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Impact of Inflammatory Bowel Disease on Patient's Quality of Life – A Review

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Abstract

Background: *Nowadays, the need to increase patients' quality of life in terms of their mental and physical health is increasingly being discussed. The incidence of inflammatory bowel disease continues to rise, and it is associated with the creation of many difficulties for these patients that interfere with their daily lives.*

Objectives: *The purpose of this work was to summarize challenges that patients with inflammatory bowel disease have to deal with on a daily basis, and to assess the impact of these problems on their quality of life.*

Material and methods: *This paper was written based on a review of the knowledge contained in scientific studies conducted around the world. We have drawn conclusions guided by recent reports that address various aspects of daily life of IBD patients.*

Results: *Inflammatory bowel diseases are characterized by persistent and recurrent symptoms mainly from the gastrointestinal tract, but also from other organs. This leads to deterioration of patients' mental health and can be a risk factor for psychological disorders. Changes in the body and the treatment used make it difficult for patients to function on a daily basis. All the issues raised are reflected in the assessment of the quality of life of patients with inflammatory bowel disease.*

Conclusions: *The multifaceted nature of inflammatory bowel disease, which affects many aspects of patients' lives, reduces their quality of life.*

Key words: *inflammatory bowel disease; quality of life; mental health*

Intruduction and purpose

In recent years, the incidence of Inflammatory Bowel Disease (IBD – Inflammatory Bowel Disease), which includes Crohn's Disease (CD – Crohn's Disease) and Ulcerative Colitis (UC – Ulcerative Colitis), has been increasing markedly. Their

pathogenesis is not fully understood. The key mechanism causing symptoms is inflammation involving the gastrointestinal mucosa. In CD, inflammatory changes can occur along the entire length of the gastrointestinal tract, from the mouth to the anus, while in UC, only the large intestine is affected by inflammation. The most common symptoms of IBD are abdominal pain, diarrhea, the presence of blood or mucus in the stools, vomiting, weight loss, and chronic fatigue. They are recurrent and cause a lower quality of life for this group of patients. These diseases are characterized by the occurrence of periods of exacerbations (periods of disease activity) and remissions, which also show a correlation with the patient's well-being. In IBD, extraintestinal symptoms are often present, as inflammation can also develop in other areas of the body, such as the skin, oral cavity, and joint system [1–3]. They are estimated to occur in up to 50% of IBD patients, with those with UC and women at higher risk. Extraintestinal symptoms are another problem patients face, reducing their quality of life and requiring specialized therapy [4]. In the last century, mainly surgical treatments for IBD were used, however, in recent years, therapeutic options have changed dramatically with the introduction of biologic drugs. These include, for example, adalimumab, infliximab, golimumab, vedolizumab, ustekinumab. They can be administered subcutaneously or by intravenous infusion. The therapeutic goal of these drugs is to achieve and maintain remission. As of today, it is not possible to cure patients with IBD. This chronic disease is associated with intractable symptoms and side effects of treatment, which afflict patients in various areas of life and lead to a significant reduction in the quality of life [1]. Nowadays, an increasing number of studies and statistics investigate and analyze the quality of life of patients with inflammatory bowel diseases [5].

State of knowledge

Quality of life

According to the WHO, quality of life for patients is a term that describes an individual's perception of his or her place in society, culture, and values he

or she appreciates [6]. Knowledge of the problems that reduce the well-being of patients is used in modifying the treatment. Depending on which age, social, cultural group patients belong to, their values and needs are different. The whole process of getting to know patients more deeply, including in the psychosocial sphere, leads to a better understanding of the disease entity, the alleviation of symptoms, and the selection of optimal care. Recently, it has been said that the quality of life index can be a strong predictor of patient survival. Treatment decisions based on patients' needs can influence therapeutic successes [7]. Various tools are currently being used to assess patients' quality of life, such as the EUROHISQoL and the Inflammatory Bowel Disease Questionnaire (IBDQ), which is specifically dedicated to IBD patients [5]. Each scale has some inaccuracies, which are due to the natural and inherent problems of inflammatory bowel disease patients. Significant differences in the subjective assessment of quality of life have been noted between older and younger patients, as the values needed in life change with age [8]. The aforementioned IBDQ questionnaire is the best tool to reflect the quality of life of people with IBD. It contains 32 questions that are divided into four categories to be assessed by the patient: bowel symptoms, systemic symptoms, social perspective, and emotional perspective [8, 9]. The Inflammatory Bowel Disease Questionnaire (IBDQ) can be scored from 32 to 224, with a cutoff point of 169. A score of at least 169 indicates a normal quality of life, similar to healthy individuals [10]. Knowles et al. in their meta-analysis noted a reduction in the quality of life of IBD patients compared to healthy individuals; however, this is similar to patients with other conditions, e.g., irritable bowel syndrome, hepatitis, rheumatoid arthritis, multiple sclerosis [5]. Disease activity is important in assessing patient well-being, as the quality of life index was significantly lower in patients in the active phase of the disease compared to those in remission [11]. Leone et al. conducted a prospective study in which no patient achieved a satisfactory quality of life score on the Inflammatory Bowel Disease Questionnaire (IBDQ – the Inflammatory Bowel Disease Questionnaire), one of the more commonly used methods to assess the impact of the disease on the quality of life of people with IBD [12].

Problems of IBD patients in daily life

IBD patients face many challenges in their daily lives. Byron et al. in their meta-analysis gathered data from 11 studies, nine of which were conducted in Europe and two in Canada. A total of 565 patients were studied, of whom 365 had CD and 200 had UC. Each group of subjects identified disease-related problems in broad aspects such as daily life, work, family relationships, interpersonal relationships, social integration, and sexuality. Decreased quality of life is definitely influenced by clinical symptoms. Patients primarily pointed to persistent abdominal pain, diarrhea, vomiting, chronic fatigue. In addition, factors that can exacerbate symptoms were identified. These included intense physical exertion, family troubles, and a poor diet containing highly processed foods and spicy foods. IBD patients indicated that for them social exclusion, loss of social contacts, and change in the realization of life goals were significant problems. In most cases, there was a deterioration of mental health, reflected in depression and anxiety disorders [1]. IBD patients feel a lot of pressure from their environment. Their own expectations of themselves, as well as society's expectations, can lead to a loss of control over their emotions, particularly when they feel no sense of support from loved ones. Of note is the fact that they have a small number of friends, and often relationships with family are highly developed [13]. During the course of the disease, interpersonal relationships are undoubtedly affected. During periods of exacerbation, the patient often has to depend on another family member, leading to a swapping of social roles, and participation in family life is hampered. This is a major challenge for partners, parents, and other loved ones, and even a test for the quality of family ties. Because of the aforementioned factors that exacerbate IBD symptoms, patients have to avoid certain foods, which is the reason for limited social outings, less frequent eating out, precise shopping, and travel planning. In addition, IBD patients struggle with thoughts of unpredictable onset of clinical symptoms [1]. An increase in tension, anxiety, the occurrence of intrusions can be associated with trying to control unpredictable situations in which clinical symptoms such as diarrhea, abdominal pains appear. These are moments that embarrass the patient and

often result in social withdrawal [12]. Children and adolescents with IBD show a higher risk of psychosocial problems, behavioral disorders, and difficulties in dealing with emotions. Reduced quality of life in pediatric patients is also associated with comorbid problems that arise from the impact of the disease on the body, such as delayed puberty, short stature, and concern about side effects of drug therapy [6]. Much attention is now being paid to the need to improve the quality of mental health in patients with inflammatory bowel disease. Reducing psychosocial stress, daily conversations, and consultation with physicians can be an effective way to improve the quality of life of these patients through a better understanding of their disease [14].

Depression and anxiety

Outwardly, it may appear that all is well with the patient, but inwardly the patient often struggles with feelings of anxiety, fatigue, and helplessness [1]. Patients with IBD are at risk of developing depression and anxiety disorders [15–17]. Navabi et al. conducted a retrospective study on 432 patients with IBD, which showed that as many as 44.4% of the subjects had symptoms of depression and anxiety disorders. Among these subjects, the majority were women. Dysfunctions involving mental health were more common in patients with CD compared to those with UC [15]. Elbay et al. in their cross-sectional study raise the important issue of overlapping psychological problems such as excessive worrying, recalling negative memories, feelings of hopelessness, and pessimism, which lead to anxiety and depression. It also suggests that these difficulties may stem from the symptoms of the disease, as significantly higher levels of worry and recurrent negative thinking were observed in patients in the active phase of the disease compared to those in remission [17].

Chronic fatigue

In recent years, people with IBD have been complaining more frequently about feelings of chronic fatigue, a major problem that undermines patients' quality of life [18, 19]. Patients' fatigue levels are similar to patients with other

chronic diseases, such as rheumatoid arthritis, liver disease, irritable bowel syndrome [19]. Fatigue is described as a feeling of mental exhaustion and lack of energy, which prevents people from functioning properly throughout the day. It causes a reduced ability to work mentally and physically, and thus reduces productivity. In addition, fatigue often co-occurs with depression, anxiety disorders, and sleep disorders [18, 19]. Chavarria et al. in their prospective study found that IBD patients complaining of fatigue had a reduced quality of life index compared to IBD patients without fatigue. However, no differences in quality of life were observed between CD and UC patients experiencing fatigue [18]. Due to the significant impact of psychological symptoms: depression, anxiety disorders, and obsessions on the reduction of quality of life, it is recommended to include psychological treatment and behavioral therapy in the group of patients affected by these symptoms [3, 16].

Sleep disorders

Sleep is undoubtedly an important element needed for the body's daily functioning and contributes to maintaining proper regulation of the immune system, as disorders associated with it increase the secretion of pro-inflammatory cytokines that participate in the dysregulation of the immune response and lead to inflammation in IBD patients. Ballesio et al. observed in their meta-analysis that poor sleep is responsible for impaired mental and physical health as a result of increased disease symptoms caused by pro-inflammatory mediators [20]. Sleep disorders are a factor that reduces patients' quality of life and worsens the course of the disease [20–22]. Salwen-Deremer et al. in their study outlined the main sleep problems in IBD patients, the most common of which appeared to be insomnia. Disorders of different categories can co-occur, as evidenced by the fact that more than 30% of the subjects suffered from at least two sleep-related problems. Insomnia was more common in patients with active disease compared to those in remission, and was similar for both CD and UC [21]. It is noted that there is a tendency for sleep disorders to co-occur with clinical symptoms of IBD, mainly gastrointestinal, as sleep deprivation is associated with hypersensitivity to pain stimuli [22].

Newer studies suggest that patients with inflammatory bowel disease may suffer from disturbed physiological sleep architecture. It has been proven that patients show more micro-awakenings in the EEG and have a lower percentage of deep sleep in their total sleep time. Their sleep cycles are dominated by light sleep. Anxiety and internal fear of having to use the restroom at night probably lead to micro awakenings, which disrupts the physiological sleep architecture [23]. In addition, these problems have an impact on the deterioration of mental health, the appearance of symptoms of depression, mood disorders and, consequently, a reduced quality of life [22, 23].

Relationships and sexuality

The decision to start a family is not an easy one. Some patients give up having children because of the difficulties involved in getting pregnant, maintaining a pregnancy, and raising a child. An undeniable problem is the treatment of inflammatory bowel diseases, as the drugs can potentially affect the pregnant woman and her unborn child [1, 24]. The issue of family life and sexuality in IBD patients is very important. The symptoms and consequences that these diseases bring have the effect of reducing attraction to a potential partner. Chronic fatigue, medications taken, and other factors contribute to a weakened libido [1]. In the body, increasing inflammation and the continued production of inflammatory mediators, such as corticotropin, which is responsible for stress reactions, causes disturbances in the hypothalamic-pituitary axis [16]. This process disrupts and impairs the function of the gonads [25]. In addition, patients are embarrassed about themselves because some have to wear stoma bags, from which an unpleasant odor can rise. In turn, others suffer from skin irritation and lesions, which they describe as unattractive [1]. Zhang et al. in their meta-analysis noted a correlation between inflammatory bowel disease and sexual dysfunction, which includes, for example, erectile dysfunction, decreased libido, and pain during sexual intercourse. IBD patients are characterized by an increased risk of these disorders, and the risk is higher during periods of exacerbation. The increased risk of sexual dysfunction is also associated with the need to take certain medications – corticosteroids, as well

as the presence of comorbidities, past surgeries, concomitant depression, or being over 50 years old [25].

Pregnancy problems

Inflammatory bowel disease is most often diagnosed between the ages of 20 and 29. This is the childbearing years, so the diagnosis of the disease usually complicates the life plans of most patients. Pregnancy of an IBD patient has a high risk of complications such as miscarriage, premature birth, low birth weight of the baby [24, 26, 27]. Periods of disease exacerbation can have a negative impact on the neurological development of the unborn child. For this reason, studies emphasize the need to achieve remission, which is crucial for safe maintenance of pregnancy and successful delivery. Unfortunately, a sizable number of pregnant women with IBD discontinue medications during pregnancy without consulting their doctor, putting themselves at risk of exacerbating the disease. This is detrimental to the baby as well, as inflammatory mediators can worsen fetal well-being. In recent years, biologic drugs have begun to be introduced on a large scale, and have become a target for safety studies of their use in pregnant women [24, 26]. Nielsen et al. observed in their meta-analysis that the incidence of pregnancy complications in IBD patients taking biologics was not higher compared to healthy pregnant women [24]. The safety of these preparations is emphasized, as they have little or no effect on fetal development. No increased risk of perinatal complications was noted in pregnant women who took biologics during the third trimester of pregnancy [24, 28]. In addition, their use is not associated with an increased incidence of congenital malformations in the child. Uncontrolled inflammation that takes place in the pregnant woman's body significantly increases the risk of complications during pregnancy and during delivery. For this reason, biological treatment should be maintained during pregnancy, and any modification of treatment should be selected appropriately to avoid exacerbation of the disease [24]. The risk of disease activity after delivery is related to factors to which the woman was exposed during pregnancy, e.g., interruption of biological therapy, cesarean section, active disease during conception. Increased estrogen

levels during pregnancy may protect against exacerbations by stabilizing the intestinal barrier and inhibiting the migration of pro-inflammatory factors. There is a decrease in estrogen levels during the perinatal and postpartum period, which may explain the increased risk of exacerbations after birth. Additional studies are also suggested to support the assumption that breastfeeding reduces the risk of IBD exacerbations [28]. Pregnant patients with inflammatory bowel disease have an increased risk of venous thromboembolism compared to healthy pregnant women. This is due to physiological changes that occur in a woman's body, such as thrombocytosis, but IBD also directly contributes to the increased risk of this condition. Both have similar effects leading to the stimulation of the clotting cascade and the formation of clots in the vessels [27].

Intercurrent disease

1. Celiac disease is a chronic autoimmune disorder that often co-occurs with IBD due to similar immunological, genetic, and environmental factors that affect the increased permeability of the intestinal barrier to antigens, leading to inflammation within the intestinal mucosa [29–31]. In both celiac disease and IBD, especially CD, patient-reported symptoms and test results can be similar. In both celiac disease and IBD, patients report similar symptoms [32]. Pinto-Sanchez et al. in their meta-analysis noted the interplay between the two disease entities, which translates into an increased risk of IBD in patients with celiac disease and an increase in the prevalence of celiac disease among IBD patients [29]. The co-occurrence of both diseases contributes to a worse prognosis, treatment outcomes, increased incidence of colorectal cancer, non-Hodgkin's lymphomas and primary sclerosing cholangitis, and increased mortality from complications of The co-occurrence of both diseases contributes to a worse prognosis, treatment outcomes, increased incidence of colorectal cancer, non-Hodgkin's lymphomas and primary sclerosing cholangitis, and increased mortality due to complications [32].

2. There is now a correlation between the occurrence of IBD and alopecia, especially alopecia areata, due to similar immunological and genetic backgrounds. It is more common in patients with UC than in those with CD, probably due to the dominance of the pro-inflammatory pathway, which is more characteristic of UC. On the other hand, hair loss may be due to drug therapy based on TNF-alpha inhibitors. An undeniable issue is the impact of alopecia on the patient's mental health, which is worsened, as the patient may develop emotional disturbances and negative self-perception, leading to a reduced quality of life [33].
3. Rheumatoid arthritis (RA – Rheumatoid arthritis), as another autoimmune, chronic and progressive disease in which multiple, symmetrical joints are affected by inflammation, leading to bone tissue degradation, shows a similar pathogenesis to IBD. Due to similar clinical manifestations, the diagnosis and differentiation of arthritis directly related to inflammatory bowel disease and early RA as a comorbid condition can be difficult. The complaints associated with both conditions can cause disability and reduced quality of life for patients [34].
4. Primary sclerosing cholangitis (PSC – Primary sclerosing cholangitis) is an autoimmune, progressive disease in which biliary and hepatic symptoms result from an ongoing inflammatory process in the intrahepatic and extrahepatic bile ducts, leading to their fibrosis [35, 36]. Fraga et al. in their study observed an increased incidence of PSC in patients with IBD, with a significantly higher incidence in those with UC, which may be related to the presence of risk factors such as whole bowel involvement (pancolitis), male gender, and non-smoking. The coexistence of both disease entities contributes to liver failure and the development of gastric tract cancer, and these complications worsen the prognosis of patients. The mortality rate of the population suffering simultaneously from IBC and PSC is significantly higher compared to patients with IBD alone [36].

Psychiatric disorders

Increased IBD activity may be a factor in the onset of psychiatric disorders, with immune reactions leading to stimulation of inflammatory pathways cited as a potential cause [37, 38]. The development of mental defects is influenced by the patient's clinical condition, living under constant stress, fear of sudden onset of exacerbations, fear associated with the risk of cancer or the need for surgery, as well as treatment – corticosteroid therapy can trigger the development of nervous disorders [38]. There is a correlation between the occurrence of mental defects and an increase in the number of suicide attempts and suicides in patients with IBD, which is reflected in a worsening of the course, prognosis of the disease, as well as a reduction in the quality of life of patients [37, 38].

Deficiencies in patients with IBD

Nowadays, vitamin D is believed to have anti-inflammatory effects and is involved in regulating the human immune response. It is responsible for stabilizing the intestinal barrier by reducing its permeability to pro-inflammatory factors that lead to inflammation within the intestinal mucosa [39–41]. Vitamin D deficiency is very common in patients with IBD. Gubatan et al. in their meta-analysis observed that low vitamin D levels increase the risk of symptom exacerbation, which is associated with reduced quality of life for patients [39]. In addition, vitamin D supplementation may have potential benefits due to its immunomodulatory effects, which improve the clinical status of patients with IBD [39, 42]. The need for further studies to confirm the validity of vitamin D supplementation in patients with IBD is emphasized [40, 42]. In inflammatory bowel diseases, elemental deficiencies often occur as a result of impaired absorption in the gastrointestinal tract, which can have a negative impact on the patient's clinical condition in the form of: increased disease activity, increased clinical symptoms and malnutrition. Due to diarrhea and therapeutic interventions such as the presence of stomas or fistulas, there is an increased loss of zinc from the body. Deficiencies of this element are common in patients

with IBD, especially those with CD, because the inflammatory process in this disease involves the proximal segment of the intestine, as a result of which zinc is not sufficiently absorbed by the pathologically altered intestinal mucosa. This condition can manifest itself in delayed growth in young people, delayed sexual maturation, the presence of skin and eye lesions, impotence, hypogonadism in men. Significant deficiencies of this element in the body of patients have a significant impact on weight loss, malnutrition, deterioration of the general condition, which translates into a reduced quality of life for this group of patients [43]. IBD patients often suffer from anemia, which is a combination of iron deficiency anemia and chronic disease anemia [44, 45]. Reduced iron concentration is caused by its impaired absorption in the intestines and reduced intake due to a lack of appetite [45]. Anemia is associated with cognitive decline in children, growth retardation, and reduced quality of life, and is the cause of more hospitalizations in this group of patients [45, 46].

Psychological treatment

IBD patients' lack of knowledge about their disease is associated with increased symptoms of depression, anxiety, and stress, and negatively affects their quality of life. Hunt et al. in their randomized clinical trial demonstrated the efficacy of self-help cognitive-behavioral therapy based on increasing awareness among patients about the difficulties associated with their disease through a publicly available manual. The results of this method significantly depend on the commitment and the time devoted by the patient, but in the perspective of the results obtained, it seems to have positive effects, as patients experienced a significant reduction in anxiety and depressive symptoms and their quality of life improved [16]. Nowadays, am increasing number of studies on the impact of disorders related to the microbiome-gut-brain axis on human mental health are emerging, so various psychological therapies have begun to be applied to IBD patients with the goal of improving their quality of life. Periods of disease exacerbation resulting in increased secretion of pro--inflammatory cytokines and disruption of intestinal barrier function increase the risk of depression and anxiety. Riggott et al. noted in their meta-analysis

that psychological therapies can only improve the psychological well-being of patients with IBD in the short term, and that the quality of life of patients who underwent the study may improve only temporarily [47]. Wynne et al. in a randomized trial demonstrated the effectiveness of acceptance and commitment therapy on improving the mental health and quality of life of people with IBD. The method involves learning about and accepting the undesirable situation that is the disease, and is designed to help the patient to adapt to its course and the difficulties it entails [48]. In the future, psychological therapies may be very successful in improving patients' well-being, but at present there is a need for further research that takes into account the individual characteristics of patients, which would argue for their significant impact on improving their quality of life [16, 47].

Conclusions

Nowadays, a great deal of attention is paid to assessing the quality of life of patients with inflammatory bowel disease, who face many problems every day. These individuals have to face a new reality that affects them at the time of diagnosis, as IBD significantly changes the patient's daily functioning and confronts them with difficult choices. The persistent clinical symptoms and their recurring nature negatively affect the patient's mental health, often leading to depression, anxiety disorders and, in a few cases, suicide among this group of patients. Pro-inflammatory pathways, which are responsible for the development of inflammation, can initiate the onset of other autoimmune diseases or exacerbate diseases that already exist. In recent years, psychological therapies are becoming the subject of research, which may have significant benefits for patients in the future. In addition, attention is being paid to the role of the physicians and medical staff in the effectiveness of patient therapy. All the aspects discussed in this paper confirm the fact that the quality of life of patients with IBD is significantly impaired, and more studies presenting potential opportunities to improve the well-being of these patients are needed. Understanding the problems affecting the patient's well-being and perception in society is helpful in conducting effective treatment and modifying it.

The quality of life index is an important element in providing individualized assistance to patients and should not be ignored in the therapeutic process.

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