Journal for ReAttach Therapy and Developmental Diversities
eISSN: 2589-7799
2023 September; 6(1): 2299-2305

A Comprehesive Review on Inflammatory Bowel Disease with Homoeopathic Insight

Dr. Gyanendra Kumar Rai[1], Prof . (Dr.) Ahijit Chattopadhyay[2], Dr. Anand Kumar Jaiswal[3], Dr. Anurag Yadav[4]

[1]PhD Scholar (Tantia University) BHMS M.D.(Hom)
[2]BHMS M.D.(Hom)
[3]Lecturer State BKHM College & Hospital Deokali, Ayodhya BHMS M.D.(Hom)
[4]Lecturer, SRHPM State Homoeopathic Medical College & Hospital Barhalganj, Gorakhpur BHMS, MD(Hom)

Abstract-
Ulcerative colitis (UC) and Crohn's disease (CD) are comprising as chronic inflammatory bowel diseases (IBD), a heterogeneous state of chronic intestinal inflammation with no exact known cause having similar symptoms that lead to digestive disorders and inflammation in the digestive system. The pathogenesis of IBD is complex. Recent studies have greatly improved our knowledge of the pathophysiology of IBD, leading to great advances in the treatment as well as diagnosis of IBD. A number of factors can be attributed to the prevalence of CD and UC, some of which include geographical location, inappropriate diet, genetics, and inappropriate immune response. Conventional therapies are inadequate and are associated with several systemic side effects due to lack to localization of active moiety at the inflamed site. In this review we provide researchers and patients with new insights into this field and facilitate access alongwith hoomeopathic treatments.

Keywords: Inflammatory bowel disease, ulcerative colitis, Crohn's disease, Homoeopathy.

Introduction-

Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract, which clinically contains Crohn's disease, ulcerative colitis, and other conditions [1]. The inflammation of the intestinal mucosa in IBD is characterized by episodes of abdominal pain, diarrhea, bloody stools, weight loss, and the influx of neutrophils and macrophages that produce cytokines, proteolytic enzymes, and free radicals that result in inflammation and ulceration [1, 2].
Inflammatory bowel disease (IBD) includes ulcerative colitis (UC) and Crohn's disease (CD). UC was first described in 1859 , and CD in 1932 [3]. Both UC and CD are chronic and debilitating diseases without a real cure. As of 2017, 6.8 million IBD cases were reported globally, with an increase in age-standardized prevalence rates from 79.5 per 100,000 population in 1990 to 84.3 per 100,000 population in 2017 [4]. More than 1.6 million people in the United States , 250,000 in the United Kingdom [5], 260,000 in China , and 85,000 in Australia are affected by IBD [8]Since 1990, the incidence rate of IBD in Western countries was shown to be stable or started to drop, but the incidence rate in newly industrialized countries of Asia, Africa, and South America was increasing . It affects both children and adults. It is estimated that UC affects 2.6 million in Europe and 1.2 million people in North America . Approximately 25% of these patients are diagnosed before the age of 18 years. The disease often begins in adolescence and approximately 25% of patients with IBD are younger than 20 years [9].
Crohn's disease usually involves the terminal ileum, cecum, perianal area, and colon, but it can affect any region of the intestine in a discontinuous pattern . In contrast, ulcerative colitis involves the rectum and can affect part of the colon or the entire colon in a continuous pattern . Crohn's disease exhibited histologically a thickened submucosa, transmural inflammation, fissuring ulceration, and granulomas, whereas the inflammation in ulcerative colitis is limited to the mucosa and submucosa with cryptitis and crypt abscesses [10].

Although the cause of IBD remains unknown, considerable progress has been made in recent years to unravel the pathogenesis of this disease. Studies have provided evidence that the pathogenesis of IBD is associated with genetic susceptibility of the host, intestinal microbiota, other environmental factors, and immunological abnormalities [11,12].
Accordingly, clinical, endoscopic, histologic, and radiological tests are used to diagnose UC. About 7-10% of IBDs are unclear [13,14]. UC and CD are related diseases but there are contrasting features with regards to the clinical presentation, the site of involvement and extent of inflammation across the bowel wall[15]. IBD is a life-long condition associated with considerable ongoing morbidity and can affect an individual's social and psychological wellbeing, particularly if their disease is poorly controlled.Therefore, this review paper aims to investigate the prevalence, causes, diagnosis, and treatment strategies for patients with IBD.

Epidemiology-

Over 6.8 million people are estimated to be living with IBD worldwide, with 300,000–500,000 people currently living with a diagnosis of IBD in the UK[6–8]. A 2018 population-based cohort study published in 2020 estimated UK point prevalence as 276 cases of CD per 100,000 people and 397 cases of UC per 100,000[16].
Up to 90% of people with UC will experience one or more relapses after the first episode; early relapse or active disease in the first two years following diagnosis is associated with a poorer outcome. IBD most commonly occurs between the ages of 15 and 40 years, although it can occur at any age, with 15% of cases diagnosed in individuals aged over 60 years [17].

Pathophysiology-

The exact cause of IBD is uclear. It is believed thatGenome-wide association studies (GWAS), next generation sequencing studies, and other analysis have identified over 240 nonoverlapping genetic risk loci, of which around 30 genetic loci are shared between Crohn's disease and ulcerative colitis.[18] Nucleotide-binding oligomerization domain 2 (NOD2) is the first gene found to be associated with Crohn's disease, which is frequently mutated in patients with Crohn's disease, occurring in around one-third of the patients.[19] GWAS has identified numerous single-nucleotide polymorphisms (SNP) in *IL-23R*, with high association for Crohn's disease and ulcerative colitis.[20] Also, although many individuals carry IBD-associated risk loci, only a small population develops IBD. Therefore, additional environmental factors and alterations to the interactions between the gut microbiota and mucosal immune system are required for the development of IBD.
Intestinal microbiota is the major environmental driver of IBD. The gut microbiota can be influenced by diet, probiotics, prebiotics, antibiotics, exogenous enzymes, fecal microbiota transplantation, and other environmental factors .[21] These microorganisms contain around 100-fold as many genes present in the human genome . This gut microbiota is necessary for intestinal homeostasis and function, health, and disease.[22]
Food intake is an important environmental factor that affects the development of IBD [23]. Studies have provided evidence that intake of fruit and vegetable has been associated with decreased risk of Crohn's disease [24]; intake of fast foods containing many fat and sugar-rich foods may exacerbate the development of Crohn's disease [23]. Smoking is another example of a disease-specific modifier that seems to worsen Crohn's disease while being protective against ulcerative colitis [25] There are other environmental factors that influence the development of IBD, including but not limited to psychological stress, appendectomy, diet, and medications [26]

CLINICAL PRESENTATION-

1. The most consistent feature of UC is the presence of blood and mucus mixed with stool, accompanied by lower abdominal cramping which is most intense during the passage of bowel movements. CD presents with early satiety, nausea, emesis, epigastric pain, or dysphagia.
2. Fevers are seen in 40% of patients with IBD at the time of presentation
3. Weight loss is observed more frequently with CD than with UC.
4. Delayed growth,Chronic undernutrition resulting due to anorexia and abdominal discomfort, as well as increased losses due to a protein-losing enteropathy, is considered to be a major etiologic factor in growth delay
5. arrest of sexual maturation may occur concurrently with growth failure in children.
6. Arthralgias and arthritis occasionally precede intestinal manifestations of IBD.
7. Mucocutaneous lesions like Oral aphthoid ulcers occur commonly with IBD
8. Autoimmune hepatitis
9. Nephrolithiasis occurs predominantly as uric acid calculi in UC and oxalate calculi in CD.
10. As a complication of prolonged corticosteroid use Osteopenia (reduced bone mass) can occur.

CAUSES

The exact understanding cause is difficult to discuss but bacteria viruses and antigens trigger the immune response of the body to produce and inflammatory response in the GIT. Study reported that some hereditary genetic and environmental factor may also contribute[28]
Age, ethnicity, genetics, medication, and smoking are risk factors for both
UC and CD. The anti-inflammatory drug can also cause or worsen IBD
Age, ethnicity, genetics, medication, and smoking are risk factors for both
UC and CD. The anti-inflammatory drug can also cause or worsen IBD

RISK FACTORS

Age, ethnicity, genetics, medications and smoking are risk factors for both UC and CD the anti inflammatory drugs can also cause or worsen IBD. [28]

DIAGNOSES-

IBD is diagnosed using a combination of clinical assessment, endoscopic procedures, radiologic imaging, and histological testing [29], as shown in Table1. The following are important diagnostic steps.
Strober W, Lúdvíksson BR, Fuss IJ. The pathogenesis of mucosal inflammation in murine models of inflammatory bowel disease and Crohn disease. Ann Intern Med 1998;128:848-56. doi: 10.7326/0003-4819-128-10-199805150-00009, PMID 959919
Strober W, Lúdvíksson BR, Fuss IJ. The pathogenesis of mucosal inflammation in murine models of inflammatory bowel disease and Crohn disease. Ann Intern Med 1998;128:848-56. doi: 10.7326/0003-4819-128-10-199805150-00009, PMID 959919
Strober W, Lúdvíksson BR, Fuss IJ. The pathogenesis of mucosal inflammation in murine models of inflammatory bowel disease and Crohn disease. Ann Intern Med 1998;128:848-56. doi: 10.7326/0003-4819-128-10-199805150-00009, PMID 959919

Diagnostic Criteria	Ulcerative Colitis	Crohn's Disease
Clinical Presentation	Chronic symptoms such as constipation urgency, abdominal discomfort, and bloody diarrhea are among the symptoms that are persistent and recurrent.	Chronic Symptoms that are persistent and recurrent include fever, lethargy, weight loss, diarrhea, and stomach pain.
Endoscopic Findings	Continuously inflammation that is only present in the colon and rectum.	Transmural inflammation that may affect any area of the digestive system. commonly impacts the colon and terminal ileum, but it can also affect other organs.
Histopathology	Inflammatory infiltrates in the lamina propria as well as crypt deformation, cryptitis, and crypt abscesses may be visible in biopsy samples.	Transmural inflammation, granulomas, and intermittent gastrointestinal involvement can all be seen in biopsy samples.
Classification System	The Montreal classification system is mainly used to categorize the anatomical level of ulcerative colitis involvement. It encompasses subtypes such as: 1. Pancolitis 2. Left-sided colitis 3. Proctitis.	The Montreal classification system is largely used to categorize the severity of Crohn's disease based on: 1. The location 2. Behavior 3. Age of diagnosis 4. Progression of the disease, It contains classifications for the location (L1-L4), (B1-B3), age at diagnosis (A1-A3), and progression (P) of the disease.

Table 1: Diagnostic criteria for ulcerative colitis and Crohn's disease include classification systems such as Montreal classification.

TREATMENT-

The main objective of the diagnosis and treatment of the disease is to reduce the symptoms and improve the patient's health, to completely eliminate the symptoms of the disease or keep the disease at a fixed stage and avoid the surgical treatment. By carefully examining the clinical symptoms of the patient and performing several tests, the severity of the disease, as well as the areas affected by the disease, can be determined. the objectives of the medical treatment were described as follows:

1.Clinical treatment and improvement of the individual's clinical condition,
2.Reducing the clinical side effects of the patient,
3.Improving the quality of life,
4.Reducing the drug poisoning,
5.Nutritional support for the patient, and
6.Restricting the patient's need for admission or surgery.

Anti-inflammatory and immunomodulator drugs

This can be achieved by using anti-inflammatory drugs such as corticosteroids and aminosalicylic acids, other drugs are immunomodulators, such as adalimumab, infliximab, natalizumab azathioprine, mercaptopurine, methotrexate, and certolizumab. These compounds efficiently trigger a Th2-mediated response that dampens Th1-mediated inflammation to regulate the immune system. This drug suppresses the immune system so that inflammation-inducing chemicals are not released. These drugs also neutralize the protein in the body that causes inflammation

Antibiotics

Ciprofloxacin and metronidazole can also be prescribed to eradicate the infection if any.

Other drugs

To give more relief to the patient, antidiarrhea drugs, painkillers, and nutrient and vitamin supplements are often prescribed to the patient. As diarrhea is a common symptom, it should be treated.

Special diet

In cases that are accompanied by weight loss, the gastroenterologist may recommend a special diet that can be induced through a feeding tube. Care is taken that no food particle can struct in GIT and cause blockage.

Surgery

In severe cases, the colon part or entire colon is surgically removed when other options of treatment do not work. If the damaged portion is removed, then the remaining normal portion of the intestine is reconnected. In case the entire colon is removed, the surgeon creates a permanent opening in the abdomen called an ileal stoma through which stools pass in the bag [30].

Lifestyle modification

Home-based remedies are also found useful in some cases of IBD. The symptoms may be relieved. There is no evidence of food that can affect IBD but limiting dairy products, limiting meals, drinking plenty of fluids, multivitamins, and mineral supplements are found useful. In addition, stress management, smoking cessation, relaxation, and breathing exercises are proven beneficial [30].

COMPLICATIONS

IBD if left untreated can eventually turn into a severe life-threatening disease. 1% of severe patients present with massive hemorrhage. Toxic megacolon is noted with haustrations, especially in UC. 10% of patients have obstruction caused by benign stricture formation with one-third of stricture (narrowing of the bowel) occurring in the rectum [8]. Anal fissures, perianal abscesses, or hemorrhoids are occasionally developed in UC patients and extensive perianal lesions occur in CD patients. In addition to the above symptoms, profuse bleeding from ulcers, perforation or bowel rupture, fistula, malnutrition, weight loss, and anemia due to bleeding are occurring commonly. UC has a more increased risk of colon cancer. Blood clot formation, cholangitis, and bowel obstruction are also some complications. IBD is not only linked with colon complications, but it can also have an impact on the skin, and joints, and may result in eyes, liver, kidney, and bone disorders. Arthritis is more common [31]

Homeopathic Management for IBD

1. Mercurius Corrosivus: For Blood and Mucus in Stool. This medicine is suited to those patients who pass bloody stools and pieces of mucous membranes with their stool. The patient has a constant urge to pass stool, but only a small amount of heated, foul-smelling excrement is passed . There is recurrent urge of stool with no satisfaction. There are cutting pains in the rectum accompany the passage of stool.

2. Colchicum Autumnale: For Ulcerative Colitis with Jelly-like Mucus in Stool. Colchicum Autumnale is suited to those patients of Ulcerative Colitis who complain of excessive jelly-like mucus in stool. Patients usually have intense nausea and are unable to endure the stench of cooking food, particularly eggs, fish, and meat. Possibly causes unconsciousness. Vomiting mucous, bile, and food.

3. Arsenicum Album: For Ulcerative Colitis with Stool foul-smelling stool containing dark-colored blood. This medication can provide significant relief whenever alcoholic beverages, juicy fruit, or cold beverages aggravate the disease. Burning discomfort in the abdomen and rectum.. Patients are relieved by warm drinks.
4. Phosphorus: For Ulcerative Colitis with Stool Containing Blood and Greenish Mucus Phosphorus is indicated to those patients in whom there is Stool with blood and green mucus that is quite unpleasant and contains extreme offensiveness. The situation generally worsens in the morning hours.There is excessive craving for cold drinks, ice cream and juicy things.
5. Aloe Socotrina: For Loose Stool. Aloe Socotrina is for those patients who suffered from loose stool worsen quickly after eating or drinking anything. There is sudden urge to pass stool and patient has to rush to the toilet to pass the stool. There are cutting pains in lower abdomen which get worse before and during passing stool and relieved after passing the stool. Faintness usually follows stool. It also helps with diarrhea that worsens after drinking alcohol
6. Podophyllum Peltatum: For Crohn's Disease with Diarrhoea Podophyllum Peltatum is given for Crohn's Disease with diarrhoea and when the stool is watery, greenish and very offensive. The diarrhoea mainly gets worse in the morning but in the evening, the stool is normal. There is prolapse of rectum before or during stool. The patient is thirsty for large quantities of cold water.
7. Cinchona Officinalis: For Crohn's Disease with Diarrhoea Worse at Night Cinchona Officinalis is prescribed to treat Crohn's Disease where the diarrhoea get worse at night. There is excessive flatulence in the whole abdomen along with diarrhoea. Diarrhoea also get worse by taking milk or fruits.
8. Argentum Nitricum: For Crohn's Disease with Watery Green Stool and Flatulence Argentum Nitricumis is also indicated for Crohn's Disease where there is watery green stool accompanied by discharge of loud and noisy flatus. The diarrhoea mainly gets worse by over- eating sweets or after any emotional excitement. There is unusual craving for sweets.
9. Gambogia is a rare and very beneficial remedy for diarrhoea in Inflammatory Bowel Disease. The stool is very profuse, watery and involuntarily passes out. Diarrhoea worse in hot weather.
10. Sulphur is the another remedy for those patients who suffered from IBD with diarrhoea that get worse in the morning. Patient have to rush out of bed early morning to pass out stool. The soles of feet, palms and head are hot.
11. Nux Vomica is indcated for Inflammatory Bowel Disease with tenesmus. The patient suffered from ineffectual but constant urge to pass stool. The stool is scanty with no satisfaction. There is recurrent urge to pass stool at very short intervals. There is pain in the abdomen which is relieved for a little while after passing of stool, but reappears very soon.
12. Mercurius Solubilis is another remedy which is indicated for tenesmus in Inflammatory Bowel Disease. The stool is slimy, blood-stained accompanied with excessive chilliness.

CLINICAL PRESENTATION

Maximum gastrointestinal diseases have the same symptoms including diarrhea, pain, and bleeding. The typical symptoms of IBD are diarrhea, rectal bleeding, abdominal pain, and tenesmus. The symptoms may be severe depending on the extent of the disease. The symptoms are present for weeks or months. If the disease extends to the rectum, bleeding is there through the feces. Sometimes, mucus and pus are also observed in stools. Nocturnal or postprandial diarrhea is observed. Severe cramping pain is also there. These all symptoms may accompany a fever, weight loss, loss of appetite, and anemia due to blood loss. These symptoms can eventually lead to peritonitis, perforation, proctitis, pancolitis, and proctosigmoiditis [11,1

REFERENCE-

1. Szigethy E., McLafferty L., and Goyal A., Inflammatory bowel disease, *Child and Adolescent Psychiatric Clinics of North America*. (2010) 19, no. 2, 301–318, https://doi.org/10.1016/j.chc.2010.01.007, 2-s2.0-77952810795, 20478501.
2. Stokkers P. C. and Hommes D. W., New cytokine therapeutics for inflammatory bowel disease, *Cytokine*. (2004) 28, no. 4-5, 167–173, https://doi.org/10.1016/j.cyto.2004.07.012, 2-s2.0-9644252669, 15588691
3. Mulder, D.J.; Noble, A.J.; Justinich, C.J.; Duffin, J.M. A tale of two diseases: The history of inflammatory bowel disease. *J. Crohn's Colitis* 2014, *8*, 341–348. [Google Scholar] [CrossRef] [Green Version]
4. Alatab, S.; Sepanlou, S.G.; Ikuta, K.; Vahedi, H.; Bisignano, C.; Safiri, S.; Sadeghi, A.; Nixon, M.R.; Abdoli, A.; Abolhassani, H.; et al. The global, regional, and national burden of inflammatory bowel disease in 195 countries and territories, 1990–2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol. Hepatol* 2019, *5*, 17–30. [Google Scholar] [CrossRef] [Green Version]
5. Aniwan, S.; Tremaine, W.J.; Raffals, L.E.; Kane, S.V.; Loftus, E.V., Jr. Antibiotic Use and New-Onset Inflammatory Bowel Disease in Olmsted County, Minnesota: A Population-Based Case-Control Study. *J. Crohn's Colitis* 2018, *12*, 137–144. [Google Scholar] [CrossRef] [PubMed]

6. Ng, S.C.; Tang, W.; Ching, J.Y.; Wong, M.; Chow, C.M.; Hui, A.J.; Wong, T.C.; Leung, V.K.; Tsang, S.W.; Yu, H.H.; et al. Incidence and phenotype of inflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. *Gastroenterology* 2013, *145*, 158–165. [Google Scholar] [CrossRef] [PubMed]
7. Kaplan, G.G.; Ng, S.C. Globalisation of inflammatory bowel disease: Perspectives from the evolution of inflammatory bowel disease in the UK and China. *Lancet Gastroenterol. Hepatol*. 2016, *1*, 307–316. [Google Scholar] [CrossRef]
8. Baldassano RN, Piccoli DA. Inflammatory bowel disease in pediatric and adolescent patients. Gastroenterol Clin North Am. 1999;28(2):445–58. doi: 10.1016/s0889-8553(05)70064-9. [DOI] [PubMed] [Google Scholar]Inflammatory Bowel Disease National Action Plan 2019. Available online: https://www.crohnsandcolitis.com.au/site/wp-content/uploads/National-Action-Plan-FINAL-08-03-2019.pdf (accessed on 12 December 2019).
9. Asakura, K.; Nishiwaki, Y.; Inoue, N.; Hibi, T.; Watanabe, M.; Takebayashi, T. Prevalence of ulcerative colitis and Crohn's disease in Japan. *J. Gastroenterol.* 2009, *44*, 659–665. [Google Scholar] [CrossRef]
10. Monteleone G., Fina D., Caruso R., and Pallone F., New mediators of immunity and inflammation in inflammatory bowel disease, *Current Opinion in Gastroenterology*. (2006) 22, no. 4, 361–364, https://doi.org/10.1097/01.mog.0000231808.10773.8e, 2-s2.0-33746263856.
11. Kaser A., Zeissig S., and Blumberg R. S., Inflammatory bowel disease, *Annual Review of Immunology*. (2010) 28, no. 1, 573–621, https://doi.org/10.1146/annurev-immunol-030409-101225, 2-s2.0-77952316009, 20192811.
12. Cummings JF, Keshav S, Travis SP. Medical management of Crohn's disease. BMJ. 2008;336(7652):1062. doi: 10.1136/bmj.39547.603218.AE. [DOI] [PMC free article] [PubMed] [Google Scholar]
13. Tremaine WJ. Diagnosis and treatment of indeterminate colitis. Gastroenterology & hepatology. 2011;7(12):826. [PMC free article] [PubMed] [Google Scholar]
14. Guindi M, Riddell R. Indeterminate colitis. J Clin Pathol. 2004;57(12):1233–44. doi: 10.1136/jcp.2003.015214. [DOI] [PMC free article] [PubMed] [Google Scholar]
15. Hendrickson BA, Gokhale R, Cho JH. Clinical Aspects and Pathophysiology of Inflammatory Bowel Disease. *Clin Microbiol Rev* 2002;15:79–94. doi:10.1128/cmr.15.1.79-94.2002
16. Pasvol TJ, Horsfall L, Bloom S, *et al*. Incidence and prevalence of inflammatory bowel disease in UK primary care: a population-based cohort study. *BMJ Open* 2020;10:e036584. doi:10.1136/bmjopen-2019-036584
17. Lamb CA, Kennedy NA, Raine T, *et al*. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019;68:s1–106. doi:10.1136/gutjnl-2019-318484
18. Mirkov M. U., Verstockt B., and Cleynen I., Genetics of inflammatory bowel disease: beyond _NOD2_, *The Lancet Gastroenterology & Hepatology*. (2017) 2, no. 3, 224–234, https://doi.org/10.1016/S2468-1253(16)30111-X, 2-s2.0-85012250195.
19. Bamias G., Nyce M. R., De La Rue S. A., and Cominelli F., New concepts in the pathophysiology of inflammatory bowel disease, *Annals of Internal Medicine*. (2005) 143, no. 12, 895–904, https://doi.org/10.7326/0003-4819-143-12-200512200-00007, 2-s2.0-33644873228, 16365470.
20. Ahern P. P., Schiering C., Buonocore S., McGeachy M. J., Cua D. J., Maloy K. J., and Powrie F., Interleukin-23 drives intestinal inflammation through direct activity on T cells, *Immunity*. (2010) 33, no. 2, 279–288, https://doi.org/10.1016/j.immuni.2010.08.010, 2-s2.0-77955890952, 20732640.
21. Richard M. L. and Sokol H., The gut mycobiota: insights into analysis, environmental interactions and role in gastrointestinal diseases, *Nature Reviews Gastroenterology & Hepatology*. (2019) 16, no. 6, 331–345, https://doi.org/10.1038/s41575-019-0121-2, 2-s2.0-85062478688, 30824884.
22. Saleh M. and Elson C. O., Experimental inflammatory bowel disease: insights into the host-microbiota dialog, *Immunity*. (2011) 34, no. 3, 293–302, https://doi.org/10.1016/j.immuni.2011.03.008, 2-s2.0-79952745080, 21435584.
23. Hibi T. and Ogata H., Novel pathophysiological concepts of inflammatory bowel disease, *The Journal of Gastroenterology*. (2006) 41, no. 1, 10–16, https://doi.org/10.1007/s00535-005-1744-3, 2-s2.0-33644500497, 16501852.
24. Dolan K. T. and Chang E. B., Diet, gut microbes, and the pathogenesis of inflammatory bowel diseases, *Molecular Nutrition & Food Research*. (2017) 61, no. 1, https://doi.org/10.1002/mnfr.201600129, 2-s2.0-84994666611, 27346644.
25. Lakatos P. L., Environmental factors affecting inflammatory bowel disease: have we made progress?, *Digestive Diseases*. (2009) 27, no. 3, 215–225, https://doi.org/10.1159/000228553, 2-s2.0-70349921972, 19786744.
26. Ho S. M., Lewis J. D., Mayer E. A., Bernstein C. N., Plevy S. E., Chuang E., Rappaport S. M., Croitoru K., Korzenik J. R., Krischer J., Hyams J. S., Judson R., Kellis M., Jerrett M., Miller G. W., Grant M. L., Shtraizent N., Honig G., Hurtado-Lorenzo A., and Wu G. D., Challenges in IBD research: environmental triggers, *Inflammatory Bowel Disease*. (2019) 25, no. Supplement_2, S13–S23, https://doi.org/10.1093/ibd/izz076, 3109570

27. Barbara A Hendrickson, Ranjana Gokhale , Judy H Cho ; clinical aspects and pathophysiology of inflammatory bowel disease; Clin Microbiol Rev. 2002 Jan;15(1):79–94.doi: 10.1128/CMR.15.1.79-94.2002 https://pmc.ncbi.nlm.nih.gov/articles/PMC118061/
28. https://www.researchgate.net/publication/371081983_A_REVIEW_ON_INFLAMMATORY_BOWEL_DISEASE
29. Gecse KB, Vermeire S: Differential diagnosis of inflammatory bowel disease: imitations and complications. Lancet Gastroenterol Hepatol. 2018, 3:644-53. 10.1016/s2468-1253(18)30159-6
30. Kugathasan S, Saubermann LJ, Smith L, Kou D, Itoh J, Binion DG, et al. Mucosal T-cell immunoregulation varies in early and late inflammatory bowel disease. Gut 2007;56:1696-705.
31. Shanahan F. Inflammatory bowel disease: Immunodiagnostics, immunotherapeutics, and ecotherapeutics. Gastroenterology 2001;120:622-35. doi: 10.1053/gast.2001.22122
32. Boericke W. Boericke's New Mannual of Homeopathic Materia Medica with Repertory, Third Revised and Augmented Edition, New Delhi, B Jain Publishers, 2010.
33. Clarke JH. Dictionary of Practical Materia Medica, Student's Economy Edition, New Delhi, B. Jain Publishers, 1996.
34. Allen TF. The Encyclopaedic of Pure Materia Medica, New Delhi, B Jain Publishers, 1982.