Neuroendocrinology Letters Volume 36 No. 8 2015
ISSN: 0172-780X; ISSN-L: 0172-780X; Electronic/Online ISSN: 2354-4716
Web of Knowledge / Web of Science: Neuroendocrinol Lett
Pub Med / Medline: Neuro Endocrinol Lett

Quality of life in adolescents with inflammatory bowel disease and their parents – comparison with healthy controls

Daniela Jelenova [1], Jan Prasko [1], Marie Ociskova [1], Eva Karaskova [2], Martina Hunkova [1], Jana Kolarova [2], David Vydra [2], Michaela Holubova [1,3], Radovan Hruby [4], Klara Latalova [1], Vladimir Mihal [2]

1 Department of Psychiatry, Faculty of Medicine and Dentistry, University Palacky Olomouc, University Hospital Olomouc, Olomouc, Czech Republic
2 Department of Pediatrics, Faculty of Medicine and Dentistry, University Palacky Olomouc, University Hospital Olomouc, Olomouc, Czech Republic
3 Department of Psychiatry, Hospital Liberec, Czech Republic
4 Outpatient Psychiatric Department, Martin, Slovak Republic

Correspondence to: Jan Prasko
Department of Psychiatry, Faculty of Medicine and Dentistry
University Palacky Olomouc, University Hospital Olomouc
I. P. Pavlova 6, 77520 Olomouc, Czech Republic.
e-mail: praskojan@seznam.cz

Submitted: 2015-11-17 Accepted: 2015-12-27 Published online: 2015-01-23

Key words: **inflammatory bowel diseases; Crohn disease; ulcerative colitis; quality of life; anxiety; depression; parenting styles**

Neuroendocrinol Lett 2015; **36**(8):787–792 **PMID:** 26921580 NEL360815A02

Abstract

OBJECTIVE: Inflammatory bowel diseases (IBD) are chronic diseases with a significant impact on quality of life (QoL). The aim of the study was to examine the QoL in children with IBD and their families, depression and anxiety for both the children and their parents.

METHODS: Participants were 29 adolescents with IBD (19 individuals suffered from the Crohn disease, another ten had ulcerative colitis) and 40 healthy controls of the same age (13–16 years). The probands and their parents completed questionnaires measuring the quality of life (KidScreen-10, PedsQL), depression (CDI, BDI-II), and anxiety (SAD, BAI).

RESULTS: The QoL measured by questionnaires did not differ between the adolescent participants, but it was significantly lower in the parents of the children with IBD than in the parents of the healthy controls. The parents of the IBD children scored lower in the Family Impact Module Total Scale Score and the parental Health-Related QoL Summary Score. The fathers of the IBD children also had a lower level of the Family Functioning Summary Score. There wasn't any difference in the levels of anxiety and depressive symptoms among the IBD adolescents and the controls.

CONCLUSIONS: The parents of the children with IBD experience lower QoL than the parents with the healthy children. The children with IBD show similar symptoms of depression, anxiety, and QoL as the healthy controls.

ORIGINAL ARTICLE

INTRODUCTION

Inflammatory bowel disease (IBD) is a challenging illness from medicinal, emotional, and behavior perspectives. IBD symptoms include abdominal pain, fatigue, diarrhea, rectal bleeding, growth failure, and delayed puberty. These symptoms present unique psychological and psychosocial encounters (Mackner *et al.* 2006). The patients with IBD (especially ulcerative colitis) often suffer from diarrhea with variable amounts of hematochezia. Symptoms of tenesmus and urgency are also often present. Many of other symptoms may occur, including fever and weight loss. These symptoms are particularly typical for adolescents, who make up the majority of diagnosed pediatric cases. The patients learn how to cope with the chronic disease, that is hard to discuss with others while trying to preserve a normal teenage life and deal with regular developmental issues (CCFA 2009).

Adolescence is a period of emotional, physical, cognitive, and social changes. It is also linked to the onset of pediatric inflammatory bowel disease (IBD). Diagnosis of IBD can have a challenging impact on a range of psychosocial adjustment problems. In many youths diagnosed with IBD, appropriate developmental milestones, and normal functional growth is achieved by early adulthood

The term "inflammatory bowel disease" comprises ulcerative colitis and Crohn disease, which fall into the category of autoimmune diseases. Ulcerative colitis is a chronic, recurrent disease characterized by diffuse mucosal inflammation involving the colon. Ulcerative colitis invariably involves the rectum and may extend proximally in a continuous fashion to involve a part or all of the colon. Crohn disease is a chronic, recurrent disease characterized by patchy transmural inflammation involving any segment of the gastrointestinal tract from the mouth to the anus. Crohn disease and ulcerative colitis may be associated in 50 % of patients with extraintestinal manifestations, including oral ulcers, oligoarticular or polyarticular nondeforming peripheral arthritis, spondylitis or sacroiliitis, episcleritis or uveitis, erythema nodosum, pyoderma gangrenosum, hepatitis and sclerosing cholangitis, and thromboembolic events. Although ulcerative colitis and Crohn disease appear to be distinct entities, the same pharmacologic agents are used to treat them. The unpredictable nature of the disease can significantly stress adolescent, and therefore, can lead to higher levels of anxiety and depression (Drell & White 2005). Despite advanced research, there are still no specific therapies for these illnesses. The mainstays of treatment are 5-aminosalicylic acid derivatives, corticosteroids, and immunomodulating agents (such as mercaptopurine or azathioprine and methotrexate).

Ulcerative colitis and Crohn disease were described in the early works as psychosomatic illnesses, but no specific causative psychogenic factors have ever been demonstrated. As well as in other chronic medical illness, patients with more psychological distress tend to be more sensitive to severe physical illness with poorer functional capacity, but a causal relationship with IBD illnesses is not clear (Sewitch *et al.* 2001). Nevertheless, psychological distress does appear to exacerbate both symptom complaints and mucosal disease activity in ulcerative colitis (Levenstein *et al.* 1994). Disability and distress in patients with IBD are increased by concurrent psychiatric disorders (Walker *et al.*, 1996). For example, depression may predict relapse in adult individuals with IBD (Kurina *et al.* 2001; Mittermaier *et al.* 2004), and also, be a significant predictor of poor quality of life, independent of disease severity in IBD (Zhang *et al.* 2013). It may be a better predictor of subjective impairment IBD than inflammatory activity (Cuntz *et al.* 1999). Although psychotherapy has been shown to improve the psychological outcomes in individuals with IBD, the evidence for its efficacy in improving physical symptoms and reducing disease severity remains limited and is mixed (Knowles *et al.* 2013).

A diagnosis of a chronic disorder, such as IBD, can have a challenging effect on a variety of psychosocial adjustment problems. In many adolescents diagnosed with IBD, proper growing markers, and normal functional development is completed by early adulthood. However, an overall adolescent adjustment may vary based on aspects such as IBD progress (e.g., chronic non-remitting versus remitting) and treatment (e.g. high dose steroids, surgery), and longer-term symptoms (e.g., growth and puberty postponement) may play a role. In addition to the illness factors, maturation of emotional regulation, cognitive capacity, and impulse control across development can also influence the adolescents´ adaptation to illness. In general, children developing a persistent disease at a younger age are better able to integrate the disease as part of their self-concept. In adolescents, when self-identity is unstable, dealing with a disease such as IBD can be particularly challenging. Adolescents may feel shame linked to fecal incontinence, poor body image due to steroid-induced weight gain, social fears due to school absenteeism, and a loss of social learning opportunities. In addition to age, factors such as family and social support, the degree of disruption of the usual adolescent activities, and degree of stress, both early life and ongoing life stressors, may impact how adolescents will respond to having IBD. It is imperious for physicians and psychologist to pay attention to such psychosocial factors in assessing how an adolescent is coping with IBD.

Additionally, anxiety and depression can significantly impact disease management (including treatment adherence) and the outcomes (Mussell *et al.* 2004). The occurrence of anxiety and depression in the patients with IBD is also associated with other gastrointestinal problems that are typical for IBD: abdominal pain, bloating, and emptying disorders. The presence of these additional symptoms is associated with the largest

decrease in the quality of life in the patients with IBD (Simren *et al.* 2002). These issues clearly show that it is important to consider the dimension of physical and psychological disorders simultaneously because IBD is a group of chronic illnesses with a significant impact on quality of life (QoL) of the patients and their caregivers.

The aim of the study was to examine the quality of life, depression, and anxiety in the adolescents with IBD and their parents and compare their results with the healthy control group.

METHOD

Sample

The patients were recruited in the years 2013–2015 from the Department of Pediatrics, University Hospital Olomouc, Czech Republic. The participants were 29 adolescents with IBD and 40 healthy controls of the same age (13–16 years). Written informed consent was signed by all subjects and their parents. All patients had been monitored for IBD; 19 patients were diagnosed with Crohn disease and 10 with ulcerative colitis. The patients had to be diagnosed with IBD, at least, six months before included in the group of the chronically ill patients. The diagnosis was confirmed by a detailed examination, blood labs, and colonoscopy performed by a specialist. There were 15 boys and 14 girls. According to PUCAI (Pediatric Ulcerative Colitis Activity Index) and PCDAI (Pediatric Crohn Disease Activity Index), 25 children were in remission, and 4 presented low disease activity at the time of the assessment.

Assessment

The main assessment tools were used for measuring the level of depression (CDI in children, BDI-II in parents), anxiety (SAD in children, BAI in parents), and quality of life (KidScreen-10 in children, PedsQL in parents). All questionnaires are self-report scales, and they were fulfilled at home. The control group of children completed them at school.

The ***CDI*** (Children's Depression Inventory) is a psychological instrument widely used to assess depressive symptoms in children and adolescents (Kovacs 1992). The self-rating scale is composed of 27 items that are grouped into five-factor areas, including Negative Mood, Interpersonal Problems, Ineffectiveness, Anhedonia, and Negative Self-Esteem. High scores reflect more serious depressive symptomatology. A score greater than 19 is considered as a cut-off score for a depressive disorder.

The ***SAD*** (The Scale of Anxiety in Children; Müllner *et al.* 1983) measures the state anxiety and trait anxiety in two 20-items scales; each item is rated on the 3-point range.

The ***BDI-II*** (Beck Depression Inventory, the second version) is intended for assessing subjective depressive symptoms in adults (Beck *et al.* 1961). This self-rating scale with 21 depression indicators includes somatic and cognitive-affective symptoms; each item is rated on a 4-point scale. Scores of 19 or above indicate a possible depression.

The ***BAI*** (Beck Anxiety Inventory) is a self-rating scale with 21 anxiety indicators focusing primarily on physiological manifestations of anxiety in adults. The items are rated on a 4-point scale; a score of 16 or above indicates a possible anxiety disorder (Beck *et al.* 1988).

PedsQL Family Impact Module is a parent-reported tool that measures the effect of the chronic pediatric disorders on the patient health-related quality of life (HRQoL) and their family functioning (Varni *et al.* 2004). This 36-item questionnaire contains eight dimensions: physical functioning, emotional functioning, social functioning, cognitive functioning, communication, worry, daily activities, and family relationships. The questionnaire is designed to assess both parent self-reported functioning and parent-reported family functioning; in our study, we used only self-reported parental functioning. The items are rated on a 5-point Likert scale, and then linearly transformed to a 0–100 scale. The higher scores point to the better quality of life.

KidScreen-10 measures children's and adolescent´s subjective health and well-being (Ravens-Sieberer *et al.* 2005). It was developed as a self-report questionnaire appropriate for the healthy and chronically ill children and teenagers aged from 8 to 18 years. The KidScreen-10 is a short version of the KidScreen-52 and KidScreen-27 instruments. It includes ten items from the 10 HRQoL dimensions: Physical; Psychological Wellbeing; Moods and Emotions; Self-Perception; Autonomy; Parent Relations and Home Life; Social Support and Peers; School Environment; Social Acceptance (Bullying); and Financial Resources. Each question is rated on a 5-point response scale. A higher score is indicative of a better HRQoL.

Statistical analysis and ethics

Demographic, clinical, and psychological data were analyzed using descriptive statistics. The Shapiro-Wilk W test determined normal distribution of the demographic and clinical variables. Group differences between patients and controls were analyzed using unpaired t-tests. The Chi-square test or Fisher´s exact test were used for the analysis of categorical data. Pearson's correlation analysis calculated the relations between variables with normal distribution. Spearman´s rank correlation was used for variables with non-normal distribution. GraphPad PRISM (version 5.0) was used for statistics. The level of significance was set at 5%.

The research was carried out in agreement with the latest version of the Declaration of Helsinki, and written informed consent was obtained from all subjects after the nature of the procedures had been fully explained. The local Ethical Committee of University Hospital Olomouc approved this project.

RESULTS

Demographic and clinical characteristics

The participants were 29 adolescents with IBD and 40 healthy controls of the same age (13–16 years). 19 patients were diagnosed with Crohn disease and 10 with ulcerative colitis (Table 1). The diagnosis was established by the recommended diagnostic approach (Levine *et al.* 2014, IBD WGESPGHN 2005). The treatment was based upon the current guidelines (Ruemmele *et al.* 2014, Turner *et al.* 2012). The median duration of the treatment was 13 months (interquartile range 8–44 months). Clinical activity of the illness was evaluated according to the Pediatric Crohn's Disease Activity Index (PCDAI) (range from 0 to 100 points) and Pediatric Ulcerative Colitis Activity Index (PUCAI) (range from 0 to 85 points) (Hyams *et al.* 1991, Turner *et al.* 2009). Remission was defined as PCDAI or PUCAI of less than 10 points. Sixteen (86.4 %) patients with Crohn disease and nine (90 %) with ulcerative colitis were in remission of illness at the time of observation. Laboratory tests included CRP (C-reactive protein), thrombocytes, and hemoglobin.

As a control group, 72 children from three different high school classes were asked to participate in the study. A written consent was obtained from the parents of 42 children and questionnaires of 40 children. A possible chronic disease was assessed through an item in the KidScreen-10 questionnaire.

Demographic data

There was no statistically significant difference between the patients and the healthy controls in their mean age or gender distribution (Table 1).

Level of anxiety and depression

There were no differences between the clinical and control groups in the mean level of depression (CDI) or trait anxiety (SAD usual) (Table 1).

Tab. 1. Characteristics of the patients and controls.

	PATIENTS (n=29)	CONTROLS (n=40)	STATISTICS
Age	15.03±1.27	14.86±0.43	unpaired t-test: t=0.7766 df=67; n.s.
Age of disorder onset	12.06±3.12		
Duration of the disorder	2.98±2.85		
Male: Female	15:14	30:10	Fisher exact test; **n.s.**
CRP	1.97±2.50		
Thrombocytes	283.8±87.86		
Hemoglobin	142.00±45.34		
CDI	7.89±4.86	7.52±5.26	unpaired t-test; t=1.298 df=65; n.s.
SAD	29.08±4.70	29.22±4.54	unpaired t-test; t=0.9407 df=65; n.s.
KidS10	38.85±4.15	38.21±4.65	unpaired t-test, t=0.5804 df=65; n.s.

CRP – C-reactive protein, CDI – Children's Depression Inventory, SAD – Scale of Anxiety in Children, KidS10 – KidScreen-10

Tab. 2. Gender differences – the patients and controls.

PATIENTS	MALES (n=15)	FEMALES (n=14)	STATISTICS
Length of the disorder (in months)	38.17±35.41	33.24±34.08	unpaired t-test: t=0.3810 df=27; n.s.
CRP	1.513±1.921	2.450±2.992	Mann Whitney test: MW U=90; n.s.
Thrombocytes	295.90±50.98	270.90±116.10	unpaired t-test: t=0.7579 df=27; n.s.
Hemoglobin	138.90±8.49	145.40±65.77	Mann Whitney test: MW U=67.5; n.s.
CDI	7.39±5.80	11.38±11.09	unpaired t-test: t=1.152 df=24; n.s.
SAD	26.45±3.86	31.92±7.66	**unpaired t-test: t=2.143 df=22; $p<0.05$**
KidS10	40.62±7.32	37.54±9.24	unpaired t-test: t=0.9409 df=24; n.s.
CONTROLS	**MALES (n=30)**	**FEMALES (n=10)**	**STATISTICS**
CDI	6.67±4.67	8.63±3.50	unpaired t-test: t=1.093 df=33; n.s.
SAD	28.96±4.99	29.63±3.62	unpaired t-test: t=0.3472 df=32; n.s.
KidS10	39.00±3.50	38.00±4.90	unpaired t-test: t=0.6473 df=33; n.s.

CRP – C-reactive protein, CDI – Children's Depression Inventory, SAD – Scale of Anxiety in Children, KidS10 – KidScreen-10

Quality of life

The quality of life measured by KidScreen-10 was similar in both groups. There were no statistically significant differences between the patients and controls (Table 1).

Gender differences in the patients and controls

There was no significant difference between male and female patients in clinical results and psychological measurements, except for a higher level of anxiety in women measured by SAD (Table 2). No significant differences between males and females in the control group were found.

Parents´ quality of life and levels of anxiety and depression

The quality of life measured by the questionnaires did not differ between the adolescent groups, but it was significantly lower in the fathers and the mothers of the adolescents with IBD than in the parents of the healthy controls (Table 3). There was a statistically significant difference between the level of depression measured by BDI-II in the fathers of the patients than in the fathers of the controls, but not in the mothers of both groups. Other significant results took place in the measurement of the general anxiety using the BAI: the mothers of the patients were statistically significantly more anxious than the mothers of the controls, but there were no differences in the level of anxiety in the fathers of both groups.

DISCUSSION

The adolescents with IBD and the healthy controls showed similar levels of quality of life. The results are surprising because a significant number of studies described a lower quality of life in the patients with IBD (Cuntz *et al.* 1999; Drell & White 2005). This discrepancy is not easy to explain. Adolescents' overall adjustment may eventually vary based on influences such as the IBD course and treatment, and longer-term symptoms may play a role. Nevertheless, it could be connected with the inclusion criteria of the study – most patients were in remission of the disorder and only four presented mild disease activity. It is possible that quality of life would be lower in the acute or newly diagnosed patients. Also, hospitalized patients could reach lower levels of quality of life.

However, there were significantly lower scores on the quality of life in the parents (both fathers and mothers) of the adolescents with IBD than in the parents of the healthy controls. How to explain that children with the illness displayed the same quality of life as the healthy controls, but the mothers and fathers of the chronically ill adolescents had a lower quality of life than the parents of the controls? One could speculate that the parents with the chronically ill child restricted their lives because of the child illness. This hypothesis cannot be tested in our cross-sectional study. Future studies using prospective longitudinal design should address this issue.

The adolescents with IBD and the healthy controls showed similar levels of the depressive symptoms, trait anxiety or state anxiety. The results are also surprising because there were reports of a higher level of anxiety and depression in the patients with IBD (Cuntz *et al.* 1999). Explaining this discrepancy could be the same as in the quality of life scores. The degree of anxiety and depression may be higher in the acute, newly diagnosed or hospitalized patients.

The parents of the IBD adolescents expressed a higher mean level of anxiety (mothers) and depression (fathers) than the parents of the healthy control group. None of the average scores of anxiety and depression in the mothers and the fathers reached the prescribed cut-off scores for clinical diagnoses of anxiety or depression. Still, mildly elevated levels of anxiety and depression can be intuitively explained by worries about their child. These worries may have impaired the parents' quality of life. Also, the fathers of the children with IBD could experience the slightly elevated symptoms of depression due to possible limitations and tension in their families induced by a chronic health condition of their child. Thus, the deleterious effect of the children's illness on parents' quality of life may have been mediated by parental (subclinical) anxiety and/or depression. This hypothesis cannot be tested in our cross-sectional study. Future studies using prospective longitudinal design should also address this issue.

Tab. 3. Parental level of quality of life, anxiety and depression.

	PATIENTS´ PARENTS	CONTROLS´ ARENTS	STATISTICS
F-PQL-G	70.19±14.84	83.47±12.95	**unpaired t-test; t=2.945 df=45; *p*<0.01**
M-PQL-G	68.14±16.68	78.42±14.90	**unpaired t-test; t=2.466 df=56; *p*<0.05**
F-BDI-II	8.70±3.41	3.48±3.37	**unpaired t-test; t= t=2.956 df=47; *p*<0.005**
M-BDI-II	7.18±7.17	6.30±6.18	unpaired t-test; t=1.226 df=57; n.s.
F-BAI	4.56±4.59	3.93±4.70	unpaired t-test; t=0.9924 df=45; n.s.
M-BAI	8.60±4.66	4.59±4.77	**unpaired t-test; t=2.063 df=57; *p*<0.005**

M-PQL-G – PedsQL, mothers' global scores, F-PQL-G – PedsQL, fathers' global scores, M-BDI – Beck Depression Inventory, mothers' scores, F-BDI – Beck Depression Inventory, fathers' scores, M-BAI – Beck Anxiety Inventory, mothers' scores, F-BAI – Beck Anxiety Inventory, fathers' scores

LIMITATIONS

There are several limits of the study that need to be stated. The most significant limitation of the study is the small number of the patients. The sample may not be representative for the populations of the adolescent IBD patients. Also, the clinical state of most of the patients was stabilized. Their mental state, as well as the mental state of their parents, could worsen when the physical health gets worse. Thus, we cannot exclude the possibility that the patients and their parents are more prone towards mental distress as we did not study patients with currently high levels and intensity of the IBD symptoms.

CONCLUSION

Children with IBD and healthy controls show similar symptoms of depression, anxiety, and quality of life. The parents of the children with IBD present lower quality of life than the parents of healthy children.

ACKNOWLEDGEMENT

Supported by IGA MZ CR NT 14281-3.

Disclosure: *The authors report no conflicts of interest in this work.*

REFERENCES

1 CsaCFoA: About the Epidemiology of IBD.2009 http: //www.ccfa.org/resources/epidemiology.html.
2 Cuntz U, Welt J, Ruppert E, Zillessen E (1999). Determination of subjective burden from chronic inflammatory bowel disease and its psychosocial consequences. Results from a study of 200 patients. Psychotherapie Psychosomatik, Medizinische Psychologie. **49**: 494–500.
3 Drell MJ & White TJH (2005). Children´s reaction to illness and hospitalization. In: Sadock BJ and Sadock VA (Eds): Kaplan & Sadock´s Comprehensive Textbook of Psychiatry. 8th ed, vol II. Lippincott Williams & Wilkins, Philadelphia; 3425–3434.
4 Hyams JS, Ferry GD, Mandel FS, Gryboski JD, Kibort PM, Kirschner BS, Griffiths AM, Katz AJ, Grand RJ, Boyle JT, *et al.* (1991). Development and validation of a pediatric Crohn's disease activity index. J Pediatr Gastroenterol Nutr. **12**(4): 439–447.
5 IBD Working Group of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (2005). Inflammatory bowel disease in children and adolescents: recommendations for diagnosis-the Porto criteria. J Pediatr Gastroenterol Nutr. **41**(1): 1–7.
6 Knowles SR, Monshat K & Castle DJ (2013). The efficacy and methodological challenges of psychotherapy for adults with inflammatory bowel disease: a review. Inflammatory Bowel Disease. **19**: 2704–2715.
7 Kurina LM, Goldacre MJ, Yeates D, Gill LE (2001) Depression and anxiety in people with inflammatory bowel disease. Journal of Epidemiology and Community Health. **55**: 716–720.
8 Levenstein S, Prantera C, Varvo V, Scribano ML, Berto E, Andreoli A, Luzi C (1994). Psychological stress and distress activity in ulcerative colitis: a multidimensional cross-sectional study. American Journal of Gastroenterology. **89**: 1219–1225.
9 Levine A, Koletzko S, Turner D, Escher JC, Cucchiara S, de Ridder L, Kolho KL, Veres G, Russell RK, Paerregaard A, Buderus S, Greer ML, Dias JA, Veereman-Wauters G, Lionetti P, Sladek M, Martin de Carpi J, Staiano A, Ruemmele FM, Wilson DC (2014). ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. J Pediatr Gastroenterol Nutr. **58**(6): 795–806.
10 Mackner LM, Crandall WV, Szigethy EM (2006). Psychosocial functioning in pediatric inflammatory bowel disease. Inflamm. Bowel Dis. **12**(3): 239–244.
11 Mittermaier C, Dejaco C, Waldhoer T, Oefferlbauer-Ernst A, Miehsler W, Beier M, Tillinger W, Gangl A, Moser G (2004). Impact of depressive mood on relapse in patients with inflammatory bowel disease: a prospective 18-month follow-up study. Psychosomatic Medicine. **66**: 79–84.
12 Mussell M, Bocker U, Nagel N, Singer MV (2004). Predictors of disease related concerns and other aspects of health-related quality of life in outpatients with inflammatory bowel disease. Eur J Gastroenterol Hepatol. **16**: 1273–1280.
13 Ruemmele FM, Veres G, Kolho KL, Griffiths A, Levine A, Escher JC, Amil Dias J, Barabino A, Braegger CP, Bronsky J, Buderus S, Martín-de-Carpi J, De Ridder L, Fagerberg UL, Hugot JP, Kierkus J, Kolacek S, Koletzko S, Lionetti P, Miele E, Navas López VM, Paerregaard A, Russell RK, Serban DE, Shaoul R, Van Rheenen P, Veereman G, Weiss B, Wilson D, Dignass A, Eliakim A, Winter H, Turner D; ECCO/ESPGHAN (2014). Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease. J Crohns Colitis. **8**(10): 1179–1207.
14 Sewitch MJ, Abrahamowicz M, Bitton A, Daly D, Wild GE, Cohen A, Katz S, Szego PL, Dobkin PL (2001). Psychological distress, social support, and disease activity in patients with inflammatory bowel disease. American Journal of Gastroenterology. **96**: 1470–1479.
15 Simren M, Axelsson J, Gillberg R, Abrahamsson H, Svedlund J, Bjornsson ES (2002). Quality of life in inflammatory bowel disease in remission: the impact of IBS-like symptoms and associated psychological factors. Am J Gastroenterol. **97**: 389–396.
16 Turner D, Hyams J, Markowitz J, Lerer T, Mack DR, Evans J, Pfefferkorn M, Rosh J, Kay M, Crandall W, Keljo D, Otley AR, Kugathasan S, Carvalho R, Oliva-Hemker M, Langton C, Mamula P, Bousvaros A, LeLeiko N, Griffiths AM; Pediatric IBD Collaborative Research Group (2009). Appraisal of the pediatric ulcerative colitis activity index (PUCAI). Inflamm Bowel Dis. **15**(8): 1218–1223.
17 Turner D, Levine A, Escher JC, Griffiths AM, Russell RK, Dignass A, Dias JA, Bronsky J, Braegger CP, Cucchiara S, de Ridder L, Fagerberg UL, Hussey S, Hugot JP, Kolacek S, Kolho KL, Lionetti P, Paerregaard A, Potapov A, Rintala R, Serban DE, Staiano A, Sweeny B, Veerman G, Veres G, Wilson DC, Ruemmele FM; European Crohn's and Colitis Organization; European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (2012). Management of pediatric ulcerative colitis: joint ECCO and ESPGHAN evidence-based consensus guidelines. J Pediatr Gastroenterol Nutr. **55**(3): 340–361.
18 Walker EA, Gelfand MD, Gelfand AN, Creed F, Katon WJ (1996).. The relationship of current psychiatric disorder to functional disability and distress in patients with inflammatory bowel disease. General Hospital Psychiatry.**18**: 220–229.
19 Zhang CK, Hewett J, Hemming J, Grant T, Zhao H, Abraham C, Oikonomou I, Kanakia M, Cho JH, Proctor DD (2013). The influence of depression on quality of life in patients with inflammatory bowel disease. Inflammatory Bowel Disease. **19**: 1732–1739.