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OVERVIEW OF INFLAMMATORY BOWEL DISEASES

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Abstract

Introduction: Inflammatory bowel diseases (IBDs) are complex, long-term inflammatory disorders of the gastrointestinal (GI) tract with an unknown etiology. IBDs are made up of ulcerative colitis (UC) and Crohn's disease (CD), two idiopathic disorders. Though the exact cause, course, and severity of these disorders remain unknown, it is believed that a variety of factors, including genetic, environmental, immunological, physiological, psychological, and gut microbiome factors, interact to influence these aspects of the disease.

Aim of the Study: This present review discusses the diagnosis, treatment, and oversight of inflammatory bowel disease. It also highlights the importance of the interprofessional team in enhancing patient outcomes.

Methodology: The present review is a comprehensive research of PUBMED since the year 1991 to 2022.

Conclusion: Inflammatory bowel disease (IBD) is an idiopathic disease that results in an immunological response to the host's intestinal microbiota that is dysregulated. Research on variables influencing the onset and severity of IBDs has attracted a lot of attention in the last few decades. It is becoming more evident that a variety of factors, including genetic, environmental, psychological, autonomic, immunological, and gut microbiota, interact and contribute to the disease manifestations and persistence of inflammatory bowel diseases (IBDs), even though the genesis of these illnesses is not fully understood. The role of genetic susceptibility and its probable co-dependency with other mediators, such as environmental, immune, and microbial factors, has been highlighted.

Keywords: Inflammatory bowel diseases, Ulcerative colitis, Crohn’s disease etc.

Introduction

Inflammatory bowel disease (IBD) is characterized by recurrent episodes of gastrointestinal tract inflammation brought on by an aberrant immune response to gut microbiota. Two forms of idiopathic intestinal disease that are distinguished from one another by their location and degree of involvement in the bowel wall are combined to form inflammatory bowel disease. Diffuse inflammation of the colonic mucosa is a symptom of ulcerative colitis (UC). Proctitis, the most common form of ulcerative colitis (UC), can also affect the sigmoid (proctosigmoiditis), the entire colon up to the cecum (pancolitis), or somewhere in between. Drug selection for Crohn's disease depends on the disease's location and behavior. Modern IBD treatments have advanced to include biological therapies, such as anti-TNF medications, which are primarily based on monoclonal antibodies or fusion proteins. These biological treatments have a high index of remission despite their high cost, which allows for a notable decrease in hospital stays and surgical cases. Additionally, novel cytokine blockers and migration inhibitors offer a promising substitute for treating IBD patients.[1]

Both Crohn's disease and ulcerative colitis have a wide range of extraintestinal symptoms in addition to the GI tract. While the disorders can be distinguished in the majority of patients, in at least 10% of cases, the features are so similar that the two disorders cannot be initially distinguished. There is a genetic predisposition to both disorders; they are both extremely morbid, and neither is curable. Lastly, there is a higher chance of colorectal cancer with both.[1]

It seems that the intestinal milieu plays a more important role in immune homeostasis than previously believed. The result of this intricate interaction between environmental, microbial, and genetic factors is a persistent activation of the immune and nonimmune mucosal responses. The intestinal mucosa normally experiences "controlled" inflammation, which is governed by a finely balanced population of Th1, Th17, Th2, Th3, Th9, and Treg cells. Chronic inflammatory conditions in patients with inflammatory bowel diseases (IBD) are caused by an immunological imbalance of the intestinal mucosa, primarily due to cells of the adaptive immune system that react to self-antigens.[2]

Epidemiology

Prior to 1960, the prevalence of Crohn's disease was significantly lower than that of ulcerative colitis. According to more recent data, Crohn's disease incidence has risen close to ulcerative colitis incidence. IBD is thought to be the cause of 100,000 hospital admissions and 700,000 doctor visits annually. With an incidence of 70–150 cases per 100,000 people, ulcerative colitis or Crohn's disease affects about 1-2 million people in the United States. For ulcerative colitis, the incidence of IBD in North America varies from 2.2 to 19.2 cases per 100,000 person-years to 3.1 to 20.2 cases per 200,000 person-years. The prevalence of adult ulcerative colitis in the United States was found to be 238 per 100,000 people, while data from a large study based on insurance claims indicated the prevalence to be 201 per 100,000 people.[3,4]

Incidence of ulcerative colitis was 7.3 cases per 100,000 people annually, with a prevalence of 116 cases per 100,000 people in Olmstead County, Minnesota; incidence of Crohn's disease was 5.8 cases per 100,000 people annually, with a prevalence of 133 cases per 100,000 people in the same population of European descent. In comparison to Asia or Africa, IBD is far more common in North America and Europe. According to estimates, the incidence and prevalence of African Americans are similar to those of European Americans, with Jewish populations of middle-European descent having the highest rates.[5,6]

Even though IBD primarily affects people between the ages of 15 and 30, up to 25% of patients will experience IBD by adolescence. The age distribution of newly diagnosed cases of IBD is bell-shaped, with the majority of new diagnoses being made in people between the ages of 15 and 40. The peak incidence of the disease occurs in the early years of the second decade of life. Patients between the ages of 55 and 65 experience a second, smaller peak in incidence, which is rising. Ten percent or so of IBD patients are under the age of eighteen. For Crohn's disease and ulcerative colitis, the male-to-female ratio is roughly 1:1, with a slightly higher incidence in women. Young adults, or those in late adolescence to the third decade of life, are most frequently diagnosed with both diseases.[7]

Types of Inflammatory Bowel Diseases

1. Ulcerative Colitis (UC)
2. Crohn's Diseases (CD)

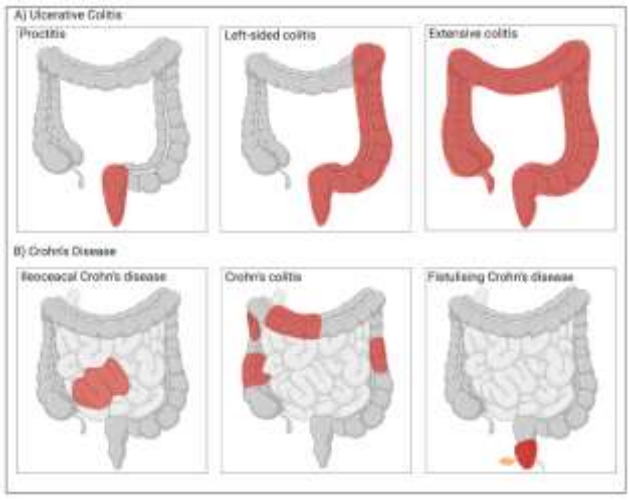

Fig. 1 Depicting different types of IBDs present in different parts of the intestine.[8]

Ulcerative colitis is always present with mucosal inflammation and causes edema, ulcers, bleeding, and loss of electrolytes. In ulcerative colitis, the inflammation typically begins in the rectum and continues unabatedly all the way to the proximal colon. In Crohn's disease, any part of the gastrointestinal tract can be impacted, which can also cause strictures, inflammation, and the formation of fistulas.[9]

Pathophysiology

IBD has been associated with inflammatory mediators, and research indicates that these mediators are crucial to the pathophysiological and clinical features of these disorders. The pathophysiology of CD and UC differs greatly from one another. The pathophysiology of UC is strongly associated with changes in the luminal microbial diversity (dysbiosis), and impairment of the epithelial and mucus layer barrier through disruption of tight junctions. When macrophages are exposed to different antigenic stimuli, they release cytokines, which bind to various receptors and have endocrine, paracrine, and autocrine effects. Lymphocytes are differentiated into various T cell types by cytokines. Type 1 (Th-1) helper T cells are primarily linked to Crohn's disease, while Th-2 helper T cells are primarily linked to ulcerative colitis. The immune reaction causes an ongoing inflammatory process by upsetting the intestinal mucosa. [8,10]

There is an increased intestinal epithelium permeability because of the impaired tight junctions and the mucous layer. This allows more luminal antigens to be absorbed. Toll-like receptors (TLRs) on non-pathogenic bacteria (commensal microbiota) cause antigen-presenting cells (APCs) to become activated which in turn activates Naïve CD4+ T-cells and start their differentiation into Th-2 effector cells, which generate pro-inflammatory cytokines like IL-5, IL-6, IL-13, and TNF-α. The nuclear factor κB (NF-κB) pathway is activated by TNF-α and IL-1, thereby facilitating the expression of genes related to cell survival and inflammation. Therefore, UC is predominantly a Th2-mediated immune disorder [11]

APCs, such as macrophages and dendritic cells, are stimulated by the uptake of luminal microflora, and this leads to the production of proinflammatory cytokines like IL-6, IL-23, and TNF-α. The expression of master transcription factors aids in the activation of APCs and the subsequent differentiation of naïve CD4+ Th cells into Th1 and Th17. More T cells enter the lamina propria of the high endothelial venule when α4β7-bearing lymphocytes bind to MAdCAM-1. Therefore, CD is a Th1 cell-mediated immune disorder.[12]

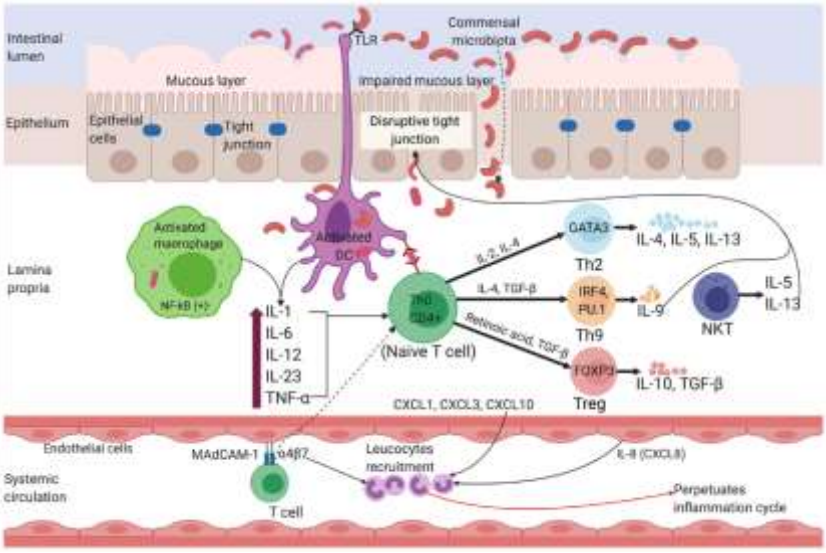

Fig.2 Pathophysiology of Ulcerative Colitis [8]

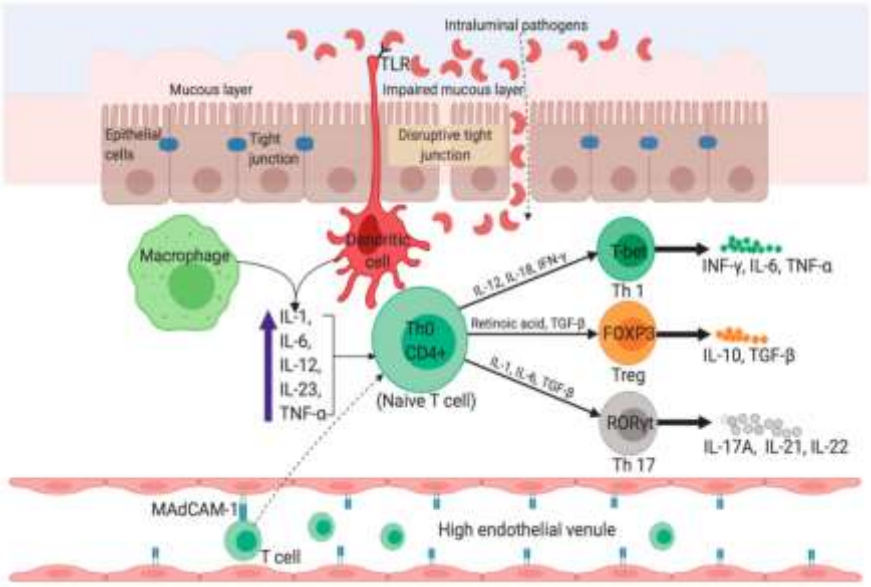

Fig.3 Pathophysiology of Crohn's disease[8]

Histopathology

Active disease presents with pronounced natural killer T cell, macrophage, dendritic cell, and neutrophil infiltration of the lamina propria. The levels of TNF-a, IL-1b, interferon-gamma, and cytokines of the interleukins-23-TH17 pathway increase with the number and activation of these cells. In ulcerative colitis, only the mucosa and submucosa are affected which results in the formation of mucosal ulcers and cryptic abscesses. Biopsy specimens show crypt abscesses, crypt distortion, and neutrophilic infiltrate. In ulcerative colitis, granulomas are not observed. The existence of pseudopolyps is another characteristic of ulcerative colitis. In Crohn's disease, granulomas may be observed, and the entire intestinal wall is affected. The hallmarks of Crohn's disease are lymphocytic infiltrates and transmural inflammation. [9]

Signs and Symptoms

The most typical sign of ulcerative colitis is bloody diarrhea, which may or may not include mucus. Abdominal pain. tenesmus, a feeling of incomplete evacuation are some other symptoms frequently reported by patients. Abdominal pain usually in the left upper or lower quadrant may be the most common finding during the physical examination. Indications of an acute abdomen, such as guarding, rebound tenderness, or percussion tenderness, call for a toxic megacolon to be looked into.[9,14]

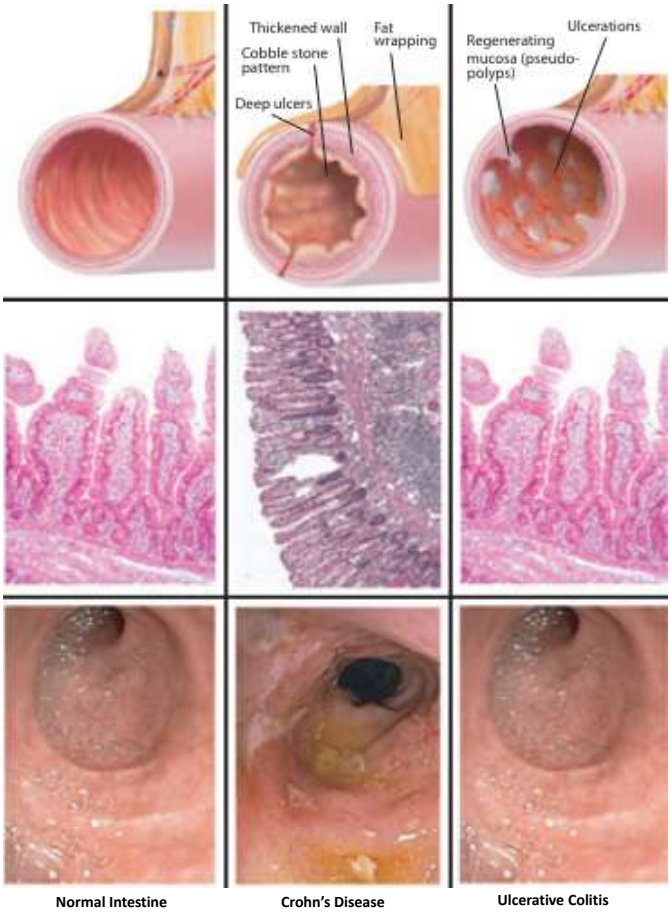

Fig.4 Comparison of Histopathological and Endoscopic features of Ulcerative Colitis, Crohn's diseases with normal Intestine.[13]

Crohn's disease manifests varies greatly depending on which part of the gastrointestinal tract is affected. Depending on the underlying cause of the inflammation, fistula formation, or stricture formation, different symptoms may appear. Weight loss, non-bloody diarrhea, and pain in the right lower quadrant all point to a possible Crohn's disease flare-up. Fecaluria, pneumaturia, and rectovaginal fistulas can all be caused by fistula formation. A lower quadrant mass on the right suggests an abscess. Patients often present with systemic symptoms, such as fever, sweats, weight loss, arthralgias, and malaise. A low-grade fever could be the precursor to a flare-up. Patients frequently experience fatigue, which is linked to the pain, inflammation, and anemia that come with the course of their illness. Recurrences can be brought on by mental stress, infections or other acute disease, dietary issues, pregnancy, antibiotic or cathartic use, or therapy noncompliance. [14]

World Gastroenterology Organization (WGO) indicates symptoms like nausea and vomiting (more common in Crohn's disease), abdominal cramping and pain, diarrhea, constipation, bowel movement abnormalities, and rectal bleeding.[15]

Extraintestinal findings like arthropathy or skin disorders may occur rarely. On the other hand, occult intestinal disease may be identified as a result of metastatic Crohn's disease symptoms on the skin, muscles, or bones. There are many skin manifestations that occur secondary to IBDs such as aphthous stomatitis, erythema nodosum, pyoderma gangrenosum, and various mucocutaneous and cutaneous lesions.[16]

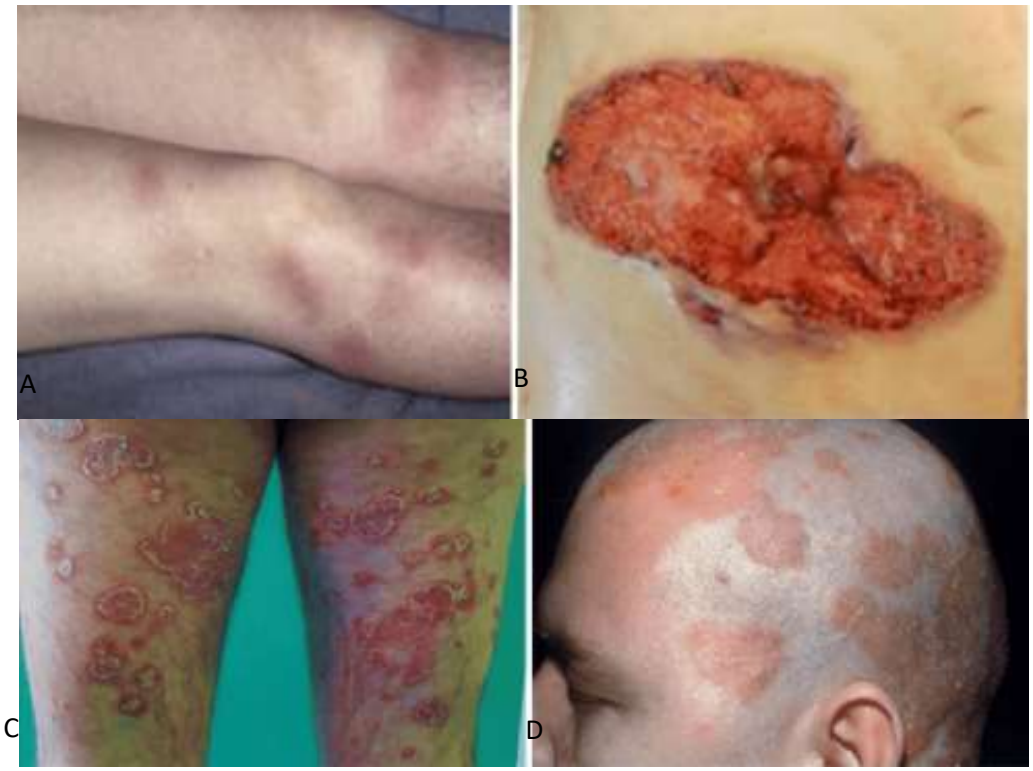

Fig. 5 A. Erythema Nodosum, B. Pyoderma Gangrenosum, C. Mucocutaneous reaction, D. Cutaneous lesion on the scalp. [16]

Diagnosis and Management

A combination of imaging findings, endoscopic biopsies, inflammatory laboratory markers, clinical findings, and physical examination are needed to diagnose inflammatory bowel disease (IBD). Microcytic anemia, leukocytosis, and thrombocytosis are examples of hematologic findings. Elevations in inflammatory markers are frequently observed, including the erythrocyte sedimentation rate (ESR) and high-sensitivity C-reactive protein (hs-CRP).[17]

Physical Examination – Tachycardia, fever, dehydration anxiety, abdominal distension, chills, lethargy, anemia, pallor, fistulas, abscesses, and rectal prolapse in Crohn's disease, upon digital rectal examination occult blood is observed growth retardation in children.[8]

Serological studies – Certain patients with ulcerative colitis have been found to have perinuclear antineutrophil cytoplasmic antibodies (pANCA), while patients with Crohn's disease have been found to have anti-Saccharomyces cerevisiae antibodies (ASCA). While the opposite pattern—positive ASCA, negative pANCA—is more specific for Crohn's disease, the combination of positive pANCA and negative ASCA has a high specificity for ulcerative colitis. [15]

Radiography – Plain and upright X-rays show a toxic megacolon, an edematous irregular colon, free air, or bowel obstruction. While, in barium enema double contrast, ulcerative colitis is indicated by a lead pipe appearance; Crohn's disease is indicated by the rectum being spared; and mucosal inflammation is indicated by thumb printing. Additionally, the barium studies might show stricture formation and skip lesions in the ileum, which are signs of Crohn's disease.[18]

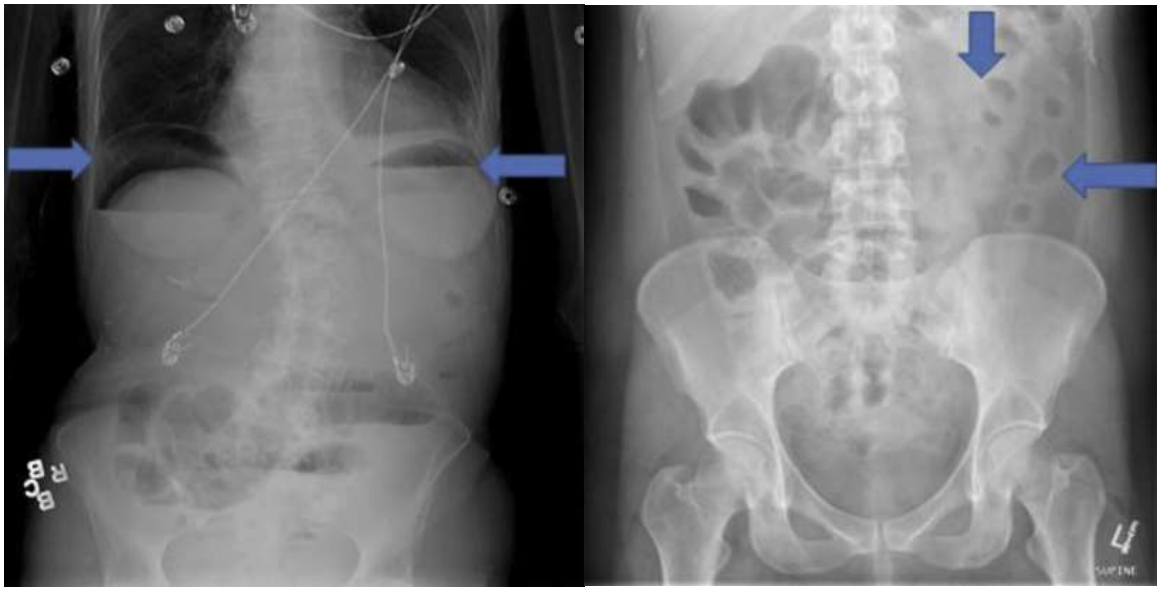

Fig. 6 Arrows indicating pneumoperitoneum (Right – Crohn's disease) and thumbprinting (Left – Ulcerative Colitis) [18]

Magnetic resonance imaging (MRI), computed tomography (CT), and ultrasound (US) have all been used to diagnose inflammatory bowel disease (IBD) or screen for complications. When used by qualified individuals, the right lower quadrant can be examined for ileal disease. Rectal fistulas can be evaluated with MRI. CT is most frequently used to check for intestinal blockage or perforations. When planning an operation or performing an assessment for strictures, CT enterography can be useful. To obtain biopsies to confirm an IBD diagnosis, endoscopy evaluation with esophagogastroduodenoscopy, colonoscopy, or both is imperative.[18]

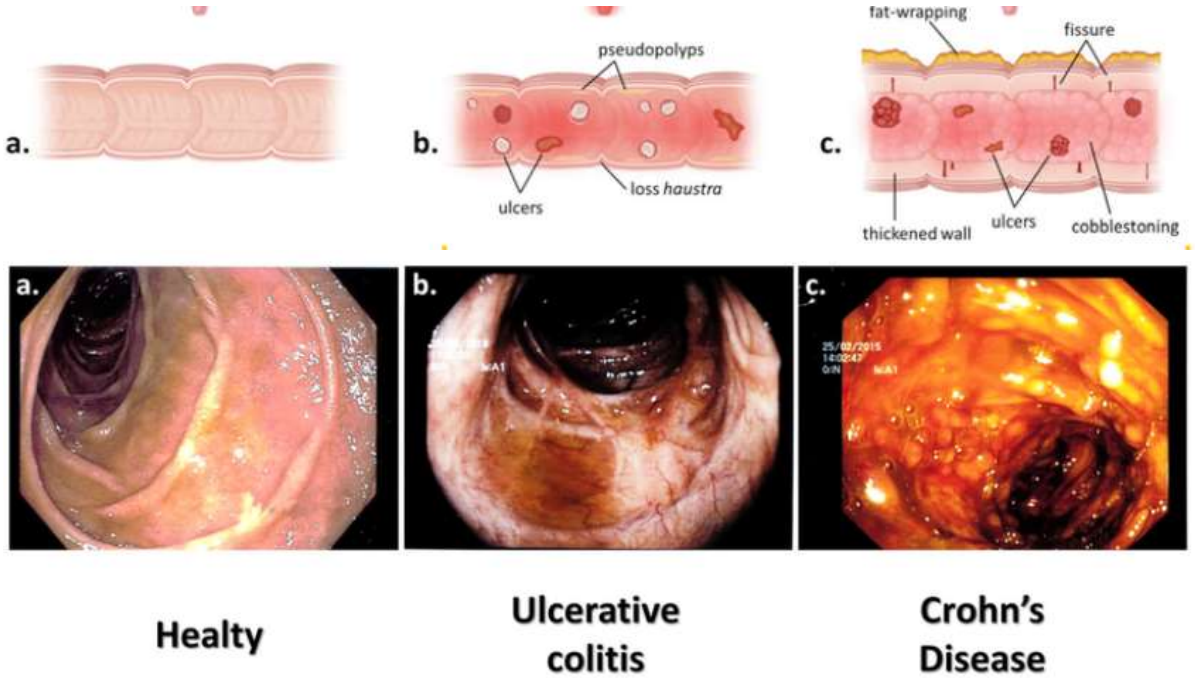

Fig. 7 Depicting the typical endoscopic findings of IBDs [19]

The three stages of IBD treatment are mild, moderate, and severe disease management. The course of treatment for UC is largely determined by the disease's severity and the existence of extraintestinal symptoms. Aminosalicylate medications such as mesalamine are the mainstays for patients with mild to moderate disease confined to the rectum. Although mesalamine is given rectally, it can be used in conjunction with oral therapy to either initiate or sustain remission. Immunomodulators such as TNF-

alpha monoclonal antibodies (infliximab) or oral glucocorticoids may be an option for patients with moderate disease who are refractory to mesalamine. For uncontrolled disease, up to 25% of all UC patients will need a total colectomy. For cases that are elective, proctocolectomy combined with ileal pouch-anal anastomosis (IPAA) is the preferred technique.[20]

The area of the GI tract affected, the severity of the fistulizing or structuring, and any extraintestinal complications all affect how a CD is treated. Mesalamine is typically the first line of treatment for mild ileocecal disease. To minimize systemic side effects, oral budesonide, a steroid with significant first-pass metabolization, can be used to further enhance the treatment. Prednisone-based systemic steroid therapy is required for more severe disease. An immunomodulating medication such as 6-mercaptopurine, azathioprine, or low-dose methotrexate is added for patients who are unable to wean. The administration of anti-tumor necrosis factor, or anti-TNF, is recommended for patients with moderate to severe illness. Patients must undergo a purified protein derivative (PPD) test to check for latent tuberculosis before starting biologic therapy. For patients with severe fistulizing disease, surgical intervention—including diverting ostomy—may be required. [20]

Conclusion

Ulcerative colitis and Crohn's Disease are similar and yet distinct diseases that make up inflammatory bowel diseases. Both diseases have a complex pathophysiology involving an interplay of intestinal microbes and aberrant immune responses. This review provides a basic overview of both diseases discussing their etiopathogenesis, diagnosis, and treatment. There has been considerable improvement in the medical management of mild and moderate cases, but unfortunately, severe cases are dealt with surgical removal of affected parts. Further research is needed to help improve patient outcomes, especially in severe cases.

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