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REVIEW ARTICLE

A COMPREHENSIVE REVIEW ON THE MANAGEMENT OF ULCERATIVE COLITIS: FROM GLOBAL EPIDEMIOLOGY TO PERSONALIZED THERAPEUTICS

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Abstract:
Ulcerative colitis (UC) is a chronic, immune-mediated inflammatory disease of the colonic mucosa, characterized by a relapsing and remitting course. Once considered a disease of the Western world, its incidence and prevalence are rising rapidly in Asia, including Bangladesh, creating a significant healthcare burden. The clinical presentation is heterogeneous, ranging from mild distal disease to life-threatening acute severe colitis, often accompanied by debilitating extra-intestinal manifestations. Diagnosis is multifaceted, relying on clinical suspicion, confirmed by endoscopic and histological evidence of chronic colitis, after the exclusion of infectious mimics. The management paradigm has shifted profoundly from symptomatic control to a proactive "treat-to-target" (T2T) strategy, with the goal of achieving sustained deep remission (clinical and endoscopic). This evolution has been fueled by an expanding therapeutic armamentarium, including a growing number of biologic therapies targeting specific immune pathways and novel small molecule drugs. This review provides a detailed, contemporary overview of UC, with a special focus on the changing epidemiology in Asia, the intricacies of medical and surgical management. The future of UC care lies in truly personalized medicine, guided by predictive biomarkers and a shared decision-making model.

Keywords: *Ulcerative Colitis, Inflammatory Bowel Disease, Asia, Bangladesh, Biologics, JAK Inhibitors.*

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Introduction:

Ulcerative colitis (UC) is a chronic, relapsing form of inflammatory bowel disease (IBD) characterized by idiopathic inflammation confined to the colonic mucosa. It remains a significant global health concern because of its considerable impact on morbidity and quality of life. UC invariably involves the rectum and extends proximally in a continuous pattern to affect a variable length of the colon. In contrast, Crohn's disease (CD) can involve any segment of the gastrointestinal tract—from the mouth to the anus—and typically demonstrates a discontinuous or "skip lesion" pattern.[1]

IBD encompasses two major chronic inflammatory disorders: UC and CD. Diagnosis requires a composite assessment of clinical presentation along with endoscopic, radiological, and histopathological findings. In approximately 10–15% of patients, distinguishing UC from CD remains challenging, and such cases are categorized as inflammatory bowel disease–unclassified (IBD-U), historically referred to as indeterminate colitis.[2]

Despite a favorable survival rate, Ulcerative Colitis (UC) can be highly debilitating. Roughly one in seven patients (15%) faces an aggressive form of the condition, with a subset of these individuals needing hospitalization for acute episodes. The disease's profound effect on quality of life is worsened by a high incidence of co-occurring anxiety and depression, often leading to social and professional impairment. Furthermore, UCthat persists over many years carries a well-established risk of developing dysplasia and Colorectal Cancer (CRC), a risk largely driven by the extent of UC involvement in the bowel and the duration of chronic mucosal inflammation.[3]

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Therapeutic strategies have dramatically improved in the last decades, expanding beyond immunosuppressive and immunomodulator drugs which includes introduction of biologics, small molecules and biosimilars. Some patients still need surgery for medically refractory disease.[4]

Once considered a disease of the western world, its incidence and prevalence are rising rapidly in Asia, including India and Bangladesh, creating a significant healthcare burden.This article offers a detailed exploration of Ulcerative Colitis. It is systematically structured to first analyze the clinical features and diagnostic pathways, then transition into the multi-modal management strategies.

Epidemiology: The rising tide in Asia

While the highest reported prevalence remains in Europe and North America (over 500 per 100,000 persons), the rate of increase in these regions has plateaued. In contrast, Asia is now experiencing the most rapid rise in incidence globally.The rising incidence in Asia and other developing regions is strongly correlated with urbanization, industrialization, and changes in lifestyle—a collective phenomenon often referred to as "Westernization".[3]

Bangladesh, representative of the South Asian region, is reporting a steady increase in UC cases. A study from Bangladesh Medical University (BMU) highlighted that UC patients in Bangladesh often present at a younger age (mean age in the 3rd-4th decade) and with moderate-to-severe disease activity. The most common extent at diagnosis was left-sided colitis, similar to Indian data. UC may present at all ages & have shown no gender difference, though diagnosis before the age of 5 years or after 75 years is uncommon. The peak incidence of UC occurs in the 2nd and 4th decades of life.The incidence is much lower before the age of 15 years.[4,5]

Clinical features and disease classification:[4,6]

Onset of symptoms UC is usually insidious often present for weeks before medical advice is sought. UC manifests through a spectrum of intestinal and systemic symptoms. A thorough understanding of its presentation is crucial for timely diagnosis and appropriate management.

- **Intestinal Manifestations:** The core symptoms are directly related to colonic inflammation and its consequences.
- **Bloody Diarrhea:** This is the hallmark of UC. The frequency and volume of bloody stools correlate with disease severity.
- **Rectal Urgency and Tenesmus:** Inflammation in the rectum leads to a compelling and often painful sensation of the need to defecate, even when the bowel is empty. This is one of the most debilitating symptoms for patients.
- **Abdominal Pain:** Typically, crampy and located in the lower abdomen, it is often relieved by defecation.
- **Disease Extent and Distribution:** The Montreal classification is widely used to define disease extent:
  - **E1 - Ulcerative Proctitis:** Inflammation limited to the rectum (d"15 cm from anal verge). Symptoms are predominantly rectal bleeding, urgency, and tenesmus.
  - **E2 - Left-sided UC (Distal UC):** Inflammation extends proximal to the rectum but no further than the splenic flexure. This includes proctosigmoiditis.
  - **E3 - Extensive UC:** Inflammation extends proximal to the splenic flexure, may involve whole colon (**Pancolitis**). Patients with pancolitis are at higher risk for severe attacks, colorectal cancer, and often have more systemic symptoms.

Extra-intestinal manifestations can occur in 20–35% of patients and can precede intestinal symptoms in up to 25% of patients.Among these extra-intestinal manifestations, peripheral arthritis is most common; primary sclerosing cholangitis and pyoderma gangrenosum are more common in ulcerative colitis than in Crohn's disease.Besides these oculars (Anterior uveitis,episcleritis),few renal & respiratory features alsodocumented.The risk of venous thromboembolism is increased by two to four times, and is greater when the patient is admitted with a severe flare-up or is being treated with corticosteroids.[4]

UC mimics: A variety of both infectious &non-infectious diseases masquerade the clinical features of UC & need to be considered cautiously in establishing the correct diagnosis (Table I).

Table -I

Infectious disease	Non-infectious disease
TB	Ischemic colitis
Salmonella	Diversion colitis
Shigella	Diverticular colitis
CDI	Drugs(NSAIDS) Colitis
CMV	Radiation colitis
Amebic colitis	Solitary rectal ulcer syndrome
Helminthiasis	
Sexually transmitted disease	

Diagnosis and comprehensive assessment.[4-8]

Diagnosis of UC needs combinations of compatible clinical features, endoscopic appearance, histological findings.

Endoscopic evaluation:

Colonoscopy, ileal intubation with biopsies is the most sensitive and specific tool to establish a diagnosis of ulcerative colitis. Classic endoscopic features of **mild ulcerative colitis**are erythema, vascular congestion, and partial loss of the visible vascular pattern. **Moderately active colitis** is characterized by a complete loss of vascular pattern, blood adherent to the surface of the mucosa, erosions, and mucosal friability. **Severe colitis** is defined by spontaneous bleeding and ulceration.A minimum of two biopsies should be obtained from at least six different areas (e.g., terminal ileum, ascending, transverse, descending, sigmoid colon, and rectum), including macroscopically normal areas).[4-6]

- **Laboratory Investigations:**
  - **Inflammatory Markers:** C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) are often elevated during active disease, though they can be normal in mild or limited disease.
  - **Hematological Tests:** Complete blood count may reveal anemia (iron deficiency due to chronic blood loss or anemia of chronic disease), leukocytosis, or thrombocytosis.
  - **Serum Biochemistry:** Albumin levels may be low in severe disease. Liver function tests are essential to screen for PSC.
  - **Stool Studies:** This is a critical step. Tests for *Clostridium difficile* toxin, stool culture for enteric pathogens, and microscopy for ova and parasites are mandatory to exclude infectious colitis. **Fecal Calprotectin** has emerged as a cornerstone non-invasive test. It is a protein derived from neutrophils and is highly sensitive and specific for intestinal inflammation. It is invaluable for differentiating IBD from irritable bowel syndrome (IBS) and for monitoring disease activity and response to therapy.[7]
- Plain X Ray abdomen: to exclude obstruction and toxic megacolon etc.
- **Cross-sectional Imaging:** While colonoscopy is primary, **CT- Enterography** or **MR Enterography** are invaluable in certain scenarios:[6]
  - Assessing the small bowel to help rule out Crohn's disease.
  - Evaluating for complications in severe UC, such as toxic megacolon or perforation.
  - When colonoscopy is incomplete or contraindicated.
- **Disease activity assessment**: Assessment of disease activity is important for prognostication& therapeutic decision making.There are different clinical activity indices e.g. Truelove & Witts classification(Table II), Mayo score(0-12 range), Lichtiger score, Ulcerative Colitis Endoscopic Index of Severity (UCEIS) etc..

However, Truelove &Witts classification is a reliable & simple to use in clinical practice though it is most applicable for extensive colitis.[8,9]

Table II

Truelove and Witts criteria (1955)

Mild Disease	Moderate disease	Severe disease
<4 stools /day	Intermediate between mild & severe	>6 stools /day with blood
No fever, No tachycardia		Fever>37.5 C Heart rate>90/min
Mild anaemia of	ESR<30	Anemia Hb< 75% normal ESR>30mm of Hg

Management[9-11]

Management of UC always involve a prompt & accurate diagnosis as well as meticulous effort to exclude UC mimics. Assessment of the patient's risk for poor outcomes & categorization of disease severity are also needed to guide treatment decision.Early initiation of effective, safe, and tolerable medical therapies (Both induction & maintenance of remission) can optimize the long term worse outcome of disease. The optimal goal of management is:

- Sustained and durable steroid-free remission (Symptomatic, endoscopic & histologic), accompanied by appropriate psychosocial support, normal health-related quality of life (HRQoL) & social functioning.
- Prevention of morbidity including hospitalization and surgery.
- Prevention of cancer.

In fact, an MDT approach can achieve the maximum management goal involving: Gastroenterologist, GI Surgeon, Internist, Radiologist, Histopathologist, Nutritionist & Psychologist.

Medical Management:

Selection of therapies promptly depends on disease severity, extent of disease as well as cost & affordability.

Table III

Commonly used agents in management of UC

Group	Agents	Formulations
Anti-inflammatory	5-aminosalicylates.	**Oral, Suppository.**
		Foam, Enema
	Corticosteroid	Oral, IV, supp. Enema
	Budesonide	Oral
Immunomodulator	**Azathioprine**	**Oral**
	MTX	Oral& IV
	Cyclosporin	Oral& IV
Biologics	Infliximab, Adalimumab	IV Or S/C
	Golimumab	
	Vedolizumab	
	Ustekinumab	
	Guselkumab,	
	Mirikizumab,	
	Risankizumab	
Small molecules	Tofacitinib	**Oral**
	Filgotinib	
	Upadacitinib	
	Ozanimod	
	Etrasimod	
Other medicines	Anti-diarrheal	**Oral**
	Anti-spasmodic	

Two phases of medical management for active UC (Induction of remission and Maintenance of remission):

Table IV

Mildly active UC

Induction Of remission	Maintenance Of remission
Mildly active UC of any extent	**Ulcerative proctitis: R**ectal 5-ASA dose
Low dose 5-ASA	of 1 g daily for maintenance of remission.
(2.0–2.4 g/day)	**Mildly active left-sided or extensive**
	UC: Oral 5- ASA therapy (I.5 to 4.8 g/d)

Table IV

Mildly to moderately active ulcerative proctitis

Induction of remission	Maintenance Of remission
Rectal 5-aminosalicylate acid (5-ASA) dose of 1 g/daily If not respond: 1. Tacrolimus suppository 2. Beclomethasone suppository 3. Topical corticosteroids (suppository, foam, enema)	Oral 5-ASA I.5 to 4.8 g/d for maintenance

Table V

Mildly to moderately active left-sided UC

Induction Of remission	Maintenance Of remission
Rectal 5- ASA enemas dose of at least 1 g/daily combined with oral 5-ASA dose least 2.0 g/daily	Oral 5-ASA I.5 to 4.8 g/d for maintenance
Intolerant or Nonresponsive: Oral budesonide Multi Matrix System (MMX) 9 mg/d	

Table VI

Mildly to moderately active extensive colitis

Induction Of remission	Maintenance Of remission
Oral 5-ASA at dose at least 2.0 g /day	Oral 5-ASA I.5 to 4.8 g/d for maintenance

- Mildly to moderately active UC of any extent not responding to oral 5-ASA, addition of budesonide MMX 9 mg/d to induce remission is recommended.
- Patients with UC of any extent who fail to respond to 5-ASA therapy, oral systemic corticosteroids are another option to induce remission.Dose: Prednisolone 40-60mg/day then tapered off over 6-12 weeks.
- Mildly to moderately active UC with prognostic factors associated increased risk of hospitalization or surgery should be treated with therapies for moderate-to-severe disease.
- Mildly to moderately active UC always be reassessed to assess response to induction therapy within 8 weeks.

Table VII

Moderately to severely UC

Induction of remission	Maintenance Of remission
• oral budesonide • oral systemic corticosteroids *Cilinical response is expected within 5-7 days Of Rx	• Thiopurines for maintenance of remission. Azathioprine 2-3mg/kg/day. *Before starting TPMT&NUDT15 activity should be done. TPMT has limited value in Asian.
Biologics: • Anti-tumor necrosis factor (TNF) therapy(infliximab) combined with a thiopurine Dose:5-10mg/kg week 0,2 & 6	• Infliximab 5mg/kg every 8 weeks
Other biologics as an alternative 1. Adalimumab, golimumab 2. Vedolizumab 3. Ustekinumab 4. Guselkumab, 5. Mirikizumab, 6. Risankizumab	Tofacitinib 5-10mg twice a day
• JAK inhibitor Tofacitinib 10mg twice a day for 8 weeks Or, Upadacitinib 45mg/d for 8 weeks	Upadacitinib 15-30 mg/d

Moderately to severely active UC who failed 5-ASA therapy previously & in whom advanced therapies with biologics or JAK inhibitors are used for induction of remission 5-ASA has no role as added therapy.

Before starting biologics TB, HBV, HCV & HIV should be excluded & appropriate vaccination. During the biologics use regular monitoring CBC, LFTs, Creatinine & therapeutic drug monitoring must be done. The withdrawal of a drug should be individualized based on patient preference, disease activity markers, risk of relapse, safety, and cost.[11,12]

Acute Severe Ulcerative Colitis (ASUC):

ASUC patients need hospitalization, close monitoring and ruling out any complication.

Evaluation of indication of surgery is important.

Modified ASUC Criteria:

≥6 bowel movements along with ≥1 of:

- Tachycardia
- Fever
- Hemoglobin< 10.5gm/dl
- CRP >5mg/dl

Day 0:

- Baseline investigations:

Stool microbiology including C difficile

- Assess for toxic megacolon
- Sigmoidoscopy within 24hrs to rule out CMV
- Venous thromboembolism prophylaxis (LMWH)
- Withhold 5-ASA
- Start IV corticosteroid (Methylprednisolone 40-60mg/day Or Hydrocortisone 100mg 3-4 times a day) for 3-5 days
- Assess symptoms & CRP daily

Day 3:

If <4 bowel movement/day for 2 days & no rectal bleeding

- Transition to oral prednisolone 40mg/day
- Treat as outpatient**.**

If no clinical response

- IV cyclosporin Or Infliximab, Tofacitinib / Upadacitinib
- Daily abdominal examination
- Daily symptoms assessment
- Daily CRP

Day 6:

If response (<4 bowel movement/day for 2 days & no rectal bleeding)

- Maintenance with thiopurine, Infliximab, Tofacitinib, Upadacitinib

If no response with cyclosporine Or biologics therapy Or

Toxic megacolon,Colonic perforation,Severe refractory hemorrhage requires surgery[11,12]

Role of surgery:

Remission rates range between 30% & 40% with most advanced therapies & data suggest that colectomy rates are not decreasing despite biologics.

Indication of surgery in UC:

- Fulminant colitis
- Toxic megacolon
- Perforation
- Massive Hemorrhage
- Unresponsive to medical Rx within 7 days of rescue therapy.
- High grade dysplasia/Ca
- Large gut obstruction

Restorative proctocolectomy and ileal pouch anal anastomosis (IPAA) is the surgical intervention of choice to avoid a permanent stoma[10,13]

Disease monitoring:[4,9-12]

Historically, symptomatic relief was the primary therapeutic target in patients with ulcerative colitis but treatment goals have evolved continuously.Now a days disease monitoring done by

a. Clinical response

b. Endoscopic assessment could be done with proctosigmoidoscopy

c. Normalization of biomarkers (CRP and fecal calprotectin)

d. Intestinal ultrasonography

e. Therapeutic drug monitoring in biologics user

f. Surveillance colonoscopy programs to detect CRC:First screening colonoscopy 8 yrs after onset of symptoms for all patients except patients with primary sclerosing cholangitis, begin at time of diagnosis &continue annually.

g. Routine visits are recommended to monitor for relapse & address health maintenance.

h. Patients with UC should be screened for coexistent anxiety & depressive disorders & when identified, patients should be provided with resources to address these conditions.

i. Patients receiving immunosuppressants or biologics should have their vaccination status reviewed regularly and should have integrated screening programs.

Special situations:

Pediatric Ulcerative Colitis

UC in children presents unique challenges. They often have more extensive disease (pancolitis in 80-90% at diagnosis) and a more aggressive course than adults. Growth failure and delayed puberty are significant concerns. Management principles are similar, but special attention is paid to nutrition, dosing (often weight based) and psychosocial impact.[4]

UC in Pregnancy:

UC patient relapse more than CD (Crohn's disease) in pregnancy. Active inflammation increases risk of infertility.Ileoanal anal J pouch operation also increase infertility. Thromboembolism is more common in pregnancy with UC.Key priority is to keep the disease in remission & continue pre pregnancy therapy to avoid flare. Flare should be treated promptly. Preconception counselling is mandatory. Majority of drugs use in UC are safe in pregnancy like 5 ASA, Steroid, Azathioprine, Cyclosporin, Antibiotic rifaximin & biologics. But, MTX & antibiotic quinolone &metronidazole should be avoided specially in 1st trimester. Vaginal delivery is not contraindicated. Cesarian section should be done in patients with ileoanal pouch operation to prevent anal sphincter injury. Withhold live vaccine infant for at least 6 months if mother take biologic therapies except certolizumab.[14]

Elderly with UC

The diagnosis and management of UC in the elderly (>60 years) can be complex due to comorbidities, polypharmacy, and altered drug metabolism. They may present with atypical symptoms. Treatment choices must balance efficacy with the increased risk of infections (with immunosuppressives) and cardiovascular events (with JAK inhibitors).

Future directions and conclusion:

The landscape of UC management is dynamic and promising. The therapeutic pipeline includes newer biologics targeting specific IL-23 subunits (e.g., guselkumab, risankizumab), other small molecules, and microbiome-based therapies like fecal microbiota transplantation (FMT).[4,15] The ultimate goal is to move towards precision medicine, using clinical, serological, genetic, and microbial biomarkers to predict disease course and response to specific therapies upfront, thereby optimizing outcomes and minimizing trial-and-error treatment.

In conclusion, UC is a complex disease whose global footprint is expanding rapidly. Its management has been transformed by a treat-to-target philosophy and a rich pipeline of advanced therapies. A deep understanding of its clinical spectrum, a methodical diagnostic approach, and a nuanced, patient-centric application of the available medical and surgical options are paramount to improving the lives of the millions affected by this chronic condition.

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