers (UC: 133.85 ± 32.89 , CD: 133.62 ± 36.63), compared to non-smokers (UC: 135.32 ± 32.41 , CD: 143.47 ± 27.44) (UC: $p=0.764$, CD: $p=0.228$).

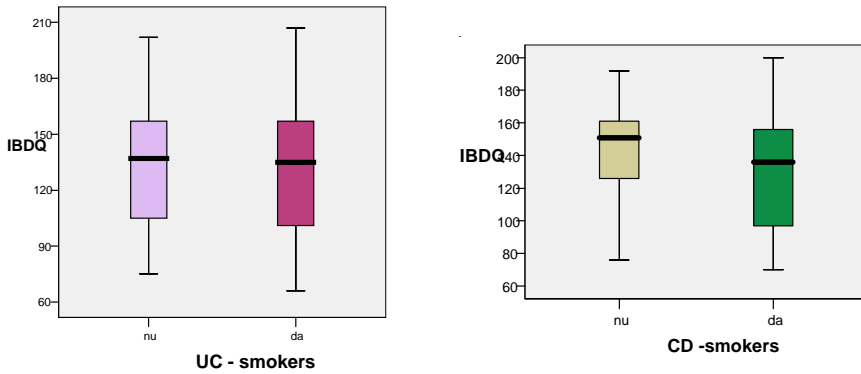


Figure 5. Average values of the IBDQ score based on smoking status

Most patients came from the urban environment (UC = 66.8%, CD = 76%). The average IBDQ score was slightly higher in the patients with UC from the urban environment (137.50 ± 31.71) compared to the number registered for the patients from the rural environment (129.19 ± 33.67) ($p = 0.100$) (Table 5). In the sample of patients with CD, the overall IBDQ score registered a slightly increased average value in the patients from the rural environment, without registering significant differences between the background environments ($p = 0.363$), (Table 6).

Table 5. UC – IBDQ total score and subscales based on background environment

IBDQ	Total sample average \pm SD (IC95%)	Urban average \pm SD (IC95%)	Rural average \pm SD (IC95%)	p
Total score	134.74 \pm 32.52 (66-207)	137.50 \pm 31.71 (77-202)	129.19 \pm 33.67 (66-207)	0.100
Bowel symptoms	33.64 \pm 8.16 (15-51)	34.61 \pm 8.06 (20-52)	32.08 \pm 8.47 (17-51)	0.062
Systemic symptoms	33.77 \pm 8.26 (17-52)	34.61 \pm 8.06 (20-52)	32.08 \pm 8.47 (17-51)	0.049
Emotional functions	33.02 \pm 9.36 (11-54)	33.52 \pm 9.25 (11-54)	32.02 \pm 9.57 (16-54)	0.302
Social functions	34.45 \pm 8.77 (17-55)	35.14 \pm 8.63 (17-55)	33.06 \pm 8.95 (18-54)	0.127

Table 6. CD – Descriptive statistical indicators of the IBDQ score based on background environment

Background environment	N	Average	Standard deviation	Standard error	Confidence interval		Min	Max	p
					-95%CI	+95%CI			
IBDQ									
rural	15	142.67	27.88	7.198	127.23	158.11	89	189	0.610
urban	48	137.77	33.51	4.837	128.04	147.50	70	200	
IBDQ-1bowel symptoms									
rural	15	30.53	7.38	1.90	26.45	34.62	16	46	0.691
urban	48	29.58	8.24	1.19	27.19	31.98	14	46	
IBDQ-2 systemic symptoms									
rural	15	33.07	7.32	1.89	29.01	37.12	19	46	0.748
urban	48	32.27	8.62	1.24	29.77	34.77	16	50	
IBDQ-3 emotional functions									
rural	15	38.93	8.13	2.10	34.43	43.43	24	48	0.611
urban	48	37.54	9.49	1.37	34.79	40.30	16	58	
IBDQ-4 social functions									
rural	15	39.73	6.84	1.77	35.95	43.52	27	48	0.462
urban	48	37.98	8.33	1.20	35.56	40.40	22	53	

Marital status did not influence QoL significantly in any of the two groups, although the IBDQ score was slightly higher in married patients (Figure 7).

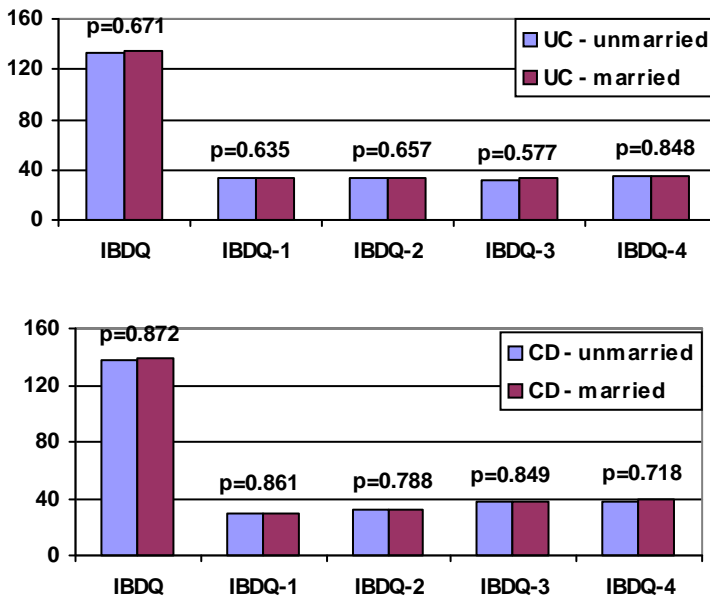


Figure 6. Average values of the IBDQ scores based on marital status in patients with UC and CD

As far as QoL depending on the type of treatment underwent is concerned, both in the patients with UC and in those with CD, corticotherapy administered during the disease activity periods was associated with lower IBDQ scores. Considering the fact that corticotherapy is administered solely during the disease activity periods, the low values of the IBDQ score can be interpreted also within the severe activity periods of the disease.

Moreover, the patients undergoing biological therapy with Ac anti-TNF- α , had a higher IBDQ score (*Tables 6 and 7*). In this sample of subjects, biological therapy was used for both inducing and maintaining remission, but the number of patients who achieved remission when assessing QoL was higher. Therefore the high QoL scores in this group of patients can be due to the weaker, or even absent symptoms.

Table 6. IBDQ score in patients with UC based on type of treatment

IBDQ score	Corticotherapy			Biological therapy		
	Yes	No	p	Yes	No	p
Total score	128.37±33.39	137.33±31.92	0.088	142.67±40.78	134.34±32.14	0.455
Bowel symptoms	31.76±8.54	34.41±7.90	0.044	35.67±10.26	33.54±8.06	0.447
Systemic symptoms	31.94±8.86	34.51±7.92	0.050	36.67±10.64	33.62±8.13	0.282
Emotional functions	31.67±9.26	33.57±9.37	0.208	35.33±11.95	32.90±9.23	0.449
Social functions	33.02±9.48	35.04±8.34	0.154	35.44±9.61	34.40±8.75	0.730

Table 7. IBDQ score in patients with CD based on type of treatment

IBDQ score	Corticotherapy			Biological Therapy		
	Yes	No	p	Yes	No	p
Total score	131.29±32.87	144.23±29.99	0.099	158.00±24.14	135.05±31.74	0.027
Bowel symptoms	28.14±7.89	30.95±7.68	0.150	35.64±6.39	28.63±7.62	0.006
Systemic symptoms	30.86±8.11	33.85±7.88	0.082	38.64±6.92	31.16±7.80	0.004
Emotional functions	35.89±9.74	39.26±8.36	0.134	40.64±7.20	37.30±9.31	0.266
Social functions	36.54±8.16	39.77±7.58	0.100	42.82±5.90	37.55±8.03	0.043

Discussions

Similarly to the data obtained from the literature, the present study confirms the fact that the disease activity is the factor likely to have the highest impact on QoL in IBD patients. To date, it has been proven that the severe activity of the disease influences negatively the QoL, both in the patients with CD and in those with UC (Zhou *et al.*, 2010; Romberg-Camps *et al.*, 2010; Mnif *et al.*, 2010; Casellas *et al.*, 2001, 2005). Moreover, the disease activity periods seem to be closely connected to fatigue and sleep disorders, the latter constituting an independent factor likely to influence QoL (Romberg-Camps *et al.*, 2010; Graff *et al.*, 2006). Under these circumstances, special attention should be paid to preserving remission. Studies have considered the use of psychotherapy in preserving disease remission; however, the effectiveness of these therapies remains controversial (Von Wietersheim *et al.*, 2006). A recent meta-analysis has shown that psychotherapy conducted on IBD patients during the disease activity periods did not influence the evolution of the disease, but it improved QoL, especially in adolescents with IBD (Timmer *et al.*, 2011). Stress reduction through psychotherapy does not determine a decrease in disease activity or the number of relapses, but it could improve QoL, especially in patients with UC (Boye *et al.*, 2011).

In the present study, both the UC and CD had a negative impact on all the aspects related to the QoL, which is likely to favour the development of depressive states and anxiety during and after periods of disease activity. The total IBDQ score in patients with UC was relatively low, compared to the sample of patients with CD. Equally, the subscores for the emotional and social components of QoL were significantly lower ($p < 0.05$) in the patients with UC, compared to the sample of patients with CD. Additionally, for the patients with CD, the bowel symptoms had a higher negative impact on the patients' QoL compared to the UC ($p < 0.05$).

Nevertheless, there are studies which demonstrated that patients with CD present more severe psycho-social dysfunctions, a lower level of wellness, anxiety and depressive states, as well as deeper effects on QoL compared to UC (Romberg-Camps *et al.*, 2010; Mnif *et al.*, 2010; Simren *et al.*, 2002).

Since the disease activity is a factor likely to have a stronger impact on QoL in patients with IBD, in our study, lower QoL scores in UC patients can be attributed to the higher number of patients with severe forms of UC compared to the patients with severe forms of CD.

The conclusion of a review on QoL in patients with CD was that QoL was more severely affected in the patients with CD compared to the control sample, or compared to the patients with UC, but also to an equal extent or even more than the patients with other medical disorders, such as rheumatoid arthritis and chronic obstructive bronchopneumopathy (Cohen *et al.*, 2002).

In the present study, the variables age, gender, and marital status did not influence the total IBDQ score and subscores. Some studies have shown that QoL is more affected in female compared to male patients with IBD (Irvine *et al.*, 1995; Casellas *et al.*, 2002; Rubin *et al.*, 2004); however, in our study, this hypothesis was not confirmed. Generally, women tend to pay more attention to the disorders they suffer from, overestimating their symptoms, being more severely affected by psychosocial factors (Maunder *et al.*, 1999; De Rooy *et al.*, 2001; Drossman *et al.*, 1989). On the other hand, even in the studies assessing QoL in the general population, women present lower QoL scores compared to men (Dimenas *et al.*, 1996). Women were generally more concerned with problems associated with their physical appearance, and the young were more concerned with the impact of the disease on their sexual life (Drossman *et al.*, 1991; Stjernman *et al.*, 2010).

Another study conducted in Sweden demonstrated that the patients with CD have the highest fears, as well as a more influenced QoL – especially in women – compared to the patients with UC. The causes of most fears were the emergence of disease complications and the lack of personal or professional achievements. The fears were higher among the female patients in all the fields of QoL assessment, except for two subjects, which did not present significant differences between the sexes: the fear regarding a possible colostomy/ ileostomy, or the lack of attractiveness (Stjernman *et al.*, 2011). It was proven that the greatest concern of the patients with IBD was the uncertain development of the disease, the side effects of the medicine, the impact of the disease on the energy level, the risk of being subject to surgical intervention, the likelihood of a stoma, the fear of becoming a burden for the others and the risk of developing a neoplasm. In the patients with CD, the main concerns were those related to vitality, being a burden for the others, not being able to reach the maximum potential, or the financial costs involved (Drossman *et al.*, 1989).

Moreover, the results of our study have shown that the smoking status did not influence QoL in the patients with IBD. However, some studies have demonstrated that smoking was associated with greater concerns and a more altered perception on the state of wellbeing among the patients with IBD (McDermott *et al.*, 2013). Another study highlighted the fact that smoking patients with CD presented lower QoL scores in all four IBDQ fields, compared to the non-smoking patients, and the male smoking patients with UC presented less intestinal disorders compared to the non-smoking patients (Russel *et al.*, 1996).

The data in the literature regarding the impact of the various types of treatment on QoL are contradictory (Romberg-Camps *et al.*, 2010; Haapamaki *et al.*, 2009; Bernklev *et al.*, 2005). In our study, corticotherapy administered during the disease activity periods was associated with lower QoL scores, while the patients under biological therapy with Ac anti-TNF- α had a higher QoL score. The aim of the

study was not to assess the effect of the treatment on QoL; therefore, QoL was assessed only in certain stages of the treatment, which would render impossible any comparison with studies directed towards these aspects only.

Nevertheless, considering the fact that corticotherapy is administered only in the disease activity periods, used for inducing remission, the low QoL scores in this sample of patients can be considered secondary to their symptomatology, and not necessarily to corticotherapy. On the other hand, biological therapy in this sample of patients was used for both inducing and maintaining remission, but the number of patients who achieved remission with biological therapy when assessing QoL was higher. Therefore the high QoL scores in this group of patients can be due to the weaker, or even absent symptoms. In another study conducted in Greece, no significant differences were noticed in the QoL scores of the patients undergoing treatment with 5-ASA derivatives, corticosteroids or immunosuppressors. However, the patients with UC treated with Ac anti-TNF- α presented lower QoL scores compared to other types of treatment. This subsample of patients showed a shorter duration of the disease and a history of surgical interventions, describing thus a higher degree of disease severity. Under these circumstances, QoL damage could be considered secondary to disease severity and not to biological therapy (Kalafateli *et al.*, 2013).

Conclusions

To conclude, the disease activity represents the factor likely to have the stronger impact on QoL in patients with IBD. The general perception on the health state in these patients is more pessimistic during the disease activity periods. The patients with UC presented relatively low IBDQ scores compared to the sample of patients with CD. Additionally, in the patients with CD, the bowel symptoms had a higher negative impact on the patients' QoL compared to UC ($p < 0.05$). Age, sex, background environment, smoking status and marital status did not influence significantly the QoL status. QoL assessment is helpful in identifying the patients requiring specialised support. Additionally, it has an important role in understanding the real impact of the disease on the patients, as well as in redefining the strategies for improving QoL in patients with IBD.

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