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Ofeliya Abdullayeva
Azerbaijan Medical University, Baku, Azerbaijan
https://orcid.org/0009-0004-3562-3002
Vugar Abdullayev
Baku Slavic University, Baku, Azerbaijan
PhD in Art History
https://orcid.org/0000-0002-4403-8778
abvugar@yahoo.de

On Non-Specific Ulcerative Colitis (Ulcerative Colitis, Uc)

Abstract

This article addresses the clinical course and therapeutic approaches to non-specific ulcerative colitis (UC), a chronic inflammatory disorder of the colon characterized by relapsing–remitting mucosal inflammation. Despite advances in therapy, achieving sustained remission remains a major clinical challenge. The multifactorial nature of UC—including genetic, immune, environmental, and microbiota-related factors—results in heterogeneous clinical presentations, complicating diagnosis and differentiation from other inflammatory bowel diseases such as Crohn's disease. The authors present clinical and therapeutic data from patients evaluated between 2001 and 2025, utilizing diagnostic methods such as computed tomography and colonoscopy. Colonoscopy remains the gold standard, enabling direct visualization and histopathological confirmation. Optimization of treatment strategies, particularly through the integration of immunomodulatory agents, is essential for prolonging remission and reducing relapse rates. While oral administration is standard, combined oral and rectal delivery may improve outcomes, especially in distal disease. Local administration via microenemas with oil-based preparations allows targeted delivery to inflamed mucosa, potentially enhancing healing and minimizing systemic effects. This approach may be especially beneficial during seasonal exacerbation periods. In conclusion, individualized multimodal therapy combining systemic and topical immunomodulation appears effective in extending remission and preventing relapse in UC patients.

Keywords: *ulcerative colitis, immunomodulators, oral administration, rectal administration, microenema therapy, inflammatory bowel disease*

Introduction

Colitis, defined as inflammation of the large intestine, represents a highly prevalent group of gastrointestinal disorders with diverse etiologies and clinical manifestations. These conditions may arise from multiple causes, including dietary (alimentary) factors, intestinal dysbiosis, and the inappropriate or unsystematic use of pharmacological agents—particularly antibiotics—each associated with distinct clinical features and therapeutic strategies (Kobayashi et al., 2020; Lichtenstein et al., 2020).

Colitis comprises a heterogeneous spectrum of diseases; however, among these, Ulcerative Colitis (UC) warrants particular attention due to its chronic, relapsing nature and complex pathogenesis. Based on our long-term clinical observations, UC represents a distinct nosological entity requiring focused investigation and tailored management approaches.

The etiological heterogeneity of UC contributes to its clinical variability and often leads to patient management across multiple medical disciplines, including internal medicine, infectious and parasitic disease units, gastroenterology departments, and even surgical clinics. This multidisciplinary involvement reflects both the systemic nature of the disease and the challenges associated with its diagnosis and treatment (Ordás et al., 2012; Ungaro et al., 2017).

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Historically, since the mid-20th century, management strategies for UC have evolved considerably. In the former Soviet Union, particularly at the Moscow Proctology Institute, treatment approaches were predominantly surgical, reflecting limited understanding of the disease's immunopathogenesis at the time (Bunin, 1972). Conservative therapies were also employed, including blood transfusions, immunomodulatory agents such as methyluracil and pentoxyl, and vitamin supplementation. During remission periods, patients were typically managed with dietary modifications and vitamin therapy.

The difficulty in achieving effective and sustained treatment outcomes in UC is multifactorial. One of the key contributing factors is the involvement of the central nervous system in modulating disease activity through the gut–brain axis, which is increasingly recognized as a significant component in inflammatory bowel diseases (Carabotti et al., 2015). Additionally, several predisposing and exacerbating factors have been identified, including improper nutrition, increased gastric acidity (hyperacid gastritis), biliary tract diseases such as cholangitis, and parasitic infections (Torres et al., 2017; Kaplan, 2015).

Epidemiologically, UC most commonly manifests in young adults, typically between the second and fourth decades of life, although it may occur at any age (Ungaro et al., 2017).

Between 2001 and 2025, among 110 patients presenting to a therapeutic clinic with a preliminary diagnosis of gastroenterocolitis, 30 patients were ultimately diagnosed with ulcerative colitis. The diagnosis was established based on a combination of detailed anamnesis, clinical examination, colonoscopic evaluation, and computed tomography findings, consistent with current diagnostic standards (Magro et al., 2020).

Clinical Characteristics, Diagnostic Findings, and Therapeutic Considerations

Among the 30 patients diagnosed with Ulcerative Colitis, 18 were female (aged 20–25 years) and 12 were male (aged 22–30 years). A significant proportion of patients reported exposure to psychological stress as a precipitating factor, consistent with current evidence highlighting the role of the gut–brain axis in inflammatory bowel diseases (IBD) (Carabotti et al., 2015; Gracie et al., 2018). Additionally, intestinal dysbiosis was identified in nearly all patients, further supporting its role in disease pathogenesis (Ni et al., 2017).

Table 1
Clinical Characteristics, Diagnostic Findings, and Contributing Factors of Patients Diagnosed with Ulcerative Colitis (n = 30)

Parameter / Characteristic	Number of Patients (n = 30)	Details / Notes
Gender	18 Female	Ages 20–25 years
	12 Male	Ages 22–30 years
Exposure to psychological stress	Majority	Reported as a precipitating factor, supporting gut–brain axis involvement (Carabotti et al., 2015; Gracie et al., 2018)
Intestinal dysbiosis	Nearly all	Supports role in disease pathogenesis (Ni et al., 2017)
Diagnosis confirmation	30	Based on anamnesis, clinical examination, colonoscopy, and CT findings (Magro et al., 2020)

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Note. The changes observed in the CT scans further corroborated the colonoscopic findings. Hemoglobin (Hb) levels were found to be low in nearly all patients, which represents a key clinical feature of the disease.

Clinical observations and laboratory investigations—particularly the frequent presence of anemia—suggest that the disease onset often occurs earlier than clinical presentation, with most patients seeking medical attention at relatively advanced stages. The predominant clinical manifestations included sudden-onset abdominal pain, often associated with prior emotional stress, bloody and mucous diarrhea, tenesmus (incomplete evacuation), anal discomfort, and borborygmi localized to the right iliac region. These findings are consistent with the typical symptomatology described in moderate-to-severe UC (Ungaro et al., 2017; Kobayashi et al., 2020).

Radiological and endoscopic assessments revealed important insights into disease extent. Notably, computed tomography findings indicated that inflammation was not confined solely to the colon but also involved segments of the small intestine. Although UC is classically defined as a colonic disease, increasing evidence suggests that backwash ileitis and extracolonic involvement may occur, raising considerations for broader classifications such as enterocolitis in selected cases (Magro et al., 2020).

Colonoscopy, performed in all patients, provided direct visualization of mucosal pathology. The findings included mucosal irritation and hyperemia, with the presence of superficial ulcers characterized by smooth margins and mucous coatings. In some cases, erosions representing early stages of ulcer formation were also observed. Specifically:

- In 16 patients, one or multiple superficial ulcers were identified in the intestinal mucosa
- In 8 patients, four or more erosions were detected
- In 6 patients, diffuse mucosal hyperemia consistent with an “irritable bowel-like” appearance was observed

These morphological features correspond to established endoscopic criteria for UC, including continuous mucosal inflammation, friability, and ulceration (Magro et al., 2020; Harbord et al., 2017).

An important clinical challenge identified in this cohort was the variability and non-specificity of presenting complaints, which frequently led patients to seek care across different specialties, thereby delaying accurate diagnosis. Among the studied patients:

- 12 initially consulted rheumatologists due to joint pain and received treatment for presumed rheumatologic conditions
- 10 were evaluated and treated by gastroenterologists and hepatologists prior to definitive diagnosis

This observation aligns with current knowledge that UC is associated with extraintestinal manifestations, particularly musculoskeletal (arthralgia, arthritis) and hepatobiliary involvement (e.g., primary sclerosing cholangitis), which may obscure the underlying diagnosis (Feuerstein et al., 2019).

Notably, when patient history (anamnesis) is carefully evaluated, a consistent pattern emerges, characterized by the coexistence of joint pain and abdominal or hepatobiliary discomfort. Some clinicians also consider the potential role of prior atypical intestinal infections in the etiopathogenesis of UC. While this remains a hypothesis, it is plausible that ascending or descending infectious processes may contribute to microbiota disruption, leading to dysbiosis and subsequent immune dysregulation—factors increasingly recognized in IBD pathogenesis (Ni et al., 2017; Kaplan, 2015).

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Table 2
Colonoscopic Findings, Initial Clinical Presentations, and Diagnostic Challenges in Ulcerative Colitis Patients (n = 30)

Parameter / Finding	Number of Patients (n = 30)	Details / Notes
Superficial ulcers (smooth margins, mucous covering)	16	Single or multiple ulcers observed in intestinal mucosa
Erosions (≥4)	8	Represent early stages of ulcer formation
Diffuse mucosal hyperemia ("irritable bowel-like" appearance)	6	Consistent with early mucosal inflammation
Initial specialty consulted due to presenting complaints		
– Rheumatologists (joint pain)	12	Treated for presumed rheumatologic conditions; highlights extraintestinal manifestations
– Gastroenterologists/hepatologists	10	Evaluated and treated prior to definitive UC diagnosis
Endoscopic features	All 30	Continuous mucosal inflammation, friability, and ulceration (Magro et al., 2020; Harbord et al., 2017)
Clinical note	–	Variability and non-specificity of presenting complaints often delayed accurate diagnosis; consistent pattern of joint pain with abdominal or hepatobiliary discomfort observed

Therapeutic Approaches in the Modern Era

Contemporary management of UC involves a wide range of pharmacological agents; however, these therapies are predominantly symptomatic and pathogenetic rather than truly etiological. Immunomodulatory therapy occupies a central role in current treatment paradigms.

Recent advances have introduced second-generation targeted immunomodulators, particularly Janus kinase (JAK) inhibitors such as:

- Tofacitinib
- Upadacitinib
- Filgotinib

These agents have demonstrated high efficacy in inducing and maintaining remission in moderate-to-severe UC, as evidenced by multiple randomized controlled trials (Sandborn et al., 2017; Panés et al., 2018).

Compared to earlier immunomodulatory agents such as thymalin, which was used in the late 20th century, these newer therapies offer significantly improved clinical outcomes due to their targeted mechanisms of action. Nevertheless, as noted by the authors, these modern agents have not yet been

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implemented in their clinical practice and therefore require further evaluation in their patient population.

Therapeutic Strategy and Clinical Outcomes

In the management of patients under our supervision diagnosed with Ulcerative Colitis, we consider it essential to emphasize not only systemic therapy but also the significant role of local (topical) treatment modalities. In our view, optimal therapeutic outcomes in UC require a combined approach integrating both systemic and localized interventions.

The rationale for local therapy is supported by the pathophysiological involvement of the distal intestinal tract. Inflammation affecting the lower third of the small intestine, together with colonic mucosal injury and irritation—manifesting as increased stool frequency, tenesmus, and urgency—often leads to secondary involvement of the rectum and particularly the anal region. Under these conditions, the application of local pharmacotherapy becomes a clinical necessity.

It should be noted that this approach is not entirely novel. Local microenema-based therapies have been utilized since the mid-20th century in the complex treatment of intestinal infections, demonstrating favorable clinical outcomes. However, our proposed modification involves the incorporation of immunomodulatory agents—specifically methyluracil—into topical formulations. We hypothesize that the administration of such agents in combination with oil-based preparations via microenemas enhances local mucosal immunity and promotes epithelial regeneration, thereby facilitating mucosal healing.

Systemic (general) treatment, on the other hand, may include the use of immunomodulatory drugs, anti-inflammatory agents targeting colonic inflammation (e.g., aminosalicylates, corticosteroids), and supportive medications aimed at reducing stool frequency and improving stool consistency. These approaches are consistent with current internationals guidelines for UC management (Lichtenstein et al., 2020; Kobayashi et al., 2020).

Importantly, in the comprehensive management of UC patients, careful attention must also be paid to comorbid conditions, which may influence disease course and therapeutic response. Overlooking associated diseases may compromise overall treatment effectiveness.

In our clinical cohort, the simultaneous initiation of both systemic and local therapies resulted in favorable outcomes. Specifically, the combined administration of immunomodulators via oral (per os) and rectal (per rectum) routes was associated with:

- Increased rates of clinical improvement
- Prolongation of remission periods
- Reduction in relapse frequency, particularly during seasonal peaks (spring and autumn), when exacerbations are commonly observed

These findings suggest that dual-route immunomodulatory therapy may represent a promising strategy in UC management, although further controlled studies are required to validate these observations.

Conclusion

Thus, the treatment of UC, a disease characterized by a multifactorial (polyetiological) etiology, remains one of the major challenges in modern medicine. The absence of a clearly defined etiological pathway complicates the development of definitive curative therapies. While the introduction of newer-generation immunomodulators has significantly improved clinical outcomes—leading to faster symptom control and prolonged remission—achieving complete and sustained cure remains difficult.

Future research should focus on targeted therapies addressing underlying immunological and microbiome-related mechanisms, as well as personalized treatment strategies tailored to individual patient profiles.

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Proposed Therapeutic Perspective

The therapeutic approach proposed in this study may contribute to the development of a novel perspective in the management of Ulcerative Colitis. Based on diagnostic confirmation through colonoscopy and computed tomography, the identification of localized mucosal lesions—such as ulcers and erosions—highlights the importance of early initiation of targeted local therapy to prevent severe complications, including perforation.

Within this context, our findings support the necessity of *simultaneous initiation of both systemic and local treatment strategies.* Colonoscopic and radiological evidence of mucosal damage provides a clear rationale for early intervention at the site of inflammation, thereby improving therapeutic precision and effectiveness (Magro et al., 2020; Kobayashi et al., 2020).

Specifically, the combination of systemic administration of second-generation immunomodulatory agents with localized delivery via microenemas—augmented by the addition of immunomodulators such as methyluracil—appears to offer significant clinical advantages. This dual-route therapeutic model is hypothesized to:

- Accelerate mucosal healing
- Reduce the overall duration of active disease
- Prolong remission periods
- Decrease the frequency of disease relapse

These observations are consistent with emerging evidence emphasizing the importance of targeted and localized drug delivery systems in inflammatory bowel diseases, particularly for distal colonic involvement (Lichtenstein et al., 2020; Sandborn et al., 2017).

Thus, the integration of systemic and local immunomodulatory therapies may represent a promising advancement in UC treatment paradigms. However, further large-scale, controlled clinical studies are necessary to validate the efficacy and safety of this combined approach.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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