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UNDERSTANDING THE INTERPLAY BETWEEN ANXIETY AND ULCERATIVE COLITIS: PREVALENCE, BIDIRECTIONAL RELATIONSHIP, MECHANISMS, AND INFLUENTIAL FACTORS

KUMAR S AND CHITRA V*

Department of Pharmacology, SRM College of Pharmacy, SRM Institute of Science and Technology, Kattankulathur, Chennai, 603203 India

***Corresponding Author: Dr. V Chitra: E Mail: chitrav@srmist.edu.in**

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ABSTRACT

This review explores the intricate relationship between anxiety and ulcerative colitis (UC), a chronic inflammatory bowel disease (IBD). Anxiety is a prevalent psychological condition among UC patients, affecting their overall well-being. Research indicates a bidirectional relationship where anxiety can exacerbate UC symptoms and the disease's unpredictable nature can induce anxiety. Studies show a high prevalence of anxiety and depression in IBD patients, ranging from 24.4% to 31.9% for anxiety and 21.8% to 25.8% for depression. Notably, during relapses, anxiety prevalence can rise to 80%. UC significantly impacts patients' lives, affecting daily activities, self-esteem, and social interactions, extending to their families and households. Effective UC management is crucial to alleviating the emotional burden. Treatments that induce remission, including biological therapies, improve the quality of life (QoL). However, challenges like treatment contraindications persist. Patient education and psychological support are essential in holistic care. This review underscores the importance of recognizing anxiety in UC patients, its bidirectional influence, and the need for comprehensive care strategies. It provides insights into the prevalence, mechanisms, and factors influencing the anxiety-UC relationship, emphasizing the bidirectional impact on ulcerative colitis patients.

Keywords: ulcerative colitis, anxiety, prevalence, bidirectional relationship, dietary factors

INTRODUCTION

Anxiety is a state of the mind characterized by emotions of concern, uncertainty, or anxiety over an unclear situation **[1]**. This psychological condition is usually present in individuals with inflammatory bowel disease (IBD), particularly ulcerative colitis (UC) **[1], [2]**.

Individuals with UC typically display mental symptoms, including feeling depressed and anxious, due to the chronic nature of the condition and its influence on their standard of living. **[1], [3]**. Anxiety can worsen UC in a variety of ways, including by increasing symptom severity, lowering treatment compliance, and lowering life quality **[2]**. Depression or anxiety are the psychosocial disorders that IBD patients experience most frequently **[2]**.

Depression and anxiety are the psychosocial symptoms that people with IBD experience most often. With difficulties in identifying the best medications and psychological health services, mental health is an essential but underappreciated element of IBD patient care **[4]**. The rising incidence of these mental illnesses encourages mental screening for every patient initially diagnosed with IBD **[4]**.

The livelihood of people with ulcerative colitis (UC), a chronic inflammatory disease, is significantly impacted. UC affects the social, emotional, and psychological facets of well-being in addition to the physical symptoms.

The patient's standard of living has been revealed to significantly worsen as a result of the extensive effects of UC in several domains **[5]**. Due to the disease's unpredictable nature, which is characterized by periods of remission and exacerbation, patients struggle to control their symptoms and daily activities **[6]**. Daily activities, jobs, social interactions, and interpersonal relationships are commonly disrupted by the impacts of UC **[6], [7]**.

According to recent studies, patients with inflammatory bowel disease (IBD) have a greater frequency of psychological problems such as depression and anxiety when compared to the general population. In IBD patients, the lifetime prevalence of anxiety and depression ranged from 24.4 to 31.9% and 21.8 to 25.8%, respectively **[2], [4], [8]**.

In a cross-sectional study conducted in Jordan, 65.7% of ulcerative colitis patients reported symptoms of anxiety, while 58.6% reported symptoms of depression **[9]**.

In a recent systematic review and meta-analysis, the prevalence of symptoms of anxiety and depression in IBD patients was found to be high, with approximately one in three patients affected by anxiety symptoms and one in four patients affected by depression symptoms **[4]**.

In a single-centre investigation, the prevalence of anxiety in IBD patients was estimated to be between 29% and 35% during remission periods and up to 80% during relapses **[2]**.

The effects of UC go beyond physical discomfort and affect patients' emotional and psychological health as well. Due to the long-lasting and unpredictable nature of the disease, patients frequently feel mental discomfort, anxiety, and depression **[5]**. Reduced self-esteem, problems with body image, and an increase in stress are some of the emotional side effects of UC **[5]**. The anxiety of illness flare-ups and the requirement for frequent doctor visits add to the emotional burden **[5], [6]**.

The effects of UC go beyond physical discomfort and affect patients' emotional and psychological health as well. Due to the long-lasting and unpredictable nature of the disease, patients frequently feel mental discomfort, anxiety, and depression **[5]**. Reduced self-esteem, problems with body image, and an increase in stress are some of the emotional side effects of UC **[5]**. The anxiety of illness flare-ups and the requirement for frequent doctor visits add to the emotional burden **[5], [6]**.

The effects of UC are not limited to patients themselves; they also affect their families and households. The disease's symptoms, such as urgent bowel movements and fatigue, can lead to decreased participation in family activities and social events **[10]**. The need for restroom accessibility and dietary restrictions can affect family dynamics and meal planning. The emotional burden of seeing a loved one struggle with the disease also impacts family members **[10]**.

The impact of UC on patients' lives highlights the importance of effective disease management and holistic care. Treatments that induce and sustain remission offer benefits beyond clinical endpoints, restoring QoL to normal levels **[5]**. Biologic therapies have shown promise in enhancing QoL during induction and maintaining these gains long-term **[5]**. However, challenges such as treatment contraindications and loss of response need to be addressed **[5]**. Prompt diagnosis, patient education, and psychological support are essential in alleviating the emotional and social burden of UC **[7]**.

Patients with ulcerative colitis (UC) can control their anxiety in a number of ways, including through exercise, dietary modifications, psychological and physiological therapies, medication, and surgery.

In this article, we go over some of the main aspects of ulcerative colitis (UC) and how to treat anxiety in UC patients. (1) Prevalence of Anxiety in Ulcerative Colitis Patients; (2) Bidirectional Relationship: Anxiety and Disease Progression; (3) Mechanisms

Underlying the Anxiety-UC Connection; (4) Factors Influencing the Anxiety-UC Relationship.

PREVALENCE OF ANXIETY IN ULCERATIVE COLITIS PATIENTS

A study on the psychological effects of this inflammatory bowel disease focused on the incidence of anxiety in ulcerative colitis. The prevalence and effects of anxiety in individuals with ulcerative colitis have been the subject of several studies, which have provided significant insight into the subject. Data from 77 studies that used validated surveys to report the prevalence of anxiety or symptoms of depression in IBD patients have been included in this systematic review and meta-analysis. Based on 58 studies, we discovered a pooled prevalence of anxiety symptoms in IBD patients of 32.1%, whereas the prevalence of depressive symptoms was 25.2% across 75 studies. In comparison to healthy controls without IBD, the prevalence of anxiety-related symptoms was noticeably greater **[11]**.

Furthermore, differences based on gender were identified. Seven studies reported the prevalence of symptoms of anxiety in patients with IBD according to sex. The pooled prevalence of symptoms of anxiety was higher in women with IBD (33.8%) compared with men (21.8%) **[11]**.

Another study specifically demonstrated that the prevalence of anxiety and depressive symptoms in UC patients was 65.7% and 58.6%, respectively, which is higher than that reported in the general Jordanian population. There are only two local studies that examined the prevalence of anxiety and depression among Jordanians and reported rates of 23.7% and 13.3%, respectively. Remarkably, our study demonstrated higher rates of depressive and anxiety symptoms in our population compared to what we found in the literature reported from other countries. According to a recent meta-analysis, the prevalence of depression in IBD patients was 25.2%, while that for anxiety was 32.1% **[9]**.

The results of a single research centre showed that our group had significant rates of anxiety (37.1%) and depression (56.2%). Our results are consistent with those of people with chronic health conditions, who often have an elevated risk of serious depression **[2], [6]**. The findings were in accordance with recent studies, which showed that IBD patients had higher levels of depression and anxiety than those in the control group **[2]**.

When compared to healthy controls, inflammatory bowel disease (IBD) patients are more likely to have mental comorbidities. In these trials, which included 70 patients and 100 healthy volunteers, the researcher found that anxiety and depression were both rather common, with an average frequency of 18.6% and 34.3%, respectively **[12]**.

These studies provide collective information about the prevalence of anxiety in ulcerative colitis patients, which is influenced by disease activity, type of inflammatory bowel disease, gender, and both physical and physiological aspects of the management of ulcerative colitis.

BIDIRECTIONAL RELATIONSHIP: ANXIETY AND ULCERATIVE COLITIS

The bidirectional correlation between anxiety and ulcerative colitis is a complicated and fascinating phenomenon that has been examined in recent studies. The connection between the gut microbiota, metabolites, and proteins in individuals with active ulcerative colitis (UC) who also have depression and anxiety was recently studied in a published study. With more Lactobacillales, Sellimonas, Streptococcus, and Enterococcus but fewer Prevotella_9 and Lachnospira, the study indicated that patients with UC and depression or anxiety had decreased fecal microbial community richness and diversity. The study also discovered that there was a general drop in immunoglobulin proteins and that the majority of metabolites were elevated in the serum while very few metabolites were decreased. These associated proteins, metabolites, and microorganisms had extensive connections. According to the study, these gut microbiota, metabolites, and proteins might be used as clinical intervention targets for those who have UC and depression or anxiety **[13]**.

A cross-sectional study at West China Hospital explored the prevalence of anxiety and depression in Chinese patients with inflammatory bowel disease (IBD), including ulcerative colitis (UC). The study aimed to understand the impact of mental health symptoms on IBD-related factors, considering their significant burden. Among 341 IBD patients, 33.1% exhibited anxiety and depression symptoms. For Crohn's disease (CD) patients, symptoms correlated with higher Crohn's disease endoscopic scores, while UC patients with symptoms showed elevated Mayo scores and severity index values. Risk factors included CD-related surgery and disease activity for CD patients and corticosteroid use for UC patients. Effective IBD management should address mental health for better outcomes **[14]**.

The 2021 comprehensive review aimed to assess the current knowledge on the social and economic effects, current therapies, and particular unfulfilled requirements associated with comorbid anxiety or depression in IBD patients. Although there were variations in the incidence of anxiety or depression in IBD patients, the percentages were comparable to those discovered in a prior systematic study. For those with IBD and anxiety or depression, non-pharmacological therapies, including

cognitive behavioral therapy, have been demonstrated to be helpful. However, many of these individuals had inadequate access to mental health treatments. To improve outcomes for patients with IBD who also suffer from anxiety or depression, healthcare practitioners should fill any gaps in patient care. The study found several unmet requirements related to certain diseases, such as inconsistent depression screening and inadequate mental health treatment **[13]**.

Various aspects of the complicated relationship between emotional health and IBD are established. Studies repeatedly show that individuals with Crohn's disease and ulcerative colitis have a greater incidence of emotional problems than people in general **[15]**. Numerous studies indicate that psychological stress and mood problems may be responsible for IBD relapses **[1]**. Patients with IBD commonly experience anxiety and depression; according to a recent meta-analysis, anxiety is prevalent in these patients at a pooled prevalence of 31.1% and depression at a pooled prevalence of 22.3% **[16]**. There is evidence that continuous psychological distress might worsen symptoms of the disease and raise the possibility of a flare [17]. Since anxiety symptoms frequently coincide with UC flare-ups but may persist throughout remission, this theory of a connection between anxiety and UC is supported **[1]**. IBD (inflammatory bowel disease) is characterized by significant physical symptoms as well as psychosocial comorbidities. Up to 40% of IBD patients have abnormal levels of anxiety **[6]**. Although its effect on inflammation is unknown, stress, especially perceived stress as opposed to significant life events, may cause clinical flares in people with IBD **[18]**. Heart rate variability (HRV), which has been studied over time, has been linked to UC symptoms, inflammation, and physiological and emotional stress levels **[19]**. Patients with UC in deep remission frequently experience IBS-like symptoms, although they are not as prevalent as originally thought. IBS-like symptoms are linked to poor psychological health and elevated levels of blood cytokines in UC patients in deep remission **[20]**.

MECHANISMS UNDERLYING THE ANXIETY-UC CONNECTION

A. Overview of the gut-brain axis and its relevance to UC and anxiety

The gut-brain axis is a communication system that goes both ways, involving signals from the brain to the gut and vice versa. This intricate system includes hormonal, metabolic, and microbial signals **[21], [24]**. Its role is crucial in regulating digestion, metabolism, and immune function **[22], [25]**.

Recent studies have discovered that the gut-brain axis also influences cognitive

functions such as mood, anxiety levels, and stress. **[21], [24]**. Furthermore, this communication system has been linked to the development of health conditions like anxiety and depression **[22], [23], [25], [26]**.

The microbiota-gut-brain axis is a major subject in this area. It comprises a complicated interplay between the brain and the gastrointestinal organs, involving routes such as the immune system, neurotransmitters, and hormones. Activation of this axis has been associated with the emergence of anxiety disorders, suggesting a multi-faceted process. Studies have examined the therapeutic potential of modulating this axis with therapies like probiotics and antibiotics, opening the path for novel treatments **[27]**. Patients with UC typically encounter symptoms such as stomach discomfort, diarrhea, and rectal bleeding **[21]**. Chronic psychological stress, such as anxiety and depression, aggravates colitis by stimulating the hypothalamic-pituitary-adrenal (HPA) axis and altering the autonomic nervous system (ANS) **[21], [25], [27], [28]**. This is followed by an increase in the production of cytokines and proinflammatory mediators that promote disease aggravation **[21], [27], [28]**.

Furthermore, chronic or acute stress can impair the integrity of the gut lining, leading to the release of toxins. This, in turn, can alter the brain, perhaps contributing to anxiety and other mental health disorders. The gut-brain axis covers the neurobiochemical, neuroendocrine, and neuroimmune systems, highlighting the intricacy of interactions between these systems **[29]**.

Dysbiosis and inflammation in the gut have been related to a variety of mental diseases, such as anxiety and depression, which are common among UC patients. **[22], [25], [27]**.

Studies have shown that the gut-brain axis, which includes mental state, emotional control, neuromuscular function, and HPA regulation, is fundamentally and extensively regulated by the enteric microbiota **[25], [27], [30]**.

Patients with active UC accompanied by depression and anxiety showed reduced fecal microbial community richness and diversity, with disordered gut microbiota metabolism and proteomics **[25], [27], [30]**. Anxiety and depression are comorbid disorders linked with worsening UC outcomes **[27], [28]**. Preclinical investigations offer evidence of the concept that underlying behavioral disorder, such as depression, leads to increased sensitivity to inflammatory stimuli and that regularly used types of antidepressants protect against this vulnerability **[21], [27]**.

The gut-brain axis modulates the natural course of inflammatory bowel disease **[1], [24]**. The gut-brain axis, commonly called the gut-brain connection, involves extensive

two-way communication between the central nervous system and the enteric nervous system found in the gastrointestinal tract. This association offers insight into the interaction between anxiety and intestinal health. Understanding the function of the gut-brain axis in anxiety-related diseases like UC can lead to the development of comprehensive therapies that address both physiological and psychological components **[31]**.

The gut microbiota-brain axis has also attracted interest for its significance for behavior and brain function. Although the specific pathways remain under investigation, new technological improvements have allowed researchers to examine the relationships between gut microbiota and neuropsychiatric illnesses. This axis offers intriguing pathways for studying anxiety-related characteristics of diseases like UC **[32]**.

B. **Gut microbiota dysbiosis**

The gut-brain axis, a complex network of bidirectional communication between the stomach and the brain, plays a vital role in affecting different areas of health, including psychological well-being **[33]**. Emerging data indicates that worry, a prevalent psychological condition, could impact the diversity of the gut microbiota, potentially leading to a state of dysbiosis **[34], [35]**]. Dysbiosis, characterized by an imbalance in the microbial community, can impair normal metabolic processes inside the gut, eventually influencing the synthesis of metabolites and short-chain fatty acids (SCFAs) that play a major role in inflammation management **[36]**.

The activation of the HPA (hypothalamic-pituitary-adrenal) axis is triggered by anxiety, which can have an impact on ulcerative colitis (UC). This in turn can disrupt the nervous system (ANS) and cause changes in the immune and inflammatory functions that are crucial for inflammatory bowel disease (IBD) **[35]**. Patients who experience ulcerative colitis and also suffer from depression and anxiety might exhibit lower diversity and abundance in their fecal microbial community, indicating an unstable gut microbial profile **[37]**. Moreover, there is evidence linking anxiety and depression to an imbalance in the gut microbiota that leads to inflammation **[38]**. The ability of the gut microbiota to generate inflammation emphasizes its significance in health.

The pathophysiology of UC is significantly linked to the mucosal immune imbalance against the gut microbiota as well as the host **[21]**. The gut microbiota can promote inflammation of the gut, which can lead to tissue damage caused by dynamic complexes of cells and cytokines **[21], [39]**.

The gut microbiota is capable of metabolizing food components, such as

polysaccharides and proteins, into SCFAs **[40]**. SCFAs are essential metabolites that have the potential to impact the gut-brain communication pathways. Research shows that SCFAs can exert an anti-inflammatory impact by regulating immune responses and increasing intestinal barrier integrity **[35]**. This anti-inflammatory activity of SCFAs is of particular relevance in the context of inflammation regulation and the influence of dysbiosis on gut health **[35], [41]**.

The interaction between SCFAs, the gut-brain axis, and inflammatory regulation involves mechanisms. SCFAs can attach to receptors on immune cells, triggering signalling pathways that result in the production of anti-inflammatory cytokines **[36]**. Additionally, SCFAs may impact the development of T cells, thus contributing to immune-mediated balance **[36], [41]**. These interconnected pathways underscore the role played by SCFAs in modifying the gut-brain axis and their potential impact on mental well-being.

In addition, recent studies have highlighted the bidirectional relationship between the gut microbiota and the CNS, exposing the complex mechanisms by which gut microbes regulate brain function and behavior. Gut bacteria can produce neurotransmitters and metabolites that alter mood and brain function **[42]**. Additionally, gut-derived chemicals, such as lipopolysaccharides, might promote neuroinflammation and contribute to mood disorders **[43]**. Understanding these links could pave the way for novel therapeutics targeting the microbiota-gut-brain axis to reduce anxiety and related mental health concerns **[42]**.

C. Immune dysregulation

The immune system behavior significantly influences anxiety levels in people with colitis (UC) which is a type of inflammatory bowel disease (IBD) **[44]**. This disruption, in the system arises from a combination of genetic factors, environmental influences, and immune responses **[1]**.

Understanding the nature of this phenomenon is crucial because it helps us grasp the significance of the gut-brain axis serves as a line of communication linking the nervous system and the gastrointestinal tract **[45]**. When chronic stress sets in it triggers the activation of the adrenal (HPA) axis resulting in the release of cortisol. Increased levels of cortisol impact the composition of gut microbiota. Disrupt the integrity of the gut barrier leading to heightened intestinal permeability and inflammation **[42], [46]**.

The research underscores the intricate relationship between immune dysregulation, anxiety, and UC. A dysregulation of the gut-microbiota-brain axis, intrinsically linked to the pathophysiology of IBD, aligns with mental conditions such as stress and anxiety **[1], [47]**. This axis enables two-way

interaction between gut microbiota and the central nervous system, thereby modulating immune responses and mental well-being **[42]**.

It is important to point out that stress triggers immune system dysfunction and disrupts the gut microbiota, increasing colitis and triggering inflammatory reactions **[46], [48]**. Chronic stress is also linked to altered gut lining integrity, increased inflammation, and reduced intestinal barrier function **[49], [50]**. Additionally, psychological stress may trigger an immunological response and cause a microbiota imbalance in the gut, which would contribute to immune dysregulation in IBD **[22], [47]**. The modulation of immune cell activity serves as another important mechanism. Chronic stress's impact on immune cell trafficking, activation, and cytokine production disrupts the delicate equilibrium between pro-inflammatory and anti-inflammatory responses, thereby contributing to the persistent inflammation observed in UC **[44], [45], [51]**.

While stress and anxiety themselves do not directly cause UC, their influence on disease progression is noteworthy. Anxiety's correlation with the timing and extent of UC symptoms can intensify the condition **[52]**. Moreover, the heightened prevalence of mental disorders among individuals with UC further substantiates the intricate connection between immune responses and psychological well-being **[1]**.

The role of the gut-brain-microbiota axis is paramount in this context. Stress-induced changes in the composition of the gut microbiota and its metabolites directly impact immune function, influencing immune cells and modulating inflammation within the intestine **[42], [45], [51]**.

Furthermore, the disruption of glial cells due to chronic stress establishes a link between psychological stress and inflammatory bowel disease. Glia cells, which play a pivotal role in immune responses within the gut, contribute to mediating the effects of chronic stress on IBD development **[53]**.

THE IMPACT OF DIETARY FACTORS ON ANXIETY AND ULCERATIVE COLITIS

Dietary variables have a crucial role in the delicate interplay between anxiety and ulcerative colitis (UC). This review digs into the complicated relationships between food, mental well-being, and UC, proven by evidence-based research studies.

In contrast to traditional regional diets, such as those popular in the Mediterranean, Indian, Japanese, and Southeast Asian areas, the Western-style diet (WSD) demonstrates considerably larger proportions of simple refined carbs, saturated fats, red meat, dairy products, and processed foods. Simultaneously, it indicates a lower presence of vegetables, fruits, legumes,

whole grains, raw meals, and dietary fibers in general. The WSD largely incorporates calorie-dense meals high in saturated fats, glycemic carbs, and animal proteins. Numerous research studies have examined the association between WSD and diseases such as obesity, hypertension, chronic renal disease, and numerous non-communicable diseases **[54]**.

Studies have also revealed that Western-type diets, defined by high protein, fat, salt, and sugar content but lacking in fruits, vegetables, and fiber, are connected with an accelerated risk of inflammatory bowel disease (IBD). Recent meta-analyses indicate a large relative risk for IBD of 1.92, accompanied by greater amounts of chemicals and preservatives in Western-type diets, likely contributing to the elevated IBD risk. Additionally, higher consumption of fried meals, which are commonly processed, has been connected with an amplified risk of IBD. The frying process and the changing nutritional content inside the meal, depending on the kind and quality of oil used, may account for this association **[55]**.

Dairy products are frequently avoided in the context of inflammatory bowel disease (IBD). Ice cream and cream are the main causes of symptoms, according to studies on dairy foods. Patients with Crohn's Disease (CD) have related fruit yogurt and hard cheese to the onset of symptoms. Both full-fat and low-fat cow's milk consumption have been linked to symptoms in people with ulcerative colitis (UC). Bloating, stomach pain, and diarrhea are typical IBD symptoms that are defined by lactose intolerance **[56]**.

Dietary factors, especially those affecting sulfur consumption, have been linked to the development and clinical progression of UC. This introduces a certain amount of complexity to UC administration. The prevalence of inflammation in UC indicates a relationship between dietary sulfur and disease development. High protein consumption from sources like red meat has been related to UC recurrence, perhaps mediated by sulfur-containing compounds **[57]**.

Moreover, dietary components, especially sulfur, are becoming recognized for their potential role in IBD pathogenesis, further stressing their significance for UC **[58]**. Consuming too many processed meals and sugary foods can worsen inflammation, which is a major contributing factor in many illnesses, including UC. Concerns regarding intestinal permeability and an increased risk of colitis have been related to high-sugar diets, which may have an impact on the emergence of UC **[59]**.

Additionally, the bidirectional association between food and IBD, as explained by a review of nutritional parameters and inflammatory bowel disease, highlights the

relevance of dietary shortfalls and components such as sugar in the context of IBD **[60]**. While direct linkages between excessive sugar intake and anxiety may demand future investigation, keeping a nutrient-rich diet has been proposed to have a preventive impact on psychological problems **[60]**.

Furthermore, there are many methods through which the ingestion of ultra-processed foods (UPFs) may impact the development of IBD. UPF intake could be associated with substituting unprocessed or minimally processed foods (UMPs) high in fiber. Furthermore, UPFs sometimes contain chemicals like salt, which may increase intestinal irritation. Experimental models have demonstrated that a greater concentration of sodium chloride might boost the production of inflammatory cytokines and aggravate chemically-induced colitis. UPFs commonly include emulsifiers, thickeners, and other chemicals that might cause direct intestinal irritation. Experiments employing synthetic emulsifiers such as carboxymethylcellulose and polysorbate-80 have revealed their tendency to disrupt the mucosal barrier and trigger proinflammatory alterations in the gut microbiome, culminating in colitis **[61]**.

DISEASE-RELATED STIGMA AND ITS IMPACT ON MENTAL HEALTH IN UC PATIENTS

Perceived stigma has been a significant concern for individuals living with Ulcerative Colitis (UC). Recent studies have demonstrated that this perceived stigma is closely associated with a range of adverse outcomes in UC patients **[62]**. Specifically, individuals who experience perceived stigma related to UC tend to face heightened psychological distress and a decline in their overall health-related quality of life **[63]**. This association underscores the profound influence of disease-related stigma on the mental well-being of UC patients.

Furthermore, the psychological challenges faced by UC patients, including anxiety and depression, often correspond with the severity of their disease and the burden of living with a chronic condition like UC **[64]**. The stigma associated with their disease may make these mental health problems worse and increase the impact on their emotions.

A separate study delved into the impact of Inflammatory Bowel Disease (IBD) stigma on depressive symptoms in youth. This research revealed empirical evidence that greater stigma associated with IBD results in increased worry about IBD symptoms among young individuals. This heightened worry, in turn, amplifies their perception of IBD as an intrusive force in their daily lives, impacting activities such as school and social events.[64] Ultimately, this cascade of events contributes to the development of

depressive symptoms in young IBD patients **[62]**. This study underscores the importance of addressing IBD-related stigma, particularly among the youth population, and emphasizes the need for interventions to mitigate its consequences.

CONCLUSION

In conclusion, anxiety is a significant issue for individuals with ulcerative colitis and IBD in general, affecting their mental well-being and overall quality of life. Effective disease management, including psychological support, is essential to alleviate the emotional and social burden of UC

REFERENCE

[1] A. S. Bannaga and C. P. Selinger, "Inflammatory bowel disease and anxiety: Links, risks, and challenges faced," *Clinical and Experimental Gastroenterology*, vol. 8. Dove Medical Press Ltd, pp. 111–117, Mar. 23, 2015. doi: 10.2147/CEG.S57982.

[2] S. Askar *et al.*, "The psychological impact of inflammatory bowel disease as regards anxiety and depression: a single-center study," *Middle East Current Psychiatry*, vol. 28, no. 1, Dec. 2021, doi: 10.1186/s43045-021-00154-0.

[3] X. Yuan *et al.*, "Depression and anxiety in patients with active ulcerative colitis: crosstalk of gut microbiota, metabolomics and proteomics," *Gut Microbes*, vol. 13, no. 1, 2021, doi: 10.1080/19490976.2021.1987779.

[4] S. Hu, Y. Chen, Y. Chen, and C. Wang, "Depression and Anxiety Disorders in Patients With Inflammatory Bowel Disease," *Frontiers in Psychiatry*, vol. 12. Frontiers Media S.A., Oct. 08, 2021. doi: 10.3389/fpsyt.2021.714057.

[5] M. C. Dubinsky *et al.*, "Ulcerative Colitis Narrative Global Survey Findings: The Impact of Living with Ulcerative Colitis-Patients' and Physicians' View," *Inflammatory Bowel Diseases*, vol. 27, no. 11. Oxford University Press, pp. 1747–1755, Nov. 01, 2021. doi: 10.1093/ibd/izab016.

[6] A. Armuzzi and G. Liguori, "Quality of life in patients with moderate to severe ulcerative colitis and the impact of treatment: A narrative review," *Digestive and Liver Disease*, vol. 53, no. 7. Elsevier B.V., pp. 803–808, Jul. 01, 2021. doi: 10.1016/j.dld.2021.03.002.

[7] F. Rapport, C. Clement, A. C. Seagrove, L. Alrubaiy, H. A. Hutchings, and J. G. Williams, "Patient views about the impact of ulcerative colitis and its management with drug treatment and surgery: A nested qualitative study within the

CONSTRUCT trial," *BMC Gastroenterol*, vol. 19, no. 1, Oct. 2019, doi: 10.1186/s12876-019-1085-y.

[8] E. Paulides, D. Cornelissen, A. C. de Vries, and C. J. van der Woude, "Inflammatory bowel disease negatively impacts household and family life," *Frontline Gastroenterol*, vol. 13, no. 5, pp. 402–408, Sep. 2022, doi: 10.1136/flgastro-2021-102027.

[9] G. Byrne *et al.*, "Prevalence of anxiety and depression in patients with inflammatory bowel disease," *Can J Gastroenterol Hepatol*, vol. 2017, 2017, doi: 10.1155/2017/6496727.

[10] A. Abu Sneineh *et al.*, "Prevalence of anxiety and depressive symptoms in ulcerative colitis patients in Jordan and its relationship to patient-reported disease activity," *Sci Rep*, vol. 12, no. 1, Dec. 2022, doi: 10.1038/s41598-022-11911-4.

[11] B. Barberio, M. Zamani, C. J. Black, E. V. Savarino, and A. C. Ford, "Prevalence of symptoms of anxiety and depression in patients with inflammatory bowel disease: a systematic review and meta-analysis," *Lancet Gastroenterol Hepatol*, vol. 6, no. 5, pp. 359–370, May 2021, doi: 10.1016/S2468-1253(21)00014-5.

[12] D. Desai, "Psychiatric morbidity in inflammatory bowel disease: Time to screen all the patients," *Indian Journal of Gastroenterology*, vol. 37, no. 4. Indian Society of Gastroenterology, pp. 281–283, Jul. 01, 2018. doi: 10.1007/s12664-018-0891-4.

[13] X. Gao *et al.*, "Symptoms of anxiety/depression is associated with more aggressive inflammatory bowel disease," *Sci Rep*, vol. 11, no. 1, Dec. 2021, doi: 10.1038/s41598-021-81213-8.

[14] M. C. Dubinsky *et al.*, "Burden of comorbid anxiety and depression in patients with inflammatory bowel disease: a systematic literature review," *Expert Review of Gastroenterology and Hepatology*, vol. 15, no. 9. Taylor and Francis Ltd., pp. 985–997, 2021. doi: 10.1080/17474124.2021.1911644.

[15] D. Sgambato, A. Miranda, R. Ranaldo, A. Federico, and M. Romano, "The Role of Stress in Inflammatory Bowel Diseases," *Curr Pharm Des*, vol. 23, no. 27, Mar. 2017, doi: 10.2174/1381612823666170228123357.

[16] T. H. Bisgaard, K. H. Allin, R. Elmahdi, and T. Jess, "The bidirectional risk of inflammatory bowel disease and anxiety or depression: A systematic review and meta-analysis," *General Hospital Psychiatry*, vol. 83. Elsevier Inc., pp. 109–116, Jul. 01, 2023. doi: 10.1016/j.genhosppsych.2023.05.002.

[17] E. I. Tomazoni and D. M. Benvegnú, "Symptoms of anxiety and depression, and quality of life of patients with Crohn's disease," *Arq Gastroenterol*, vol. 55, no. 2, pp. 148–153, Apr. 2018, doi: 10.1590/s0004-2803.201800000-26.

[18] J. J. Rozich, A. Holmer, and S. Singh, "Effect of Lifestyle Factors on Outcomes in Patients with Inflammatory Bowel Diseases," *American Journal of Gastroenterology*, vol. 115, no. 6. Wolters Kluwer Health, pp. 832–840, Jun. 01, 2020. doi: 10.14309/ajg.0000000000000608.

[19] R. P. Hirten *et al.*, "Longitudinal Autonomic Nervous System Measures Correlate with Stress and Ulcerative Colitis Disease Activity and Predict Flare," *Inflamm Bowel Dis*, vol. 27, no. 10, pp. 1576–1584, Oct. 2021, doi: 10.1093/ibd/izaa323.

[20] B. Jonefjäll, L. Öhman, M. Simrén, and H. Strid, "IBS-like Symptoms in Patients with Ulcerative Colitis in Deep Remission Are Associated with Increased Levels of Serum Cytokines and Poor Psychological Well-being," *Inflamm Bowel Dis*, vol. 22, no. 11, pp. 2630–2640, Oct. 2016, doi: 10.1097/MIB.0000000000000921.

[21] S. Peppas *et al.*, "The brain-gut axis: Psychological functioning and inflammatory bowel diseases," *Journal of Clinical Medicine*, vol. 10, no. 3. MDPI, pp. 1–22, Jan. 01, 2021. doi: 10.3390/jcm10030377.

[22] E. Sinagra, E. Utzeri, G. C. Morreale, C. Fabbri, F. Pace, and A. Anderloni, "Microbiota-gut-brain axis and its affect inflammatory bowel disease: Pathophysiological concepts and insights for clinicians," *World Journal of Clinical Cases*, vol. 8, no. 6. Baishideng Publishing Group Co, pp. 1013–1025, Mar. 26, 2020. doi: 10.12998/wjcc.v8.i6.1013.

[23] L. Ge *et al.*, "Psychological stress in inflammatory bowel disease: Psychoneuroimmunological insights into bidirectional gut–brain communications," *Frontiers in Immunology*, vol. 13. Frontiers Media S.A., Oct. 06, 2022. doi: 10.3389/fimmu.2022.1016578.

[24] J. A. Foster, L. Rinaman, and J. F. Cryan, "Stress & the gut-brain axis: Regulation by the microbiome," *Neurobiology of Stress*, vol. 7. Elsevier Inc., pp. 124–136, Dec. 01, 2017. doi: 10.1016/j.ynstr.2017.03.001.

[25] L. Zhao *et al.*, "Bidirectional gut-brain-microbiota axis as a potential link between inflammatory bowel disease and ischemic stroke," *J Neuroinflammation*, vol. 15, no. 1, Dec. 2018, doi: 10.1186/s12974-018-1382-3.

[26] S. Breit, A. Kupferberg, G. Rogler, and G. Hasler, "Vagus nerve as modulator of the brain-gut axis in psychiatric and inflammatory disorders," *Frontiers in Psychiatry*, vol. 9, no. MAR. Frontiers Media S.A., Mar. 13, 2018. doi: 10.3389/fpsyt.2018.00044.

[27] Y. Lee and Y.-K. Kim, "Understanding the Connection Between the Gut-Brain Axis and Stress/Anxiety Disorders," 1920, doi: 10.1007/s11920-021-01235-x/Published.

[28] C. Günther, V. Rothhammer, M. Karow, M. Neurath, and B. Winner, "The gut-brain axis in inflammatory bowel disease—current and future perspectives," *International Journal of Molecular Sciences*, vol. 22, no. 16. MDPI, Aug. 02, 2021. doi: 10.3390/ijms22168870.

[29] S. M. Collins, "Interrogating the Gut-Brain Axis in the Context of Inflammatory Bowel Disease: A Translational Approach," *Inflammatory Bowel Diseases*, vol. 26, no. 4. Oxford University Press, pp. 493–501, Mar. 04, 2020. doi: 10.1093/ibd/izaa004.

[30] "Understanding the Gut-Brain Connection | Psychology Today." https://www.psychologytoday.com/us/blog/the-brain-body-connection/202108/understanding-the-gut-brain-connection (accessed Aug. 21, 2023).

[31] "Anxiety and Gut Health: How They're Connected." https://well.org/gut-health/anxiety-and-gut-connected/ (accessed Aug. 21, 2023).

[32] L. H. Morais, H. L. Schreiber, and S. K. Mazmanian, "The gut microbiota–brain axis in behaviour and brain disorders," *Nature Reviews Microbiology*, vol. 19, no. 4. Nature Research, pp. 241–255, Apr. 01, 2021. doi: 10.1038/s41579-020-00460-0.

[33] R. G. Xiong *et al.*, "The Role of Gut Microbiota in Anxiety, Depression, and Other Mental Disorders as Well as the Protective Effects of Dietary

Components," *Nutrients*, vol. 15, no. 14. NLM (Medline), Jul. 01, 2023. doi: 10.3390/nu15143258.

[34] M. Carabotti, A. Scirocco, M. Antonietta Maselli, and C. Severi, "The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems," 2015. [Online]. Available: www.annalsgastro.gr

[35] A. Rutsch, J. B. Kantsjö, and F. Ronchi, "The Gut-Brain Axis: How Microbiota and Host Inflammasome Influence Brain Physiology and Pathology," *Frontiers in Immunology*, vol. 11. Frontiers Media S.A., Dec. 10, 2020. doi: 10.3389/fimmu.2020.604179.

[36] K. Socała *et al.*, "The role of microbiota-gut-brain axis in neuropsychiatric and neurological disorders," *Pharmacological Research*, vol. 172. Academic Press, Oct. 01, 2021. doi: 10.1016/j.phrs.2021.105840.

[37] Gut Brain Axis (GBA). (n.d.). Retrieved from https://www.physio-pedia.com/Gut_Brain_Axis_(GBA)

[38] T. Limbana, F. Khan, and N. Eskander, "Gut Microbiome and Depression: How Microbes Affect the Way We Think," *Cureus*, Aug. 2020, doi: 10.7759/cureus.9966.

[39] N. Tatiya-Aphiradee, W. Chatuphonprasert, and K. Jarukamjorn, "Immune response and inflammatory pathway of ulcerative colitis," *Journal of Basic and Clinical Physiology and Pharmacology*, vol. 30, no. 1. De Gruyter, pp. 1–10, Jan. 01, 2019. doi: 10.1515/jbcpp-2018-0036.

[40] K. Hou *et al.*, "Microbiota in health and diseases," *Signal Transduction and Targeted Therapy*, vol. 7, no. 1. Springer Nature, Dec. 01, 2022. doi: 10.1038/s41392-022-00974-4.

[41] J. Balaguer-Trias, D. Deepika, M. Schuhmacher, and V. Kumar, "Impact of Contaminants on Microbiota: Linking the Gut–Brain Axis with Neurotoxicity," *International Journal of Environmental Research and Public Health*, vol. 19, no. 3. MDPI, Feb. 01, 2022. doi: 10.3390/ijerph19031368.

[42] J. F. Cryan *et al.*, "The Microbiota-Gut-Brain Axis," *Physiol Rev*, vol. 99, pp. 1877–2013, 2019, doi: 10.1152/physrev.00018.2018.-The.

[43] A. Chakrabarti *et al.*, "The microbiota–gut–brain axis: pathways to better brain health. Perspectives on what we know, what we need to investigate and how to put knowledge into practice," *Cellular and Molecular Life Sciences*, vol. 79, no.

2. Springer Science and Business Media Deutschland GmbH, Feb. 01, 2022. doi: 10.1007/s00018-021-04060-w.

[44] Phillips, Q. (2021, August 19). *The link between mental health disorders and ulcerative colitis*. EverydayHealth.com. https://www.everydayhealth.com/ulcerative-colitis/link-between-mental-health-disorders-ulcerative-colitis/

[45] A. Kaser, S. Zeissig, and R. S. Blumberg, "Inflammatory bowel disease," *Annual Review of Immunology*, vol. 28. pp. 573–621, Apr. 23, 2010. doi: 10.1146/annurev-immunol-030409-101225.

[46] X. Gao *et al.*, "Chronic stress promotes colitis by disturbing the gut microbiota and triggering immune system response," *Proc Natl Acad Sci U S A*, vol. 115, no. 13, pp. E2960–E2969, Mar. 2018, doi: 10.1073/pnas.1720696115.

[47] Y. Oligschlaeger, T. Yadati, T. Houben, C. M. C. Oliván, and R. Shiri-Sverdlov, "Inflammatory bowel disease: A stressed 'gut/feeling,'" *Cells*, vol. 8, no. 7. MDPI, Jul. 01, 2019. doi: 10.3390/cells8070659.

[48] Y. Sun, L. Li, R. Xie, B. Wang, K. Jiang, and H. Cao, "Stress Triggers Flare of Inflammatory Bowel Disease in Children and Adults," *Frontiers in Pediatrics*, vol. 7. Frontiers Media S.A., Oct. 24, 2019. doi: 10.3389/fped.2019.00432.

[49] C. R. Shaler *et al.*, "Psychological stress impairs IL22-driven protective gut mucosal immunity against colonising pathobionts," *Nat Commun*, vol. 12, no. 1, Dec. 2021, doi: 10.1038/s41467-021-26992-4.

[50] J. M. Allen *et al.*, "Psychological stress disrupts intestinal epithelial cell function and mucosal integrity through microbe and host-directed processes," *Gut Microbes*, vol. 14, no. 1, 2022, doi: 10.1080/19490976.2022.2035661.

[51] P. J. Karl *et al.*, "Effects of psychological, environmental and physical stressors on the gut microbiota," *Frontiers in Microbiology*, vol. 9, no. SEP. Frontiers Media S.A., Sep. 11, 2018. doi: 10.3389/fmicb.2018.02013.

[52] *How and why are ulcerative colitis and stress linked?* (n.d.). How And Why Are Ulcerative Colitis and Stress Linked? https://www.medicalnewstoday.com/articles/ulcerative-colitis-and-mental-health-link

[53] Glia Cells Link Chronic Stress to Inflammatory Bowel Disease. (2023, June 8). Retrieved from

https://www.pennmedicine.org/news/news-releases/2023/june/glia-cells-link-chronic-stress-to-inflammatory-bowel-disease

[54] F. Rizzello *et al.*, "Implications of the westernized diet in the onset and progression of IBD," *Nutrients*, vol. 11, no. 5. MDPI AG, May 01, 2019. doi: 10.3390/nu11051033.

[55] N. Narula *et al.*, "Association of ultra-processed food intake with risk of inflammatory bowel disease: Prospective cohort study," *The BMJ*, vol. 374, Jul. 2021, doi: 10.1136/bmj.n1554.

[56] H. Morton, K. C. Pedley, R. J. C. Stewart, and J. Coad, "Inflammatory bowel disease: Are symptoms and diet linked?," *Nutrients*, vol. 12, no. 10, pp. 1–14, Oct. 2020, doi: 10.3390/nu12102975.

[57] S. L. Jowett *et al.*, "Influence of dietary factors on the clinical course of ulcerative colitis: A prospective cohort study," *Gut*, vol. 53, no. 10, pp. 1479–1484, Oct. 2004, doi: 10.1136/gut.2003.024828.

[58] I. M. Saracino *et al.*, "The Bidirectional Link between Nutritional Factors and Inflammatory Bowel Diseases: Dietary Deficits, Habits, and Recommended Interventions—A Narrative Review," *Foods*, vol. 12, no. 10. MDPI, May 01, 2023. doi: 10.3390/foods12101987.

[59] X. Ma *et al.*, "Excessive intake of sugar: An accomplice of inflammation," *Frontiers in Immunology*, vol. 13. Frontiers Media S.A., Aug. 31, 2022. doi: 10.3389/fimmu.2022.988481.

[60] H. Jafari-Vayghan, S. Mirmajidi, Z. Mollarasouli, F. Vahid, S. Saleh-Ghadimi, and P. Dehghan, "Mental health is associated with nutrient patterns and Index of Nutritional Quality (INQ) in adolescent girls - an analytical study," *Human Nutrition and Metabolism*, vol. 31, Mar. 2023, doi: 10.1016/j.hnm.2022.200176.

[61] C. H. Lo *et al.*, "Ultra-processed Foods and Risk of Crohn's Disease and Ulcerative Colitis: A Prospective Cohort Study," *Clinical Gastroenterology and Hepatology*, vol. 20, no. 6, pp. e1323–e1337, Jun. 2022, doi: 10.1016/j.cgh.2021.08.031.

[62] T. H. Taft, L. Keefer, C. Leonhard, and M. Nealon-Woods, "Impact of perceived stigma on inflammatory bowel disease patient outcomes," *Inflamm Bowel Dis*, vol. 15, no. 8, pp. 1224–1232, 2009, doi: 10.1002/ibd.20864.

[63] D. Luo *et al.*, "Resilience as a Mediator of the Association Between Perceived Stigma and Quality of Life Among People With Inflammatory Bowel Disease," *Front Psychiatry*, vol. 12, Aug. 2021, doi: 10.3389/fpsyt.2021.709295.

[64] C. M. Roberts *et al.*, "Illness Stigma, Worry, Intrusiveness, and Depressive Symptoms in Youth with Inflammatory Bowel Disease," *J Pediatr Gastroenterol Nutr*, vol. 72, no. 3, pp. 404–409, Mar. 2021, doi: 10.1097/MPG.0000000000002939.