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Kulchytska O.M., Kuzminova N.V., Nazarova M.S., Hnatyshyn M.S., Burdeina L.V., Kedyk I.O., Savytska O.O.
National Pirogov Memorial Medical University, Vinnytsya

FEATURES OF DEVELOPMENT, CLINICAL COURSE, AND MANAGEMENT OF OVERLAP SYNDROME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES AND IRRITABLE BOWEL SYNDROME

e-mail: olenakulchytskavnmu@gmail.com

Irritable bowel syndrome and inflammatory bowel diseases are common gastroenterological conditions that significantly affect patients' quality of life and create diagnostic challenges due to overlapping clinical manifestations. Patients with inflammatory bowel disease in remission often continue to experience symptoms characteristic of irritable bowel syndrome, forming the so-called overlap syndrome. This study analyzed clinical records and observational data of patients with a combined course of inflammatory bowel disease and irritable bowel syndrome. A comprehensive assessment of clinical manifestations, laboratory and instrumental findings, and therapeutic outcomes was performed. The results showed that overlap syndrome occurs in a significant proportion of patients with inflammatory bowel disease in remission, with the main features including persistent diarrhea, abdominal pain, increased intestinal sensitivity, and impaired quality of life. Standard anti-inflammatory therapies were found to be insufficient for controlling functional symptoms, highlighting the need for an integrated approach that combines baseline treatment of inflammatory processes with strategies for managing irritable bowel syndrome. The novelty of this study lies in the comprehensive description of pathophysiological mechanisms, clinical features, and treatment outcomes of overlap syndrome, providing practical guidance for gastroenterologists and improving the accuracy of assessing disease activity. Systematic symptom monitoring and individualized therapy were shown to enhance patient management, reduce the frequency of relapses, and improve quality of life, representing a significant contribution to global gastroenterological practice.

Key words: inflammatory bowel diseases, Crohn's disease, ulcerative colitis, irritable bowel syndrome, overlap syndrome, functional gastrointestinal disorders.

Кульчицька О.М., Кузьмінова Н.В., Назарова М.С., Гнатишин М.С., Бурдейна Л.В., Кедик І.О., Савицька О.О.

ОСОБЛИВОСТІ ФОРМУВАННЯ, КЛІНІЧНОГО ПЕРЕБІГУ ТА ЛІКУВАННЯ ОВЕРЛАП СИНДРОМУ У ХВОРИХ ІЗ ЗАПАЛЬНИМИ ЗАХВОРЮВАННЯМИ КИШЕЧНИКА ТА СИНДРОМОМ ПОДРАЗНЕНОГО КИШЕЧНИКА

Синдром подразненого кишечника та запальні захворювання кишечника – різні гастроентерологічні захворювання, що мають істотний вплив на якість життя пацієнтів. Клінічні прояви можуть бути дуже схожі, особливо при наявності синдрому подразненого кишечника з діареєю, що обумовлює певну складність у діагностиці. Синдром подразненого кишечника є функціональним розладом кишечника, що характеризується хронічними абдомінальними симптомами без структурних чи біохімічних порушень, тоді як запальні захворювання кишечника, основними з яких є хвороба Крона та неспецифічний виразковий коліт, супроводжуються морфологічно підтвердженим запаленням. У клінічній практиці все частіше спостерігається явище так званого «оверлапу» між цими станами, коли пацієнт із запальним захворюванням кишечнику у ремісії продовжує скаржитися на симптоми, що також притаманні синдрому подразненого кишечника. Це створює діагностичні труднощі, ускладнює лікування та часто призводить до неправильної оцінки активності основного захворювання. Ця стаття присвячена аналізу патофізіологічних механізмів, клінічних проявів, діагностичних підходів та терапевтичних стратегій у випадках «оверлап-синдрому» запальних захворювань кишечника та синдрому подразненого кишечника.

Ключові слова: запальні захворювання кишечника, хвороба Крона, неспецифічний виразковий коліт, синдром подразненого кишечника, оверлап-синдром, функціональні захворювання шлунково-кишкового тракту.

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Inflammatory bowel disease (IBD) encompasses complex chronic inflammatory disorders of the gastrointestinal (GI) tract of uncertain etiology, characterized by a chronic relapsing intestinal inflammation. An emerging challenge in clinical practice is understanding the prevalence and impact of comorbid irritable bowel syndrome (IBS) in patients with IBD. Every fourth patient with endoscopically confirmed quiescent IBD reports persistent GI symptoms that frequently mimic IBS manifestations [2]. IBS symptoms arise from complex interactions between biological, psychological, and social factors, such as alterations in intestinal sensory perception leading to the interpretation of normal physiological stimuli as painful (visceral hypersensitivity), and cognitive-affective processes (e.g., catastrophic thinking regarding GI symptoms) [24] etc. The overlap between IBD and IBS is associated with anxiety, depression, fatigue, sleep disturbances, and increased healthcare utilization, even when IBD is in remission [2]. This condition necessitates management strategies that extend beyond mere suppression of inflammation.

When evaluating current GI symptoms in IBD patients, it is crucial to determine whether symptoms are driven by inflammation or intestinal dysfunction, as treatment must be tailored to the underlying pathophysiological mechanism. Gastroenterologists may erroneously escalate IBD-specific pharmacotherapy when symptoms are actually caused by underlying IBS. This can result in reduced treatment effectiveness and expose patients to unnecessary risks associated with IBD medications (e.g., infections, malignancies) without any clinical benefit. Selecting effective therapy for the subpopulation of patients with overlapping IBD and IBS can improve quality of life and reduce healthcare utilization. Clinical disease activity indices are commonly used to assess IBD activity; however, these clinical parameters often overlap with IBS symptoms [22]. Consequently, when activity indices are high, clinicians frequently rely on objective markers of inflammation. However, when activity indices are low, clinicians do not always consider that GI symptoms may be related to IBS or another functional bowel disorder.

The purpose of the study was to review current evidence on the clinical, pathophysiological, and diagnostic overlap between IBS and IBD, to analyze the challenges in differential diagnosis, and to highlight approaches to effective patient management when both conditions coexist or overlap.

Materials and methods. This review analyzed scientific publications by both domestic and international authors. To conduct the review, electronic databases of medical and biological literature were used, specifically PubMed/MEDLINE, Scopus, and Web of Science. Only full-text sources were included in the analysis. The search was last performed on January 15, 2025. Publications from January 1, 2020 to January 15, 2025 were included; sources published prior to 2020 were excluded unless they represented foundational clinical guidelines (ECCO, ACG 2020, AGA 2022) or landmark systematic reviews with no more recent equivalent.

Search Strategy. Separate search queries were constructed for each database using controlled vocabulary and free-text terms combined with Boolean operators.

Database 1 – PubMed/MEDLINE.

("irritable bowel syndrome"[MeSH Terms] OR "IBS"[tiab])

AND

("inflammatory bowel disease"[MeSH Terms] OR "IBD"[tiab] OR "Crohn's disease"[tiab] OR "ulcerative colitis"[tiab])

AND

("overlap"[tiab] OR "comorbidity"[tiab] OR "differential diagnosis"[tiab] OR "clinical features"[tiab] OR "pathophysiology"[tiab] OR "management"[tiab])

NOT ("pediatric"[tiab] OR "children"[tiab] OR "animal study"[tiab])

Filters: Full text, Publication date: 2020/01/01–2025/01/15, Language: English

Database 2 – Scopus.

TITLE-ABS-KEY ("irritable bowel syndrome" OR "IBS")

AND TITLE-ABS-KEY ("inflammatory bowel disease" OR "IBD" OR "Crohn's disease" OR "ulcerative colitis")

AND TITLE-ABS-KEY ("overlap" OR "comorbidity" OR "differential diagnosis" OR "clinical overlap" OR "pathophysiology" OR "management" OR "guidelines")

AND NOT TITLE-ABS-KEY ("pediatric" OR "children" OR "animal")

AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re"))

AND LIMIT-TO (PUBYEAR, 2020, 2025)

Database 3 – Web of Science.

TS=("irritable bowel syndrome" OR "IBS")

AND TS=("inflammatory bowel disease" OR "IBD" OR "Crohn's disease" OR "ulcerative colitis")

AND TS=("overlap" OR "comorbidity" OR "differential diagnosis" OR "clinical features" OR "pathophysiology" OR "management" OR "clinical guidelines")

NOT TS=("pediatric" OR "children" OR "animal model")

Refined by: Document Types = Article OR Review

Timespan: 2020-01-01 to 2025-01-15

Inclusion and Exclusion Criteria.

Inclusion criteria: randomized controlled trials; systematic reviews and meta-analyses; analytical reviews; current clinical guidelines (ECCO, ACG, AGA); studies addressing the clinical overlap between IBS and IBD; full-text availability; English or Ukrainian language.

Exclusion criteria: publications prior to January 2020 (except pivotal guidelines); case reports and case series; conference abstracts without full-text publication; studies involving exclusively pediatric populations or animal models; duplicate records.

Study Selection and Characteristics. The study selection process followed the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) framework. Records were initially screened by title and abstract; those meeting the inclusion criteria proceeded to full-text assessment. Disagreements were resolved by consensus.

Results of the study and their discussion. IBD represents a group of chronic, immune-mediated inflammatory disorders of the GI tract of unknown etiology, characterized by a relapsing-remitting course and morphologically confirmed mucosal inflammation. The primary forms of IBD are Crohn’s disease (CD) and ulcerative colitis (UC). These entities are differentiated by the localization and depth of intestinal wall involvement [5]. Both conditions are classified by severity (mild, moderate, or severe) and anatomical distribution. The prevalence of IBD reaches nearly 0.5 % in Western populations, with a distinct upward trend in recent years [7].

The etiology of IBD remains uncertain and is likely multifactorial. Intestinal inflammation is believed to result from immune system activation

in genetically susceptible individuals exposed to environmental factors [18]. Extensive research has focused on identifying the mechanisms underlying IBD development and progression, including advances in cellular and molecular biology, understanding of immune responses and inflammatory cascades, and genetic analysis technologies. In addition, the enteric nervous system (ENS) and the gut-brain axis play important roles in IBD pathogenesis [25].

Table 1

Simplified PRISMA Flow

Stage	Description	Number of Records/Studies
1. Identified	Total number of records identified through database searching and other sources	121
2. Duplicates Removed	Number of records removed before screening (e.g., duplicates)	21
3. Screened (Title/Abstract)	Number of records screened after duplicates were removed	100
4. Assessed for Eligibility (Full-text)	Number of full-text articles assessed for eligibility against the inclusion/exclusion criteria	68
5. Included in Review	Total number of primary studies finally included in the systematic review	32

The Role of Genetics in the Development of IBD. More than 200 gene polymorphisms and genetic variants associated with IBD have been identified [11]. However, no single variant can fully explain disease development, and most individuals carrying risk alleles do not develop IBD. Genetic susceptibility alone is insufficient to account for IBD onset and progression, highlighting the importance of further research into additional factors that interact with genetic predisposition [4].

Immune Modulation and IBD. IBD is characterized by immune dysregulation during active disease, including expansion of effector T cells and excessive production of proinflammatory cytokines such as TNF-α, IL-6, and IFN-γ. The balance between proinflammatory and immunosuppressive mechanisms determines the progression of intestinal inflammation [4]. T helper 17 cells play a key role in colitis pathogenesis through IL-17 production following stimulation by IL-1, IL-6, IL-23, and TGF-β. Their development and function are strongly influenced by the intestinal microbiota [4].

Gut Microbiota and IBD. The gut microbiota plays a central role in the pathogenesis of IBD. Studies suggest that disturbances in microbiota composition may trigger maladaptive immune responses in genetically predisposed individuals, leading to loss of tolerance toward commensal microorganisms and the development of dysbiosis [4]. Although substantial evidence supports the involvement of microbiota in IBD, the specific microbial and functional changes responsible for initiating and maintaining inflammation remain under investigation [17].

IBD and Environmental Factors. Environmental factors significantly influence the development and course of IBD through interactions with genetic susceptibility, the gut microbiome, and the immune system. Urbanization, a Westernized lifestyle, diet, smoking, stress, early antibiotic exposure, and reduced microbial contact may alter microbiota composition and immune responses, increasing IBD risk and severity. Conversely, factors that promote microbial diversity, such as breastfeeding, large family size, and animal exposure, as well as appendectomy and smoking in UC, have complex and sometimes contradictory effects on disease risk and clinical outcomes [5].

Psychological Changes in IBD. IBD is associated with increased psychological distress, particularly anxiety and depression, which are more common during active disease and may affect its course and prognosis. Current evidence supports a bidirectional relationship between inflammation and the brain, whereby psychological factors can both result from and influence IBD activity through neuroendocrine and autonomic pathways. However, findings on the causal association between psychiatric disorders and IBD activity remain inconsistent, reflecting the complex and incompletely understood nature of this interaction [31].

The Gut-Brain Axis. Digestive function and homeostasis are regulated by the gut-brain axis, a bidirectional communication network between the central nervous system (CNS) and ENS [10]. This interaction involves neural, neuroendocrine, and immune pathways, particularly the H ypothalamic-Pituitary-Adrenal (HPA) axis and autonomic nervous system (ANS). The sympathetic division influences motility and immune responses, whereas the parasympathetic division exerts predominantly anti-inflammatory effects [25, 27]. Under stress, activation of the HPA axis increases glucocorticoid (GC) and catecholamine levels, enhances intestinal permeability, and contributes to dysbiosis, mucosal inflammation, and elevated pro-inflammatory cytokines (TNF-α, IL-6, IFN-γ), creating a self-perpetuating inflammatory cycle [12, 25].

Dysregulation of these pathways by stress, anxiety, or depression may impair gut motility and immune function, contributing to the development or exacerbation of IBD [10].

The ANS and IBD. The ANS provides a bidirectional connection between the brain and the gut and plays a crucial role in regulating intestinal motility, secretion, and mucosal immune responses. Immune activation triggers the “acute sickness response,” mediated by pro-inflammatory

cytokines such as IL-1, IL-6, and TNF-α acting on the CNS [12, 27].

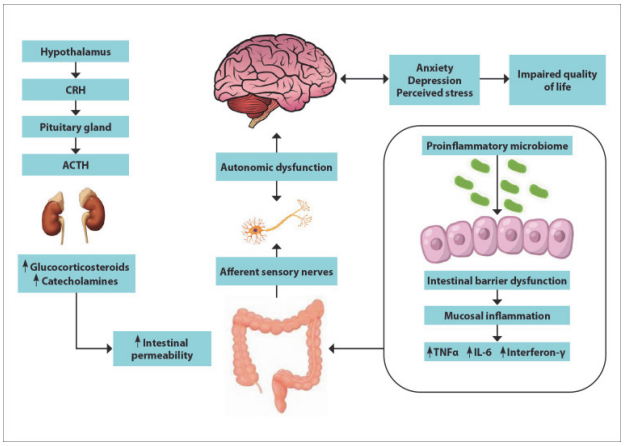

Fig. 1. Proposed neurohormonal pathways of the gut-brain axis. ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing hormone; IL, interleukin; TNFα, tumor necrosis factor alpha [12].

The gut contains an extensive neuroimmune network in which enteric neurons closely interact with immune cells. Inflammatory signals are transmitted to the brain through neural and endocrine pathways, activating central responses, including the HPA axis and the release of anti-inflammatory GC. The vagus nerve exerts anti-inflammatory effects via the cholinergic pathway, whereas the sympathetic nervous system may have both pro- and anti-inflammatory actions depending on the stage of inflammation [25].

IBD is associated with ANS imbalance, characterized by reduced vagal tone and/or sympathetic hyperactivity, contributing to chronic inflammation and autonomic dysfunction [12]. The ANS, ENS, CNS, and intestinal immune system are closely interconnected, and higher brain regions, including the prefrontal cortex, hippocampus, and amygdala, further modulate autonomic signaling and gut function [25, 32].

Psychological factors and ANS activity are closely integrated and influence patients' adaptation to disease. Although autonomic dysfunction has been reported in IBD, its severity appears to depend on coping strategies and emotional status, and the underlying mechanisms remain incompletely understood [10,12]. Both the ANS and HPA axis are activated by psychological and physical stressors, suggesting that neuropsychological factors may influence the course and severity of IBD and alter physiological responses to stress during chronic inflammation [12, 25].

Clinically, IBD is characterized by recurrent periods of disease activity and remission, with common symptoms including altered bowel habits, urgency, and rectal bleeding [5].

According to the World Gastroenterology Organization, common symptom-based features of IBD include: diarrhea with blood and mucus, nocturnal diarrhea and fecal incontinence are not uncommon; constipation in some patients with UC, particularly when disease involvement is limited to the rectum; abdominal pain, tenesmus, and severe urgency; right lower quadrant pain in CD and left lower quadrant pain in UC; nausea and vomiting, which occur more frequently in CD [4].

Assessment of IBD activity and treatment response combines patient-reported symptoms with objective clinical and laboratory findings. Physical examination may reveal tachycardia, fever, dehydration, anxiety, and signs of anemia, while perianal fistulas, abscesses, and, rarely, rectal prolapse are characteristic features of CD [5].

Diagnosis is based on clinical presentation, inflammatory biomarkers, imaging studies, and endoscopic evaluation with histological confirmation. Common laboratory abnormalities include microcytic anemia, leukocytosis, thrombocytosis, and elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels [5]. In selected cases, infectious and parasitic diseases, including giardiasis, amebiasis, strongyloidiasis, yersiniosis, and tuberculosis, must be excluded.

Fecal calprotectin is a widely used marker of intestinal inflammation. This neutrophil-derived S100 family protein has antimicrobial properties and demonstrates good diagnostic performance (sensitivity 0.88; specificity 0.80) [11, 19]. Although elevated levels are not specific to IBD, fecal calprotectin remains valuable for assessing disease activity and monitoring inflammatory changes.

Fecal lactoferrin, an iron-binding glycoprotein released by activated neutrophils, is another useful biomarker of intestinal inflammation. Elevated fecal lactoferrin levels correlate with the degree of intestinal inflammation and show high diagnostic accuracy (sensitivity 0.82; specificity 0.95) in patients with IBD [7, 19].

Ileocolonoscopy with biopsy remains the gold standard for IBD diagnosis [18]. CD most commonly affects the terminal ileum and is characterized by segmental transmural inflammation, strictures, fistulas, and occasional noncaseating granulomas, although their absence does not exclude the diagnosis. In contrast, UC typically presents with continuous inflammation extending proximally from the rectum and is generally limited to the mucosa and superficial submucosa. Histological findings in both conditions include features of active inflammation and chronic mucosal injury [7].

As IBD remains incurable, treatment focuses on controlling inflammation and maintaining remission [7]. Aminosalicylates, particularly 5-aminosalicylic acid, remain first-line therapy for mild-to-moderate UC because of their anti-inflammatory and immunomodulatory properties [11]. GC, such as budesonide, suppress pro-inflammatory cytokine production and are mainly used for short-term induction of remission in moderate-to-severe disease; however, long-term use is limited by adverse effects [7, 11].

Immunomodulators, including thiopurines and methotrexate, inhibit T-cell proliferation and pro-inflammatory cytokine production. They are used for maintenance therapy when GC or aminosalicylates are insufficient, or in combination with anti-TNF agents to reduce immunogenicity [7].

Biological therapies consist of monoclonal antibodies targeting key pro-inflammatory cytokines, such as TNF (infliximab, adalimumab), IL-12/23 (ustekinumab), and IL-23 (risankizumab, mirikizumab, guselkumab), as well as integrin inhibitors (vedolizumab, natalizumab).

Newer therapeutic approaches include small-molecule drugs (SMDs), such as the oral Janus kinase (JAK) inhibitor tofacitinib, which suppresses JAK1, JAK2, and JAK3 signaling, thereby reducing T-cell and natural killer cell activity and modulating pro-inflammatory cytokine production [7, 11].

Other SMDs include sphingosine-1-phosphate receptor modulators, such as ozanimod and etrasimod, which prevent lymphocyte migration from lymph nodes into the systemic circulation, thereby reducing intestinal inflammation [18].

Furthermore, given that the gut microbiota plays an important role in the development of IBD, the use of certain antibiotics, probiotics, prebiotics, synbiotics, and postbiotics, as well as fecal microbiota transplantation, has been explored as a therapeutic strategy; however, the current evidence base remains limited [17].

IBS is a common chronic disorder of gut-brain interaction characterized by recurrent abdominal pain and alterations in bowel habits, including constipation, diarrhea, or both.

IBS affects approximately 11 % of the global population, although prevalence varies across regions [1]. Familial clustering suggests contributions from both genetic and sociocultural factors. IBS is more frequently diagnosed in women in Western countries and is most common in younger individuals, with prevalence declining after 50 years of age [29].

Despite its high prevalence and impact on quality of life, IBS remains underdiagnosed and undertreated [1]. Its pathophysiology is multifactorial and involves disturbances of the gut-brain axis, visceral hypersensitivity, altered GI motility, changes in the gut microbiota, food intolerance, and psychosocial factors [14].

Diagnosis is based on the Rome IV criteria and a targeted clinical evaluation. Abdominal pain related to defecation, together with altered bowel habits (constipation, diarrhea, or mixed patterns), represents the hallmark of IBS, while bloating is a common but nonessential symptom [1]. A positive diagnostic approach facilitates earlier diagnosis and improved patient outcomes.

Causes of IBS:

1. Gut-brain axis dysregulation is a central mechanism in IBS, leading to altered motility, increased visceral sensitivity, and changes in intestinal secretion. Genetic, hormonal, dietary, psychosocial, and epigenetic factors may contribute to this dysfunction, which is also associated with immune activation and microbiota alterations [13, 23].

2. Visceral hypersensitivity is characterized by enhanced perception of physiological and pathological intestinal stimuli due to sensitization of peripheral and central nociceptive pathways, contributing to abdominal pain and discomfort despite the absence of structural abnormalities [23].

3. GI motility disorders may result in delayed transit in constipation-predominant IBS or accelerated transit in diarrhea-predominant IBS. These abnormalities are closely linked to gut-brain axis dysfunction, visceral hypersensitivity, and dysbiosis [17].

4. Gut microbiota alterations (dysbiosis), including reduced beneficial bacteria and overgrowth of potentially pathogenic species, may affect motility, intestinal permeability, immune regulation, and sensory signaling, thereby contributing to bloating, pain, and other symptoms [28].

5. Food intolerance, particularly to fermentable oligo-, di-, monosaccharides and polyols (FODMAPs), lactose, and gluten, is frequently associated with symptom exacerbation, although dietary effects often interact with visceral hypersensitivity and psychosocial factors [15].

6. Low-grade mucosal inflammation and increased intestinal permeability, especially in post-infectious and diarrhea-predominant IBS, may enhance immune activation and neural sensitization, contributing to symptom persistence [6].

8. Psychosocial factors, including stress, anxiety, and depression, influence intestinal motility, secretion, microbiota composition, and pain perception through the gut-brain axis. Consequently, psychological interventions are considered an important component of comprehensive IBS management [17].

Thorough history-taking remains essential for identifying patients who meet the Rome IV criteria. A detailed medical history facilitates the identification of specific IBS subtypes, differentiates IBS from other conditions with overlapping symptoms, and allows for the assessment of alarm features (“red flags”) that may indicate underlying organic pathology.

According to the Rome IV criteria, an IBS diagnosis is based on recurrent abdominal pain occurring, on average, at least one day per week during the preceding three months. This pain must be associated with at least two of the following: defecation, a change in stool frequency, or a change in stool form (appearance). These criteria should be fulfilled for the past three months, with symptom onset at least six months prior to diagnosis. This structured approach promotes timely and accurate

diagnosis, enabling appropriate management while minimizing unnecessary investigations [1].

IBS Subtypes (classified based on predominant stool form using the Bristol Stool Form Scale): IBS with constipation (IBS-C): >25 % of bowel movements are types 1 or 2; IBS with diarrhea (IBS-D): >25 % of bowel movements are types 6 or 7; mixed IBS (IBS-M): Stool forms fluctuate between types 1–2 and 6–7; unclassified IBS (IBS-U): Patients meet IBS criteria, but their bowel habits cannot be reliably categorized into the three subtypes [1, 29].

Alarm Features ("Red Flags"). The presence of alarm features in a patient's history should raise suspicion for organic disease and prompt further diagnostic evaluation. These include: new-onset symptoms at age ≥50 years; hematochezia (bright red blood) or melena (black, tarry stools); fever, chills, or night sweats; nocturnal diarrhea; unintentional weight loss; a change in typical IBS symptoms (e.g., new or atypical abdominal pain); laboratory abnormalities (e.g., iron deficiency anemia, elevated CRP, fecal calprotectin, or lactoferrin); family history of GI malignancy, IBD, or celiac disease.

For patients with IBS-D, recommended investigations include serologic testing for celiac disease, measurement of fecal calprotectin or lactoferrin, and CRP to exclude IBD. Additional testing for bile acid-induced diarrhea may be considered when there is clinical suspicion. In regions endemic for giardiasis, stool antigen testing for Giardia is also recommended. Routine testing for food allergies or sensitivities, general stool analysis, or hydrogen breath testing for small intestinal bacterial overgrowth (SIBO) should be performed only when clinical suspicion specifically warrants these investigations [1].

Although IBD and IBS are nosologically distinct conditions, they share common pathogenic mechanisms, including the involvement of the CNS, ANS, and ENS in the regulation of GI function and immune responses. Consequently, the coexistence of these two disorders in the same patient is pathophysiologically plausible, clinically logical, and entirely possible. Mucosal inflammation, altered gut microbiome composition, activation of the ENS, and dysregulation of the gut-brain axis are associated with both conditions [2].

The pathway to effective IBS management is multifaceted and depends on a comprehensive understanding of the patient's symptoms, lifestyle, and preferences [20].

Management of IBS-C. Pharmacologic treatment of IBS-C primarily aims to improve intestinal transit, increase secretion, and reduce visceral hypersensitivity. First-line therapy includes soluble, non-fermentable fiber, which improves stool consistency and facilitates defecation with minimal bloating [8, 9]. Osmotic laxatives are commonly used to increase stool frequency, although their effect on abdominal pain is limited [8].

In patients with persistent symptoms, secretagogues can improve bowel function and reduce visceral hypersensitivity, while serotonergic prokinetic agents may be considered in selected cases. Newer therapies that increase luminal water content and reduce electrolyte absorption have also demonstrated efficacy, although diarrhea remains the most common adverse effect [8, 20].

Management of IBS-D. Pharmacologic treatment of IBS-D aims to reduce stool frequency and urgency, normalize intestinal secretion, and relieve abdominal pain and bloating. Antidiarrheal agents effectively control diarrhea but have limited effects on overall symptom burden [21].

Non-absorbable antibiotics may improve abdominal pain, bloating, and stool consistency and can be administered in repeated short courses when symptoms recur. Agents acting on opioid receptors are effective for diarrhea and urgency but may be limited by contraindications and adverse effects [21].

5-HT_3 receptor antagonists can improve global symptoms and abdominal pain in patients with severe, treatment-refractory IBS-D, although careful safety monitoring is required [19, 21].

Management of Global IBS Symptoms focuses on modulation of intestinal motility, visceral sensitivity, and the gut-brain axis [13]. Evidence supporting antispasmodics remains limited, resulting in cautious recommendations for their use [20].

Among neuromodulators, low-dose tricyclic antidepressants have demonstrated efficacy in reducing abdominal pain and improving overall symptoms, whereas selective serotonin reuptake inhibitors have shown limited benefit [13].

A low-FODMAP diet is the most evidence-based dietary intervention and may significantly reduce symptoms when individualized and professionally supervised [9]. Microbiome-directed therapies, including probiotics and fecal microbiota transplantation, have produced inconsistent results and currently lack sufficient evidence for routine use [28].

Psychotherapeutic interventions, particularly cognitive-behavioral therapy and gut-directed hypnotherapy, are important components of treatment, especially in refractory IBS with psychological comorbidity. Overall, the greatest benefit is achieved through a multimodal approach combining pharmacologic, dietary, and psychological strategies that address the interaction between GI symptoms and the gut-brain axis [1, 13].

The Essence of IBS and IBD Overlap Syndrome:

Overlap syndrome refers to the coexistence of features or diagnostic criteria of two distinct disorders within the same patient, often due to shared pathophysiological mechanisms or overlapping clinical manifestations [22]. In gastroenterology, it most commonly describes the coexistence of functional and organic GI disorders.

The IBS and IBD overlap syndrome is characterized by the persistence of IBS-like symptoms, including abdominal pain, bloating, and diarrhea, in patients with confirmed IBD, even during clinical, endoscopic, or histological remission [2]. This may complicate assessment of disease activity, leading to inappropriate treatment decisions and reduced quality of life.

IBS-like symptoms have been reported in approximately 30–40 % of patients with UC in remission and 40–60 % of patients with CD, particularly those with small bowel involvement, highlighting the significant clinical relevance of this condition [22].

Pathophysiological Mechanisms of the Overlap:

The development of IBS-like symptoms in patients with IBD in remission can be explained by several pathogenic mechanisms: microinflammation: Even in the absence of macroscopically visible inflammation, microscopic inflammatory changes may persist in the mucosa and contribute to symptom generation; impaired intestinal barrier function: Increased mucosal permeability promotes immune activation, leading to symptoms characteristic of IBS; dysbiosis: IBD is associated with alterations in the intestinal microbial composition. Following remission, the gut microbiota may not fully recover, thereby contributing to IBS-like symptomatology; visceral hypersensitivity: Damage to enteric nerve endings during periods of active inflammation may result in increased sensitivity to intestinal distension even after mucosal healing; psychoemotional factors: Stress, anxiety, and depression act as triggers for both IBD and IBS. In patients with a chronic course of IBD, hyperreactivity of the gut-brain axis frequently develops [2, 25].

Clinical Significance of the Overlap Syndrome:

The coexistence of IBS and IBD presents a significant diagnostic challenge, as IBS-like symptoms may mimic IBD relapse, while low-grade inflammatory activity may be mistaken for a functional disorder [2].

A major limitation is the lack of definitive objective criteria to reliably distinguish active IBD from IBS-like symptoms. Overinterpretation of abdominal pain, diarrhea, or bloating may lead to unnecessary escalation of immunomodulatory or biologic therapy despite normal inflammatory markers, whereas underrecognition of persistent inflammation may result in disease progression and poorer outcomes [22].

Key symptoms of overlap:

In patients with IBD in remission, IBS-like symptoms may persist despite the absence of active inflammation. Common manifestations include abdominal pain, altered bowel habits, urgency without relief, bloating, excessive gas production, and anxiety related to disease recurrence [2]. These symptoms can impair quality of life to a degree comparable to active IBD.

Psychological factors, particularly anxiety, depression, and heightened symptom vigilance, play an important role in overlap syndrome. Patients may develop excessive concern about intestinal symptoms, avoid social activities or certain foods, and frequently seek medical evaluation, increasing healthcare utilization [22,24].

Effective management requires a multidisciplinary approach involving gastroenterologists, psychologists or psychotherapists, dietitians, and primary care physicians. Timely recognition of IBS-related symptoms is essential to avoid unnecessary escalation of IBD therapy.

Approaches to the diagnosis of overlap between IBS and IBD. Correct differentiation between inflammatory activity and functional IBS-related symptoms in patients with IBD is critically important to avoid both overtreatment and undertreatment. The optimal diagnostic approach should be sequential, multilevel, and individualized.

Step 1: Verification of IBD remission.

Before diagnosing IBS in a patient with IBD, active inflammation must be confidently excluded. The following investigations are required: complete blood count: anemia and elevated ESR indicate an inflammatory process; CRP: elevated CRP levels are a marker of active inflammation; fecal calprotectin: <50 μg/g – active IBD is very unlikely; 50–250 μg/g – "gray zone," requiring dynamic monitoring; ≥250 μg/g – high probability of active inflammation; endoscopic examination: to assess mucosal status in cases of doubtful or persistent symptoms; biopsy: may reveal subclinical inflammation; other imaging modalities: computed tomography, magnetic resonance imaging/ computed tomography enterography (in CD); intestinal ultrasonography.

Step 2: Identification of functional symptoms.

After excluding active inflammation, attention should be paid to typical features of IBS: recurrent abdominal pain associated with defecation; changes in stool frequency and/or consistency; absence of nocturnal symptoms (suggestive of a functional origin); normal levels of inflammatory markers.

Symptom assessment should be based on the Rome IV criteria, even in patients with IBD in remission.

Step 3: Exclusion of other causes of symptoms.

It is important to consider other conditions that may mimic IBS or coexist with IBD in remission: Clostridioides difficile-associated infection, which may occur or recur even during IBD remission, particularly after antibiotic therapy or immunosuppression; other bacterial enteric infections (Salmonella spp., Campylobacter spp., Shigella spp., Yersinia enterocolitica, enteropathogenic and enteroinvasive strains of Escherichia coli); chronic carriage or subclinical

infections that may sustain diarrheal symptoms without clear signs of active inflammation; parasitic infestations (Giardia lamblia, etc.); bile acid malabsorption (especially in CD involving the terminal ileum); SIBO; medication-induced diarrhea; celiac disease, lactase deficiency; exocrine pancreatic insufficiency (particularly after resections or in concomitant chronic pancreatitis); endocrine disorders, including thyrotoxicosis or diabetes mellitus with autonomic neuropathy [1, 24].

To this end, a comprehensive set of laboratory, instrumental, and functional tests should be used, including stool bacteriological examination (multiplex PCR panel for enteric pathogens), stool testing for Clostridioides difficile (toxins A/B or PCR), breath tests for SIBO, parasitological stool examination (antigens of Giardia lamblia), tests for bile acid malabsorption (SeHCAT, where available), coprogram, fecal elastase measurement to assess exocrine pancreatic function, thyroid hormone testing (TSH ± free T4), serological markers of celiac disease, and elimination trials of specific foods (dairy products, FODMAP diet) [2].

Step 4: Assessment of psychoemotional status.

Psychoemotional factors play an important role in the structure of functional symptoms. The following aspects should be considered: levels of anxiety and depression (using HADS, PHQ-9); social factors and quality of life; presence of post-traumatic reactions (e.g., after severe hospitalizations or surgical interventions) [24].

Assessment of these factors contributes to a personalized therapeutic approach.

Management of patients with overlap between IBS and IBD.

Treatment of patients with concomitant IBS and IBD in remission requires a comprehensive and individualized approach. The primary goals are symptom relief without unnecessary escalation of IBD therapy and improvement of quality of life.

General principles of management:

– confirmation of IBD remission is a mandatory prerequisite before initiating therapy for IBS-like symptoms;

– avoidance of escalation of baseline IBD therapy in the absence of objective signs of active inflammation;

– consideration of the psychoemotional background: psychosocial support is often required, particularly in patients with long-standing disease;

– multidisciplinary team approach: gastroenterologist, psychotherapist, dietitian, and primary care physician;

– dietary therapy: a low-fiber diet (which may significantly reduce bloating, abdominal pain, and flatulence), elimination of individual dietary triggers such as lactose, gluten, caffeine, and fatty foods (based on individual tolerance and observation) [15];

– pharmacological treatment of IBS symptoms;

– psychotropic therapy: in cases of pronounced pain syndrome or concomitant anxiety/depression, antidepressants should be prescribed. Tricyclic antidepressants (amitriptyline, nortriptyline) in low doses exert effects on visceral sensitivity. Selective serotonin reuptake inhibitors are effective in IBS associated with anxiety. Prescription should follow assessment of the psychoemotional status and is often performed in collaboration with a psychotherapist [31];

– psychotherapy: cognitive behavioral therapy, relaxation techniques, and supportive counseling with a psychologist can significantly reduce symptom perception and fear of IBD relapse [24];

– control and monitoring, including reassessment of symptoms 4–8 weeks after initiation of therapy;

– dynamic adjustment of treatment depending on the dominant component (inflammatory vs functional);

– avoidance of unnecessary escalation of biological therapy in the presence of normal fecal calprotectin and other inflammatory markers, avoidance of steroid prescription without confirmed disease activity, and avoidance of neglecting the psychosomatic component of symptoms [24].

Prognosis and quality of life in overlap syndrome.

The IBS and IBD overlap syndrome significantly affects long-term outcomes, quality of life, and social functioning. Even during clinical and endoscopic remission of IBD, persistent IBS-like symptoms may cause chronic discomfort, anxiety, dietary restrictions, reduced participation in daily activities, sleep disturbances, and increased healthcare utilization [24].

Patients with IBD and concomitant IBS-like symptoms consistently report lower quality-of-life scores than those without functional symptoms [22]. Although IBS does not cause structural intestinal damage, symptom overlap may complicate assessment of IBD activity and lead to inappropriate treatment escalation, increasing the risk of adverse effects [24].

Despite growing recognition of this condition, IBS and IBD overlap syndrome remains insufficiently studied, and management strategies are often fragmented. Further research, physician education, development of standardized diagnostic and therapeutic algorithms, and implementation of digital monitoring tools may improve patient care [2].

A potential direction for the development of clinical approaches includes educational programs for physicians focused on recognition and management of overlap syndrome, development of national and international guidelines incorporating diagnostic and therapeutic algorithms for overlap, as well as digital tools (mobile applications,

questionnaires) for monitoring symptoms, stress, diet, and quality of life.

Future management of patients with IBS and IBD overlap should be based on principles such as individualized treatment, consideration of psychoemotional needs, establishment of a partnership-based physician-patient relationship, and increased patient awareness regarding the nature of their disease and symptoms [24].

Limitations. This review has several limitations. Most of the included studies were based on data obtained from patients in Western countries, which may limit the generalizability of the findings to the Ukrainian population, given differences in dietary patterns, gut microbiome composition, and the availability of certain diagnostic and therapeutic modalities. In addition, some of the analyzed studies had relatively short follow-up periods, which precludes a comprehensive assessment of the long-term consequences of the overlap between IBS and IBD, as well as the long-term effectiveness of the proposed therapeutic approaches.

Conclusion

The IBS and IBD overlap syndrome is a common but underestimated clinical phenomenon. Approximately 30–50 % of patients with IBD in remission may experience IBS-like symptoms, which significantly affect well-being and quality of life despite the absence of active inflammation.

The pathogenetic mechanisms of overlap are complex and multimodal, including disturbances of intestinal motility, alterations in the gut microbiome, impairment of the intestinal barrier, dysfunction of the gut-brain axis, visceral hypersensitivity, and psychological factors such as anxiety, depression, and stress.

The clinical diagnosis of overlap syndrome is complex and requires meticulous differential evaluation. The symptomatology of IBS may obscure or mimic exacerbations of IBD; therefore, the use of objective markers of disease activity (such as endoscopic assessment, fecal calprotectin, and CRP) is essential to prevent overtreatment or inappropriate management.

Standard pharmacological treatment of IBD is often ineffective in the presence of overlap. Functional symptoms respond poorly to immunomodulators or biologic agents, necessitating additional use of IBS-oriented therapies, including dietary interventions, antispasmodics, probiotics, psychotherapy, and psychotropic medications.

Overlap syndrome necessitates a shift in patient management strategies. Implementation of personalized treatment based on stratification by symptom profile, inflammatory activity, psychoemotional status, and life priorities is required.

Psychosocial factors play a critical role in the persistence of overlap symptoms. Patients with anxiety or depressive disorders exhibit a higher frequency of functional symptoms and poorer treatment response; therefore, psychological support should be an integral component of care.

In summary, IBS and IBD overlap is more than a coexistence of two diagnoses. It represents a unique clinical continuum requiring a careful, patient-centered approach. Timely recognition, differentiated diagnosis, and integrative management can substantially reduce disease burden, improve the effectiveness of IBD therapy, and enhance patients' quality of life.

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ORCID: Kulchytska O.M. https://orcid.org/0009-0004-7277-3675, Kuzminova N.V. https://orcid.org/0000-0003-4718-8218, Nazarova M.S. https://orcid.org/0000-0001-6981-9522, Hnatyshyn M.S. https://orcid.org/0000-0001-6510-9582, Burdeina L.V. https://orcid.org/0000-0001-7450-7777, Kedyk I.O. https://orcid.org/0000-0001-6420-6583, Savytska O.O. https://orcid.org/0009-0005-0327-4634.

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