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# Recent Updates of Ulcerative Colitis-Epidemiology, Pathophysiology, Medications Complementary Treatment and Therapies, Dietary Recommendations

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## Abstract

Ulcerative colitis is an idiopathic, chronic progressive inflammatory bowel disease of colonic mucosa, that causes the rectum and colon (Sigmoid colon) forms range from mild to severe. This chapter encompass the Ulcerative colitis- An overview. It can occur in people of any age usually in between ages of 15-30 years unless frequently in 50 years. The cause is complex and involves many factors, abnormal immune response against some micro-organisms, other environmental factors. Early diagnosing of UC with signs and symptoms like Diarrhea, Bloody stools with endoscopy biopsy. Proper treatment and medication, management, hygiene may be at lower risk. Other complication may cause Colon cancer and can be life-threatening with other co-morbidities.

**Keywords:** Ulcerative Colitis; Idiopathy; Sigmoid Colon; Endoscopy; Bloody Stools; Co-Morbidities

## Introduction

Ulcerative colitis is a chronic immune mediated inflammatory disorder of the colon, a subtype of Inflammatory Bowel Disease. And that is hypothesized to be related to exposure to environmental risk factors leading to in appropriate immune responses to enteric commensal microbes in genetically susceptible individuals. UC patient's mostly present blood in the stool and diarrhea and it is associated with major morbidities in western countries its incidence is increasing in developing countries.

This is characterized by relapsing and remitting mucosal inflammation that classically begins in the rectum and extends proximally through the colon in a continuous manner. Patients with IBD are also at a higher risk to develop colorectal cancer when compared to the average population. The etiology and the exact mechanism remain unknown despite much effort and research. IBD will become a global health problem in future and understanding its pathogenesis and developing affordable safe treatment is important [1].

## Epidemiology

UC is more prevalent than chron's disease .The health data of the entire population are recorded for epidemiological purpose. Reports have shown an increasing incidence of

IBD in recent decades. In this North America and Northen Europe have the highest incidence and prevalence rate of UC. Although the incidence of UC has stabilized in developed nations at the turn of the 21st century it has actually risen in many newly industrialized countries within South America, Asia, Africa and the Middle East. Although prevalence remains low in these countries. It is expected to climb given the rising number of new UC diagnosis. IBD emergence are strongly implicates the role of environmental risk factors to development of the disease. In 2000 there were approximately 10,000 persons diagnosed with UC in China However, by 2010 an estimated 266,394 individuals arrived a diagnosis by IBD [2].

## Pathophysiology

### Epithelial Barrier

Figure 1 depicts the pathogenesis of ulcerative colitis. The mucosal immune system's first line of defense is the stomach epithelial barrier, which separates host immune cells from luminal bacteria physically and also produces antimicrobial peptides. It is surrounded by a mucinous layer. In UC, there is a reduction in the production and modification of specific colonic mucin subtypes (mucin 2).

Increased permeability as a result of epithelial barrier degradation may be caused by improper tight junction control.

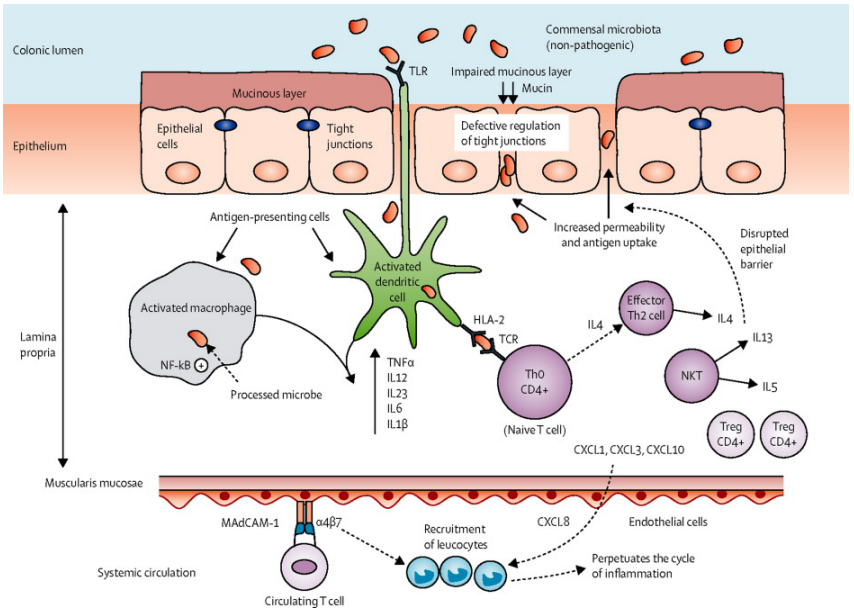


**Figure: 1** Pathophysiology of ulcerative colitis [3].

It is unknown if the malfunction occurs before ulcerative colitis or as a result of chronic inflammation, as this barrier breakdown will allow for an increase in luminal antigen uptake 2.

The intestinal epithelium also helps to the host defence by generating antimicrobial peptides (like defensins), which lessens bacterial invasion in addition to creating a physical barrier. Due to pregulated expression of specific human beta-defensin in colonic samples from ulcerative colitis patients. It is unclear whether the rise in defensin synthesis is brought on by inflammatory cytokines, bacteria, or both [4].

### Commensal Microflora

The gut immune system typically maintains a balance between dietary antigens and commensal flora tolerance while also providing optimal reactivity to enteric infections. The findings from genetically modified animal models, which produce chronic intestinal inflammation after becoming colonised with commensal gut bacteria, but will remain disease-free in bacterial-free circumstances, is plain to grasp. It has been proposed that non-pathogenic enteric bacteria have a major role in the etiology of ulcerative colitis [5].

The role of the enteric microflora in humans was also highlighted by research that contrasted Crohn's disease with ulcerative colitis in terms of the intensity of intestinal inflammation and disease phenotype. Therefore, the primary cause of ulcerative colitis is the disruption of the homoeostatic relationship between the intestinal microbiota and the mucosal immunity of the host. As a result, the commensal non-pathogenic bacteria are the target of an abnormal immune response [6].

## Antigen Recognition

- Antigens interact with macrophages and dendritic cells to activate the innate immune system. Dendritic cells have the ability to project dendrites outside the epithelium. This is connected to sample bacteria, antigens in the lumen, and intestinal epithelial cells.
- Adaptive immune responses are triggered when macrophages and dendritic cells in the lamina propria convey antigens to B cells and T cells. A greater rise in the stimulatory ability is accompanied by an increase in the number of activated and mature dendritic cells in UC patients. These levels are indicative of disease activity and show that these cells play a significant role in the initiation and maintenance of inflammation.
- Numerous microbial pattern-recognition receptors, such as Toll-like receptors (TLR) and NOD-like receptors are expressed by dendritic cells. TLR signalling plays a crucial role in providing defence against infections and safeguarding against epithelial damage. Contributing to the maintenance of the epithelial barrier and intestinal homoeostasis. TLR2 and TLR4 are not present in normal intestinal epithelial cells, which mostly express TLR3 and TLR5.In contrast; the lamina propria cells of UC patients have a substantial increase in TLR4 expression.
- The polymorphisms in TLRs can vary how susceptible a person is to enteric infections or how tolerant their adaptive immune system is to commensal bacteria. The TLR4 D299G polymorphism may be a significant risk factor for white patients.
- The nuclear factor-B (NF-B) and other transcription factors are activated when TLRs are engaged because they start the innate and adaptive immune responses. These play a crucial role in the inflammatory cascade's activation.
- Its role in chronic intestinal inflammation is multifaceted and depends on the type of cell because NF-kB controls the proinflammatory and cell survival activities in macrophages and T cells while simultaneously acting as a protective factor in epithelial cells [7].

## Deregulation of Immunological Responses

The homeostatic balance between regulatory and effector T-cells (such as T-helper [Th] 1, Th2, and Th17) is altered in the mucosa of ulcerative colitis patients. Evidence suggests that non-classical natural killer T-cells are responsible for the interleukins 5 and 13 produced by the atypical Th2 response in ulcerative colitis. Because it has cytotoxic effects on epithelial cells, such as inducing apoptosis and changing the protein makeup of tight junctions, interleukin 13 is particularly significant.

Naturally fatal the number of T-cells in an inflamed colon's lamina propria increases, and they can produce a variety of Th2 cytokines, including interleukin 4, which is quickly replaced by interleukin 13, among others [8].

Interleukin 13 may cause natural killer T-cells to respond favourably, enhancing tissue damage. Because there is evidence that blocking this interleukin and depleting natural killer T cells can stop the progression of ulcerative colitis, it appears that these two factors are important in the pathogenesis of ulcerative colitis. Severe ulcerative colitis is related to loss-of-function mutations in either interleukin-10 receptor-1 or interleukin-10 receptor, most likely as a result of a lack of interleukin-10 signalling.

In the blood, stool samples, and mucosa of patients with ulcerative colitis, tumour necrosis factor (TNF-) is raised. These results support the role of TNF- in the aetiology of the disease and the efficacy of anti-TNF therapy for ulcerative colitis.

## Leucocyte Recruitment

The production of chemoattractants like CXCL8 that draw circulating leucocytes from the systemic circulation to the inflamed mucosa (which is upregulated in patients with UC). Additionally, it is crucial for the inflammation response to be amplified.

The expression of adhesion molecules, such as mucosal addressin cellular adhesion molecule-1 (MadCAM-1), is upregulated by proinflammatory cytokines on the vascular endothelium of mucosal blood vessels, which encourages leucocyte adhesion and extravasation into the tissue, thereby sustaining the inflammatory cycle. In times of inflammation, MAdCAM-1 facilitates lymphocyte homing to gut-associated lymphoid tissue by interacting with 47 integrins.

Lymphocyte recruitment is prevented and colonic inflammation is less severe by antibodies to either MAdCAM-1 or its ligand 47 and to the 7 subunits of this heterodimeric integrin.

Several susceptibility genes for ulcerative colitis have been found thanks to genome-wide association studies, which have revolutionised the complicated field of polygenic illnesses and provided new insights into disease pathophysiology. The most important associations are found close to HLA-DRA in the major histocompatibility complex class-2 region or (84, 95% CI 9-785; p0.0001) HLA haplotype DRB1*0103 is substantially related to illness susceptibility, extensive disease, and a higher likelihood of colectomy.

There are currently 47 susceptibility loci linked to ulcerative colitis, 20 of which are also linked to Crohn's disease (for example, interleukins 23 and 10 and Janus kinase-2 pathway

genes).

The relevance of impaired barrier function in disease aetiology is highlighted by the discovery of risk loci for ulcerative colitis, such as hepatocyte nuclear factor-4, CDH1, and laminin-1, which code for proteins that are essential for epithelial cell adhesion. The first established genetic link between colorectal cancer and ulcerative colitis is a mutation in the protein E-cadherin [9].

## Intestinal Microbiota and UC

The pathogenesis of UC and the gut flora are closely related. The intestinal microbiota's stable state is crucial for preventing the out-of-control proliferation of specific microorganisms. Obesity, metabolic syndrome, immunological disorders, necrotizing enterocolitis, skin issues, UC, Crohn's disease (CD), and irritable bowel syndrome may all be influenced by intestinal microbiota dysbiosis. When the intestinal microbiota is out of balance, the body's immunity is diminished, the immune system is less effective, and the relative pathogenic factors are raised, which can lead to an invasion of the intestinal mucosa or worsen existing conditions. The interplay between the host and intestinal microbiota may play a significant role in the complex pathophysiology of UC. The host's innate and adaptive immunity often stops the invasion of dangerous bacteria while tolerating the usual microbiota. Immunity is jeopardized if the microbiota is unbalanced. Overstimulating the immune system of the gut mucosa might result in illness [10].

Gut inflammatory reactions result from intestinal microbiota disruption. The dangerous bacteria in the intestine quickly increase as a result of the change in the microbiota. The synthesis of immunosuppressive proteins and the increase in intestinal mucosal permeability caused by enterotoxin release also contribute to immunological dysfunction. Intestinal epithelial cells are directly invaded and harmed by expanding populations of pathogenic bacteria. The gut mucosal barrier is harmed by it. Due to the overgrowth of some bacteria, metabolic and energy metabolism are impacted. Additionally, intestinal inflammation and mucosal damage are caused. The function of the intestinal mucosal barrier deteriorates, the intestinal wall's ability to act as a shield is reduced, and intestinal microbiota is moved around the body, further damaging the mucosal barrier and escalating the intestinal inflammatory response. Animal studies have shown that altering gut bacterial balance can cause colitis in animal models. The absence of colitis in sterile IL-10 or HLA-B27 deletion animals suggests that intestinal microbiota is crucial for the development of UC.

Compared to healthy individuals, intestinal epithelial cells of CD patients have a high quantity of microorganisms adhering to them. One of the main reasons triggering CD and activating the gut immune system may be microbiota. Additionally, it's possible that the primary cause of IBD is the disruption of the local microbiota. The development of several kinds of immediate cell factors may result from the presence of intestinal inflammation (Figure 2) [11].

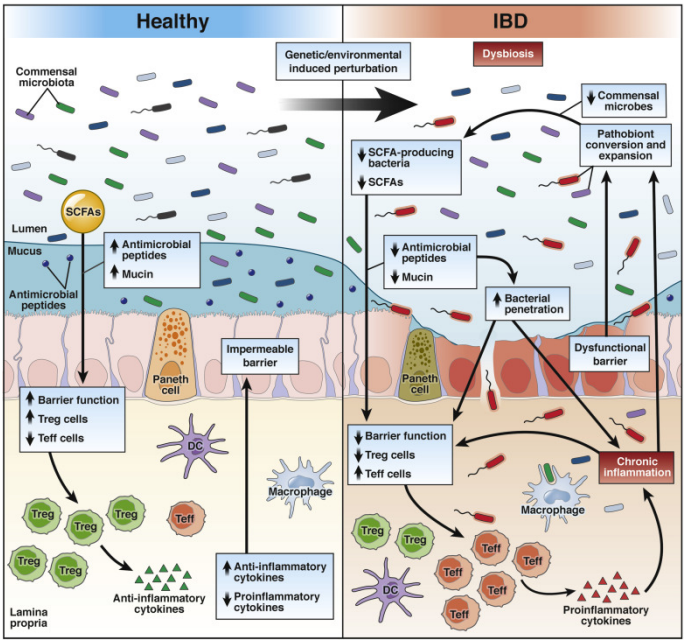


**Figure 2:** Intestinal micro biota and Ulcerative colitis.

## Presenting Signs and Symptoms

Lower abdominal cramping that is most severe during faeces and blood-and-mucus-mixed stools are the two characteristics of UC that occur most frequently. Depending on the frequency of stools, the degree of abdominal discomfort, fever, and haemoglobin and albumin concentrations, episodes are classified as mild, moderate, or severe [12].

## Diagnosing Ulcerative Colitis

A thorough physical examination and extensive medical history-taking are the first steps in the diagnosing process. Then, you could require one or more diagnostic exams. The "gold standard" for identifying ulcerative colitis is a colonoscopy and sigmoidoscopy. To rule out other illnesses, such as Crohn's disease, more testing could be required [13].

Diagnostic testing for ulcerative colitis available at Stanford Health Care includes:
Blood test: We may do a variety of blood tests using a sample of your blood, such as:

- A complete blood count to check for infections and symptoms of anemia
- An electrolyte and renal function panel to check for liver problems and electrolyte disorders
- Albumin tests to determine your dietary status

Colonoscopy or sigmoidoscopy: A tiny flexible tube and camera are inserted into your rectum to do a colonoscopy or sigmoidoscopy, which involves looking at your entire colon or just the bottom portion of it (endoscope) [14].

**Magnetic resonance imaging:** A magnetic resonance imaging exam gives you clear pictures of your small and large intestines without using radiation, and it deftly reveals tissue inflammation.
**Stool culture:** This test, also known as a fecal occult blood test (FOBT), looks for minute amounts of blood by examining a sample of your faeces under a microscope.
**Upper endoscopy:** We carefully inspect the lining of your intestines using an endoscope that we pass through your mouth and oesophagus. We might also take a tissue sample (biopsy) during an upper endoscopy and study it under a microscope.

## Diagnosis of ulcerative colitis

### Clinical Features

- Rectal bleeding
- Diarrhoea
- Urgency
- Tenesmus
- Abdominal pain
- Fever (severe cases)
- Extraintestinal manifestations

### Endoscopic Features

- Loss of vascular pattern
- Erythema
- Granularity
- Friability
- Erosions
- Ulcerations
- Spontaneous bleeding

### Pathological Features

- Distortion of crypt architecture
- Crypt abscesses
- Lamina propria cellular infiltrate (plasma cells, eosinophils, lymphocytes)
- Shortening of the crypts
- Mucin depletion
- Lymphoid aggregates
- Erosion or ulceration [15]

## Medications for Ulcerative Colitis

These medications which are used to treat the curb inflammation in your bowel. It includes sulfa drugs, corticosteroids, immunosuppressive agents, and antibiotics.

- **5-aminosalicylic (5-ASA):** The most common drugs used to treat ulcerative colitis are balsalazide, mesalamine, olsalazine, and sulfasalazine. These come in tablet and suppository form. Before utilizing one of these medications, let your doctor know if you have a sulfa allergy. They can recommend a 5-ASA without sulfa.
- **Corticosteroids:** If 5-ASA medications don't help you or if your condition is more severe, you may need to use these anti-inflammatory medications. Doctors frequently recommend these medications for brief periods of time to assist you in entering remission because they can occasionally cause negative effects and long-term consequences. Then, to prevent your symptoms for a longer time, your doctor might give you a 5-ASA medicine.
- **Immunosuppressants:** Your doctor may recommend medications like 6-mercaptopurine (6-MP), azathioprine (Azasan, Imuran), cyclosporine, and tacrolimus if corticosteroids or 5-ASA medications are ineffective (Astagraf XL, Envarsus XR, Prograf).
- **Biologics:** Adalimumab (Humira) and its biosimilars, adalimumab-atto (Amjevita), adalimumab-adbm (Cyltezo), certolizumab pegol (Cimzia), golimumab (Simponi, Simponi Aria), infliximab (Remicade), a biosimilar to Remicade, adalimumab (Entyvio).
- **Drugs that inhibit Janus kinase (JAK inhibitors):** These oral medications have a quick onset of action and

help keep ulcerative colitis in remission. The first JAK inhibitor to receive FDA approval for the treatment of ulcerative colitis is tofacitinib (Xeljanz).

- **Modulators of the Sphingosine 1-phosphate (S1P) receptor:** The first oral sphingosine 1-phosphate (S1P) receptor modulator approved for people with moderately to highly active UC is ozanimod (Zeposia) [16].

Newer medications being studied include a group called sphingosine 1-phosphate receptor modulators. These can be taken by mouth. Researchers think they may get around the anti-drug antibodies that sometimes form with medications given as a shot. Antibodies are proteins that cancel out viruses, bacteria, and other things your body doesn't recognize.

Some people get surgery to remove part or the entire colon. Your doctor may suggest this if your medicine isn't working, your symptoms get worse, or your ulcerative colitis leads to serious complications.

When you have an operation to remove your entire colon, the surgeon most often creates an opening, or stoma, in your belly wall. They attach a bag there and bring the tip of your lower small intestine through the opening. Waste passes through it and collects in a pouch, which gets attached to the stoma. You'd need to wear the pouch all the time.

A newer surgery, called a pelvic pouch or ileal pouch anal anastomosis (IPAA), doesn't create a permanent opening. Instead, a surgeon removes your colon and rectum, and your small intestine is used to form an internal pouch or reservoir that serves as a new rectum. This pouch is connected to the anus.
A procedure called a continent ileostomy (Kock pouch) is done if you want your external pouch converted to an internal one, or if you can't get the IPAA operation [17].

In this procedure, there is a stoma but no bag. Your surgeon removes your colon and rectum and creates an internal reservoir from your small intestine. They make an opening in your belly wall and join the reservoir to your skin with a nipple valve. To drain the pouch, you insert a catheter through the valve into the internal reservoir.

Other techniques are also available. All surgeries carry some risk and complications. If you have been told you need surgery to treat ulcerative colitis, you may want to get a second opinion to make sure you get the best option for you [18].

## Complementary Treatments and Therapies

The complementary treatment and therapies which is useful in the patient with Ulcerative colitis. Let's take a look at a few:

- **Mind-body therapies:** It is not unexpected that mind-body relaxation techniques may be beneficial because stress and anxiety are well-known ulcerative colitis triggers for many people. These methods aid in cultivating a strong bond between your mind and body as well as between you and the outside world. They may even motivate you to adopt new habits in your daily life. They might be beneficial even if merely to reduce UC-related anxiety and despair and enhance the quality of life. Additionally, there is some proof that practices like yoga, meditation, and gut-centered hypnotherapy may be able to ease some physical UC symptoms or flare-ups. Some of the approaches, such as cognitive behavioral therapy (a form of psychotherapy) and patient support groups, have been so effective that they have gradually entered the mainstream.
- **Vitamins and supplements:** Due to their condition, people with ulcerative colitis may not be able to fully absorb certain vitamins or minerals from their diet. Your doctor could advise using certain vitamins in these circumstances. However, before you choose to take any on your own, it's crucial to consult your doctor. If you have UC and are on other medications, several of these chemicals may be dangerous. Additionally, some patients take specific vitamins in the hope that they would help manage their UC symptoms. These might include:
- **Fish oil:** Omega-3 fatty acids, which are present in foods like fish, walnuts, flaxseed, and vegetable oils, are beneficial to your health. Among its many advantages are its ability to reduce inflammation and protect the heart. To reduce gut inflammation, some persons with UC take omega-3 supplements in the form of fish oil capsules. The effectiveness of this has not yet been established by research. If you combine fish oil with blood thinners like warfarin, it may be harmful to you and dangerous (Coumadin) [19].
- **Turmeric:** It is frequently used in South Asian and Indian cuisine. It contains a substance called curcumin, which may help some people reduce inflammation. A few small studies suggest that taking it as a capsule may be helpful for UC flare-ups, but additional study is required to confirm these findings. It might cause bloating, nausea, and diarrhea as adverse effects. Blood is also thinned by it. This test is not safe for use on expectant mothers.
- **Probiotics:** These microorganisms are beneficial. Many foods contain it. It gives your gut's microorganisms a balanced, healthy population. Some studies indicate they might be effective as supplements in reducing and preventing UC flare-ups, particularly if you have an inflammatory pouch (as a result of J-pouch surgery). It's crucial to use caution. There are many different probiotic products on the market, and additional research is required [20].

## Diet Recommendations for Ulcerative Colitis Flare

- To relieve abdominal pain and diarrhea follow a low residue diet.
- Avoid food such as fresh fruits and vegetables, prunes and caffeinated beverages these may increase the stool output.
- Avoid concentrated sweets in your diet, such as juices, candy and soda. It helps to decrease amounts of water pulled into your intestine, which may contribute to watery stools.
- Avoid alcohol consumption.
- Try to incorporate more omega-3 fatty acids in your diet. Because it have an anti-inflammatory effect. They are found in fish, including salmon, mackerel, herring and sardines.
- More frequent meals are better tolerated. This eating pattern can help to increase the amount of nutrition you receive in a day [21].

**Suggestions for first foods after a flare include:**

- Diluted juices
- Applesauce
- Canned fruit
- Oatmeal
- Plain chicken, turkey or fish
- Cooked eggs or egg substitutes
- Mashed potatoes, rice or noodles
- Bread – sourdough or white

## Conclusion

In evidence we have summarized the Ulcerative colitis-An overview with causes epidemology, pathophysiology, diagnosis, treatment and therapies, dietary recommendation for patient with mild to moderate risk, to reduce the complications of risk and factors, to overall knowledge of patients in severity of disease to prevent complications and other co-morbidities.

## References

1. Chang JT (2020) Pathophysiology of Inflammatory bowel diseases. New England Journal of Medicine 383: 2652-2664.

2. Annahazi A, Molnar T (2014) Pathogenesis of Ulcerative colitis and Crohn's diseases: Similarities, differences and a lot of things we do not know yet. Journal of J Clinical & Cellular Immunology 5: 253.

3. Schroeder KW, Tremaine WJ (1987) Coated oral 5-Aminosalicylic acid therapy for mildly to moderately active Ulcerative colitis. New England Journal of Medicine 317(26): 1625-1629.

4. Rachmilewitz D (1989) Coated mesalazine (5-Aminosalicylic acid) versus sulphasalazine in the treatment of active Ulcerative colitis: a randomized trial. British Medical Journal 298: 82.

5. Abraham C, Cho JH (2009) Inflammatory bowel disease. New England Journal Medicine 361: 2066-2078.

6. Silverberg MS, Satsangi J, Ahmad T, Arnott ID, Bernstein CN, et al. (2005) Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Canadian Journal of Gastroenterology 19: 5-36.

7. Loftus CG, Loftus EV, Harmsen WS, Zinsmeister AR, Tremaine WJ, et al. (2007) Update on the incidence and prevalence of Crohn's disease and ulcerative colitis in Olmsted County, Minnesota, 1940-2000. Inflammatory Bowel Diseases 13(3): 254-261.

8. Bernstein CN, Wajda A, Svenson LW, MacKenzie A, Koehoorn M, et al. (2006) The epidemiology of inflammatory bowel disease in Canada: a population-based study. American Journal Gastroenterology.2006; 101(7): 1559-1568.

9. Ungaro R, Mehandru S, Allen PB, Peyrin Biroulet L, Colombel JF (2017) Ulcerative colitis. Lancet 389: 1756-1770.

10. Ramos GP, Papadaki KA, (2019) Mechanisms of Disease: Inflammatory Bowel Diseases. Mayo Clin. Proc 94(1):155-165.

11. Almallah YZ, Richardson S, O Hanrahan T, Mowat NA, Brunt PW, et al. (1998) Distal procto-colitis, natural cytotoxicity, and essential fatty acids. American Journal of Gastroenterology 93(5): 804-809.

12. Hou JK, Abraham B, El Serag H (2011) Dietary Intake and Risk of Developing Inflammatory Bowel Disease: A Systematic Review of the Literature. American Journal of Gastroenterology 106(4): 563-573.

13. Ament ME, Berquist WE, Vargas J, et al (1988) Fiberoptic upper endoscopy in infants and children. Pediatrics Clinician North America 35(1): 141-155.

14. Tragnone A, Valpiani D, Miglio F, Elmi G, Bazzocchi G, et al. (1995) Dietary habits as risk factors for inflammatory bowel disease. European Journal of Gastroenterology Hepatol 7(1): 47-51.

15. Barton JR, Gillon S, Ferguson A (1989) Incidence of

inflammatory bowel disease in Scottish children between 1968 and 1983; marginal fall in ulcerative colitis, three-fold rise in Crohn's disease. Gut 30(5): 618-622.

16. Beattie RM, Schriffrin EJ, Donnet Hughes A, Huggett AC, Domizio P, et al. (1994) Polymeric nutrition as the primary therapy in children with small bowel Crohn's disease. Aliment Pharmacology Thererapy 8(6): 609-615.

17. Bonen DK, Cho JH (2003) The genetics of inflammatory bowel disease. American journal of Gastroenterology 124(2): 521-536.

18. Candy S, Borok G, Wright JP, Boniface V, Goodman R (1985) The value of an elimination diet in the management of patients with ulcerative colitis. South African Medical Journal 85(11): 1176-1179.

19. Satsangi J, Morecroft J, Shah NB, Nimmo E (2003) Genetics of inflammatory bowel disease: scientific and clinical implications. Best Practice Clinical Gastroenterology 17(1): 3-18.

20. Pallone F, Blanco Gdel V, Vavassori P, Monteleone I, Fina D, et al. (2003) Genetic and pathogenetic insights into inflammatory bowel disease. Current Gastroenterology Rep 5(6): 487-492.

21. MacDonald TT, Murch SH (1994) Aetiology and pathogenesis of chronic inflammatory bowel disease. Baillieres Clinical Gastroenterology 8(1): 1-34.