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QUALITY OF LIFE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: importance of clinical, demographic and psychosocial factors

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ABSTRACT – ***Context*** - Inflammatory bowel disease causes physical and psychosocial consequences that can affect the health related quality of life. ***Objectives*** - To analyze the relationship between clinical and sociodemographic factors and quality of life in inflammatory bowel disease patients. ***Methods*** - Ninety two patients with Crohn's disease and 58 with ulcerative colitis, filled in the inflammatory bowel disease questionnaire (IBDQ-32) and a questionnaire to collect sociodemographic and clinical data. The association between categorical variables and IBDQ-32 scores was determined using Student t test. Factors statistically significant in the univariate analysis were included in a multivariate regression model. ***Results*** - IBDQ-32 scores were significantly lower in female patients (P<0.001), patients with an individual perception of a lower co-workers support (P<0.001) and career fulfillment (P<0.001), patients requiring psychological support (P = 0.010) and pharmacological treatment for anxiety or depression (P = 0.002). A multivariate regression analysis identified as predictors of impaired HRQOL the female gender (P<0.001) and the perception of a lower co-workers support (P = 0.025) and career fulfillment (P = 0.001). ***Conclusion*** - The decrease in HRQQL was significantly related with female gender and personal perception of disease impact in success and social relations. These factors deserve a special attention, so timely measures can be implemented to improve the quality of life of patients.

HEADINGS - Inflammatory bowel diseases. Crohn disease. Ulcerative colitis. Quality of life. Questionnaires.

INTRODUCTION

Inflammatory bowel diseases (IBD), which encompasses ulcerative colitis (UC) and Crohn's disease (CD), are chronic diseases with a relapsing-remitting disease course requiring lifelong treatment. The goal of treatment for IBD is to reduce disease activity and improve patient's perception of health and health related quality of life (HRQOL).

The World Health Organization defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"[41].

Quality of life measurement is specially pertinent in inflammatory bowel disease (IBD), because it is a disabling disease[35], which typically presents in early adulthood and hence affects patients in all domains of life, namely physical, social and psychological. A significant number of patients with IBD consider that their quality of life is adversely affected by their disease[13]. This has been corroborated by studies indicating reduced quality of life compared with an age- and sex-matched population[27].

Health related quality of life studies provide insights into the influence of IBD on patient's lives, and the potential impact on professional and personal productivity. Due to the importance of HRQOL in IBD, formal questionnaires are often included as secondary outcomes in clinical trials[1, 11, 26, 39]. So, the aim of this study was to analyze the relationship between clinical, demographic and psychosocial factors and HRQOL in patients with IBD.

PATIENTS AND METHODS

During July to December 2012, one hundred and fifty patients, 92 with CD and 58 with UC, followed up in the Gastroenterology department at Centro Hospitalar do Alto Ave, Guimarães, Portugal, were prospectively interviewed during an outpatient specialist visit. A written questionnaire was filled, anonymously and without the presence of any of the assistant physicians. Some patients with difficulties to understand

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the questionnaire had help from a gastroenterology nurse. We excluded patients with hospitalization or surgery in the previous 3 months, patients seen for the first time or in urgent context, as well as those unable to fill the questionnaire. The patients were informed about the study's character and those who agreed to participate were enrolled and signed an informed consent form.

Quality of life measurement

Quality of life was measured using the 32-item Inflammatory Bowel Disease Questionnaire (IBDQ-32)[19]. This is a well-validated disease-specific instrument to measure HRQOL in patients with IBD and has previously been translated and validated for its use in Portuguese patients[36, 47]. The IBDQ-32 is a 32-item questionnaire consisting of four domains: bowel-related symptoms (e.g., loose stools, abdominal pain), systemic function (e.g., fatigue, sleep pattern), social function (e.g., ability to attend work and social events), and emotional status (e.g., anger, depression, irritability). The response for each question ranges from one to seven with one corresponding to significant impairment and seven corresponding to no impairment. The overall IBDQ score is the sum of the responses to each of the IBDQ questions. Total IBDQ score can range from 32 (very poor HRQOL) to 224 (perfect HRQOL).

Socio-demographic and clinical data

A separate questionnaire was used to collect the following socio-demographic and medical data: 1) Demographic data: age, gender, studies and working status, 2) Data on the disease character: type of IBD, year of diagnosis, number of hospital admissions, and number of IBD-related surgical procedures, 3) Data on their treatment: drugs and type (oral vs topical), 4) Psychological support, 5) Pharmacological treatment for depression or anxiety and 6) Smoking habits. The study included 150 patients. The demographic and clinical details of the study population are shown in Table 1.

Statistical analysis

Descriptive data were described as mean ± standard deviation (SD) for quantitative variables and proportions for qualitative ones. The univariate analyses explored the link between HRQOL scores and socio-demographic, clinical and psychological variables using the Student t test.

Variables which were statistically significant in the univariate analysis were included in a multivariate regression model, with the IBDQ score as the dependent variable.

The statistical analysis was performed using the SPSS version 18.0 software package. The statistical significance threshold was defined as $P<0,05$.

TABLE 1. Clinical and demographic characteristics of patients

	CD	UC
Number of patients, n	92	58
Gender, n (%)	58 (63) female	34 (58.6) female
Duration of IBD, mean±SD* (min-max)	5.4±4.8 (1-20) years	5.0±3.7 (1-16) years
Age, mean±SD* (min-max)	33.9±12,2 (17-75) years	37.7±12.4 (16-64) years
Current medical therapy for IBD, n (%)		
Oral aminosalicylates	56 (60.9)	46 (79.3)
Topical aminosalicylates	-	13 (22.4)
Steroids	7 (7.6)	1 (1.7)
Azathioprine	46 (50.0)	20 (34.5)
Biological therapy	23 (25.0)	7 (12.1)
Past IBD-related hospital admission (n/%)	65 (70.7)	24 (41..4)
Past IBD-related surgical procedure (n/%)	27 (29.3)	-
Education level (n/%)		
Primary studies	3 (3.3)	9 (15.1)
Lower secondary education	33 (35.9)	14 (24.1)
Upper secondary education	35 (38.0)	26 (44.8)
University studies	21 (22.8)	9 (15.5)
Smoking habits, n (%)	25 (27.2)	8 (13.8)

*SD: standard desviation; CD: Crohn's disease; UC: ulcerative colitis

RESULTS

Descriptive statistics for the four domains and overall score of the IBDQ-32

The mean of IBDQ-32 of enrolled patients was 159.5, ranging from 69 to 224. The vast majority of patients (76.7%) were satisfied with their life in general and about one quarter (23.3%) were unhappy.

No difference between the mean of the IBDQ-32 for CD and UC was observed (156.8 for CD and 161,2 for UC, $P = 0.482$), therefore they were considered together in the subsequent analysis. Table 2 summarizes the descriptive statistics for the four domains and overall score of the IBDQ-32.

TABLE 2. Descriptive statistics for the four domains and overall score of the IBDQ-32

	Score IBDQ-32		
	Mean	Min. (reference value)	Max. (reference value)
Bowel-related symptoms	53	22 (10)	70 (70)
Systemic function	22	8 (5)	35 (35)
Social function	29	8 (5)	35 (35)
Emotional status	15	3 (3)	21 (21)
Global	159.5	69 (32)	224 (224)

For each IBDQ-32 domain the issues more often related with a lower HRQOL were fatigue (54% of patients), frustration (42% of patients), the feeling of abdominal distention (41.3% of patients) and the difficulties in leisure activities or sports (24.7%).

Determinants of quality of life

Univariate analysis of all the psychosocial, clinical, and demographic variables revealed significant associations. The mean value of the IBDQ-32 was significantly lower among female patients (147.6 vs 178.3, $P<0.001$), patients with an individual perception of a lower co-workers support (144.6 vs 167.1, $P<0.001$) and career fulfillment (144.3 vs 174.1, $P<0.001$). Patients requiring either psychological support (147.2 vs 165.2, $P = 0.010$) or pharmacological treatment for anxiety or depression (147.2 vs 165.6, $P = 0.002$) also presented with significantly lower IBDQ-32 scores.

The remaining variables included in our study: age ($P = 0.343$), duration of IBD ($P = 0.314$), educational level ($P = 0.101$), workplace status ($P = 0.316$), IBD-related hospital admission ($P = 0.271$), IBD-related surgical procedure ($P = 0.271$), smoking habits ($P = 0.789$) and medication (topical aminosalicylates $P = 0.462$, oral aminosalicylates $P = 0.947$, steroids $P = 0.102$, azathioprine $P = 0.765$ and biological therapeutic $P = 0.190$) did not show statistically significant differences. The relationship between psychosocial, clinical, and demographic variables and the overall score of IBDQ-32 are shown in Table 3.

TABLE 3. Relationship between psychosocial, clinical, and demographic variables and the overall score of IBDQ-32 (univariate analysis)

	Score (mean) IBDQ-32	§*P* value
Type of disease		
CD	161.2	0.500
UC	156.8	
Gender		
Female	147.6	<0.001
Male	178.3	
Age		
≤30years	157.7	0.343
>30years	163.9	
Duration of IBD		
≤5years	161.8	0.314
>5years	155.6	
Educational level		
Low/Medium	153.4	0.101
High	163.4	
Working status		
unemployed	153.2	0.316
employed	160.9	
IBD-related hospital admission		
Yes	156.8	0.271
No	163.5	
IBD-related surgical procedure		
Yes	156.8	0.271
No	163.5	
Co-workers support		
High support	167.1	<0.001
Low support	144.6	
Career fulfillment		
Unaffected by the disease	174.1	<0.001
Decreased	144.3	
Smoking habits		
Yes	157.9	0.789
No	159.9	
Topical Aminosalicylates		
Yes	152.9	0.462
No	160.2	
Oral Aminosalicylates		
Yes	159.2	0.947
No	158.8	
Steroids		
Yes	138.9	0.102
No	160.6	
Azathioprine		
Yes	160.5	0.765
No	158.7	
Biological therapeutic		
Yes	151.6	0.190
No	161.5	
Psychological support		
Yes	147	0.010
No	165.2	
Pharmacological treatment of anxiety or depression		
Yes	146.1	0.002
No	165. 6	

§*P* value: level of significance

Variables statistically significant in the univariate analysis were included in a multivariate regression model (Table 4). The variable most strongly associated with lower HRQOL was female gender (P<0.001). This was followed by an individual perception of a decreased career fulfillment (P = 0.001) and a lower perceived co-workers support (P = 0.025).

TABLE 4. Multivariate regression analysis between predictor variables and IBDQ-32 scores

Variable	b	Standardized error β	β	t	*P*
Female gender	-24.85	5.26	-0.34	-4.72	**<0.001**
Lower perceived co-workers support	12.88	5.69	0.17	2.27	**=0.025**
Decreased career fulfillment	-19.51	5.56	-0.27	-3.51	**=0.001**
Psychological support	-11.71	6.09	-0.14	-1.92	=0.296
Pharmacological treatment of anxiety or depression	-6.43	6.13	-0.08	-1.05	=0.057

R^2 = 32%

DISCUSSION

The incidence and prevalence of IBD is subject to considerable variation, both between and within geographic regions, with IBD being more common in industrialized than in nonindustrialized countries. The incidence of CD in Europe ranges from 0.5 to 10.6 cases per 100,000 person-years while the estimates for UC range from 0.9 to 24.3 per 100,000 person-years. The highest incidence rates are observed in the Northern Europe, while the lowest rates are seen in Southern and Eastern Europe — suggesting a north-west/south-east gradient in IBD incidence. The prevalence of CD in Europe varies from 1.5 to 213 cases per 100,000 persons, whereas the prevalence of UC in Europe varies from 2.4 to 294 cases per 100,000 persons[7].

In Brazil, a study by Victoria et al.[48] reported an incidence of 4.48 and 3.5 cases per 100,000 inhabitants, for UC and CD, respectively. In the same study, the prevalence for UC and CD was 14.81 and 5.65 per 100,000 inhabitants, respectively. These results were similar to those presented by some countries in Eastern Europe, and only slightly smaller to those reported from countries of the Southern Europe[7].

Regardless of the country, the IBD adds substantial direct and indirect costs to both health care system and society. The impact of IBD on patients' quality of life is substantial due to early age onset, fluctuating disease course and the lack of a cure, meaning that the patients will have to deal not only with the physical impact of their disease, but also with all its social, psychological and professional disruptions.

There is little information available related to the definition of the score threshold to be reached to consider that patient's HRQOL evaluated by IBDQ-32 is normal. In this study, the average values obtained in four domains and overall score are above the expected mean values, and comparing with previous studies[29], the overall score of IBDQ-32 of this sample was higher. Our positive HRQOL scores may be explained because patients with a hospitalization or a surgery in the past 3 months and patients seen in an urgent context were excluded from this study, since it is known that adverse events, like hospitalizations or surgeries, have a negative impact on patient's quality of life[5].

In our sample, the systemic function was the most affected, as more than half of patients felt that fatigue adversely affected their quality of life. Several studies have shown that fatigue is a prevalent symptom in IBD[21, 46]. A recent review of the literature by Czuber-Dochan et al.[14], regarding fatigue in IBD patients, identified that fatigue prevalence ranges from 22% to 41% when the disease is in remission, to 86% when it is active. Fatigue may lead to considerable impairment in the patient's daily life and three studies demonstrated that it is associated with reduced HRQOL[12, 22, 38]. Therefore, easily reversible causes of fatigue should be identified and treated to prevent unnecessary patients' distress and suffering, and before more time and resource consuming investigations are undertaken.

This study shows that individuals with IBD who have an individual perception of a decreased career fulfillment, a lower perceived co-workers support and women reported lower HRQOL scores. Of these predictor variables, female gender was found to be the strongest predictor of a low HRQOL.

The effect of gender on HRQOL has previously been investigated in IBD, and female gender was found to be significantly associated with a lower HRQOL[3, 5, 10, 29]. Usually, and independently of the reported chronic disease, women´s self-rated quality of life is poorer than that of men[15, 34, 43, 49]. Several hypotheses for this finding are frequently reported in studies. Psychosocial factors may play a greater role in females than in males[5, 40]. Furthermore, females have greater disease-related concerns and worries about being treated differently as a result of their disease[31] and are also more likely to report concerns related to attractiveness and body image [8, 28].

Previous studies have shown that HRQOL is significantly impaired by work disability[2, 3, 17, 42]. The work disability rates of IBD patients range between 1.3% and 34%[45]. The frequent flares requiring hospitalization or surgical intervention often leads to sick leave and disability pensions[2, 3, 4, 6, 20, 44], which may be the main reason for the decreased career fulfillment in IBD patients.

Social support has been extensively studied and is thought to influence HRQOL in IBD patients[29, 32, 33]. However, the

specific importance of co-workers support in the HRQOL has never been previously studied. As previously stated, the ability to work of IBD patients is frequently compromised. However, the disease's impact is often not readily apparent, leading to a lack of understanding from others concerning the presence and graveness of their condition[23]. Lack of knowledge of how patients are affected by IBD may be at the origin of this behavior. Throughout the world, support groups for people with Crohn's disease and ulcerative colitis have a special role in providing information for patients and society, helping each one to deal with IBD.

Psychological variables, psychological support and pharmacological treatment for anxiety or depression were also related with a lower HRQOL in a univariate analysis, however without statistical significance in a multivariate regression model. Previous studies have found that higher levels of anxiety and depression are independently associated with lower HRQOL[16, 30] and disease activity[24, 37]. Screening for psychological morbidity, as well as patients' coping styles, should be considered at each follow up visit, and patients should be referred to a psychiatrist or psychologist, as appropriate.

Past IBD-related hospital admission and IBD-related surgical procedure were not a significant predictor of a lower HRQOL in our work. These results are supported by a study of Cassellas et al.[9], evaluating the impact of surgery on health-related quality of life, where the determining factor for a lower HRQOL was whether the patient had active disease and not whether he or she had undergone previous surgery for Crohn's disease.

Some studies have reported that HRQOL is positively influenced by biological treatment, including infliximab[18], adalimumab[25], yet in our study we did not find any significant association between medical treatment and HRQOL. However, the main aim of our study wasn´t to assess the effect of treatment on HRQOL, so the quality of life only was evaluated at a point of treatment, making it impossible to compare with studies only directed to this issue.

In conclusion, in our study we found important variables significantly related with a lower quality of life, suggesting that a HRQOL analysis has an important role in understanding the true impact of the disease on patients' lives, as well as in the redefinition of strategies to improve quality of life in IBD patients.

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RESUMO – ***Contexto*** - A doença inflamatória intestinal acarreta consequências físicas, psicológicas e sociais que podem afetar a qualidade de vida dos doentes. ***Objetivo*** - Avaliar a relação entre os fatores clínicos, demográficos e psicossociais e a qualidade de vida na doença inflamatória intestinal. ***Métodos*** - Um total de 150 doentes, 92 com doença de Crohn e 58 com colite ulcerosa, preencheram um questionário para avaliação da qualidade de vida na doença inflamatória intestinal (IBDQ-32) e um questionário para recolha de dados sociodemográficos e clínicos. A associação entre variáveis categóricas e o IBDQ-32 foi determinada com o teste t-Student. Variáveis estatisticamente significativas na análise univariada foram incluídas no modelo de regressão linear múltipla. ***Resultados*** - A análise univariada revelou uma qualidade de vida significativamente menor nas mulheres (P<0,001) e nos doentes com uma perceção individual de falta de compreensão pelos colegas de trabalho (P<0,001) e de diminuição do sucesso laboral (P<0,001). Doentes com necessidade de apoio psicológico (P = 0,010) e tratamento farmacológico da ansiedade e/ou depressão (P = 0,002) também apresentaram IBDQ-32 scores significativamente mais baixos. A análise de regressão linear múltipla identificou como preditores de diminuição da qualidade de vida o sexo feminino (P<0,001), perceção individual da falta de compreensão pelos colegas de trabalho (P = 0,025) e de diminuição do sucesso laboral (P = 0,001). ***Conclusões*** - A diminuição da qualidade de vida relaciona-se significativamente com o sexo feminino e a percepção pessoal de impacto da doença no sucesso e relações laborais. Estes fatores merecem uma atenção acrescida para que atempadamente se possam implementar medidas que possibilitem a melhoria da qualidade de vida destes doentes.

DESCRITORES - Doenças inflamatórias intestinais. Doença de Crohn. Colite ulcerativa. Qualidade de vida. Questionários.

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