International Research Journal of Pharmacy and Medical Sciences
ISSN (Online): 2581-3277

# An Overview Study of Crohn's Disease

Ram Kale[1], Pranjali Thakare[2], Sachin Pawar[4], Sudhanshu Sakharkar[3], Ajinkya Lodhe[4], Kunal Davhale[5], Avinash Solanki[6]
Dr.Vedprakash Patil Pharmacy College, Chha. Sambhaji, Nagar[1]
Laxmi Narayan College of Pharmacy, Bhopal[2]
Dr. Rajendr Gode College of Pharmacy, Malkapur[3]
Gawande College of Pharmacy Sakherkherda, Chikhli[4]
Gawande College of Pharmacy Sakherkherda, Chikhli[5]
Gawande College of Pharmacy Sakherkherda, Chikhli[6]
Gawande College of Pharmacy Sakherkherda, Chikhli[7]

***Abstract*—***Globally, there is a rising incidence of Crohn's disease. It results from a complicated interaction between environmental factors and genetic predisposition. An exploration of databases and clinical practice guidelines was conducted in order to present the most recent evidence-based method for the diagnosis and treatment of Crohn's disease patients. There isn't a single gold standard study available. Although complete ileocolonoscopy with biopsies continues to be the gold standard for diagnosis, the use of serological markers and other less invasive imaging modalities are being actively studied in the workup. When necessary, management should include food and lifestyle changes, the use of drugs to induce and remit disease, and the possibility of surgical intervention in cases where medical therapy is ineffective*.

***Keywords—*** *Crohn's Disease Diagnosis, Inflammatory Bowel Disease, Colorectal Cancer*.

## I. INTRODUCTION

A combination of genetic predisposition, environmental factors, and an inappropriate immune response to the gut microbiota results in chronic idiopathic inflammatory disorders of the gastrointestinal tract, known as inflammatory bowel diseases (IBD), which include Crohn's disease (CD) and ulcerative colitis (UC) [1]. IBD incidence has significantly increased globally since the diseases were recognized [2]. IBD prevalence increased to more than 0.3% in North America, Oceania, and some European nations during the 20th century [3]. While the frequency of IBD seems to have peaked in North America and Europe at the start of the twenty-first century, it is still rising in newly industrialized Asia, Africa, and South America [3]. The total incidence of IBD in Asia is 1.4 cases per 100,000 people, according to the Asia–Pacific Crohn's and Colitis Epidemiologic Study (ACCESS), a population-based cohort study of newly diagnosed IBD patients from 2011–2013 from 13 countries in the Asia–Pacific area [4]. Despite the fact that the incidence of IBD is still low in Asia, it is rising based on 60% of the world's population (https://www.statista.com/statistics/262881/global-population-by-continent/), and over the next ten years, the absolute number of IBD patients in Asia may surpass that of those in the West [5]. According to data from the Ministry of Health, Labour and Welfare's National Japan IBD Registry, the prevalence of IBD is likewise increasing in Japan [6]. While UC is the most common form of IBD in Asia, there has been a rise in the incidence ratio of CD. There have been reports of UC over time [7, 8]. Compared to UC, the cost of healthcare for CD patients is nearly three times higher [9].

*Natural history*

The entire gastrointestinal tract may be affected by the degenerative and progressive illness known as CD [10]. Ten years following diagnosis, the majority of patients (77–90%) experience a chronic intermittent course [11, 12]. 15% of the 213 Danish CD patients in the area alinception cohort who had been followed up for at least 7 years showed signs of deteriorating disease behavior [13]. Corticosteroids, immunomodulators, and biologics are utilized in 48–60, 32–60, and 6–20% of patients with CD, according to an Ameta-analysis of 198 population-based studies comprising 211,563 CD patients [14]. The cumulative rates of surgery vary across different populations, ranging from 29 to 49%. The use of biologics and immunomodulators has increased recently, and this has been correlated with a steady and notable decline in the number of CD surgeries performed[15, 16].

## II. EPIDEMOLOGY

There are three to twenty cases of CD for per 100,000 people.[17] Though prevalence is increasing in Asia and South America, Crohn's disease is more prevalent in the industrialized world, especially in Western Europe and North America. [18,19] Women may have a slightly higher predominance of CD than men, and Ashkenazi Jews are more likely to have CD than non-Jews. While several genetic and environmental factors have been demonstrated to raise the risk of CD and cause the abnormal gut immune response that is a hallmark of the disease, the precise etiology of the illness is unknown.[18]

## III. THE DISEASE'S LOCATION

The gastrointestinal tract can be affected in any area by Crohn's disease.[20] Thirty percent of patients only have small-bowel involvement, fifty percent have involvement of the colon and terminal ileum, and twenty percent of patients exclusively have colon involvement. Furthermore, fissures and



Ram Kale, Pranjali Thakare, Sachin Pawar, Sudhanshu Sakharkar, Ajinkya Lodhe, Kunal Davhale, and Avinash Solanki, "An Overview Study of Crohn's Disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 13-17, 2024.

fistulas, among other perianal problems, affect 25% of individuals. Less frequently (<10%), patients may exhibit extraintestinal symptoms (EIMs) of disease, upper gastrointestinal disease, or isolated perianal problems.[20]

## IV. Phenotype Of Disease

Three phenotypic subgroups of CD have been identified for research and treatment purposes: inflamatory, stricturing, and fistulizing. The hallmark of inflammatory CD is gastrointestinal tract inflammation without signs of stricturing or fistulizing illness. Patients with this inflammation may eventually develop fibrosis and luminal constriction, at which point they are diagnosed with stricturing disease. Other than surgery, there is no way to repair a flexion deficiency once it has taken place. Sustained transmural inflammation may also lead to the formation of a sinus or fistulous tract, which is a feature of fistulizing CD. Any neighboring organ, including the vagina, bladder, and other parts of the gut, can develop fistulae between it and the colon. An intraabdominal abscess may form if the sinus tract between the colon and a nearby organ is incomplete. Patients may experience difficulties with their perianals in addition to these subtypes. Perianal illness is not thought to be distinct from rather than a characteristic of the underlying luminal disease, but a complication that may arise.[20] The Montreal Classification is used to standardize the classification of diseases (Table 1). This system takes into account the patient's age at diagnosis, the CD's location, and the disease's behavior, or phenotype.

TABLE 1: Classification of Crohn Disease

| | |
|---|---|
| **Age of Diagnosis {years}** | • **< 16**<br>• **17- 40**<br>• **Over 40** |
| **Location** | • Ileal<br>• Colonic<br>• Ileocolonic<br>• Isolated upper gastrointestinal |
| **Behavior** | • Non stricturing\non penetrating<br>• Stricturing<br>• Penetrating |
| **Modifier** | • Perianal disease |

## V. Diagnostic Approach Including Phenotype And Disease Activity Assessment

The diagnosis of Crohn's disease is a clinical diagnosis that combines objective information from laboratory and imaging tests, including histopathology, with the patient's history and physical examination. It should not be supported or refuted by any one factor or outcome. It is important to differentiate between important non-infectious diagnoses (such as irritable bowel syndrome or Behçet's disease [21]) and infectious [22] diagnoses (such as Yersinia or enteroviruses) that mimic Crohn's disease, paying special attention to endemic diseases like tuberculosis. [23, 24]

Once the diagnosis of Crohn's disease is established, patients should be phenotyped according to the Montreal classification (figure 1) [25] and screened for extraintestinal manifestations [26] and associated autoimmune diseases. [27] An assessment of disease activity in com- bination with phenotype and endoscopic features helps to stratify patients and allows physicians to pick the best possible therapeutic regimen, since these factors are important predictors of disease course and complications. Whereas the anatomical location is mostly stable,[28] behaviour of Crohn's disease according to the Montreal classification varies substantially during the course of the disease. In a population based study[29] more than half of 306 patients were diagnosed between the ages of 17 and 40 years (Montreal category A2). Crohn's disease was located in the terminal ileum in 45% (L1), colon in 32% (L2), ileocolon in 19% (L3), and upper gastrointestinal tract in 4% (L4). Most patients (81%) had a non-stricturing non-penetrating phenotype (B1), 5% a stricturing (B2) and 14% a penetrating (B3 or B3p) phenotype. Almost a fifth (19%) of patients progressed to a more aggressive phenotype at 90 days and more than half (51%) at 20 years after initial diagnosis, especially when ileal and perianal involvement (fistulas) were present at the time of diagnosis.

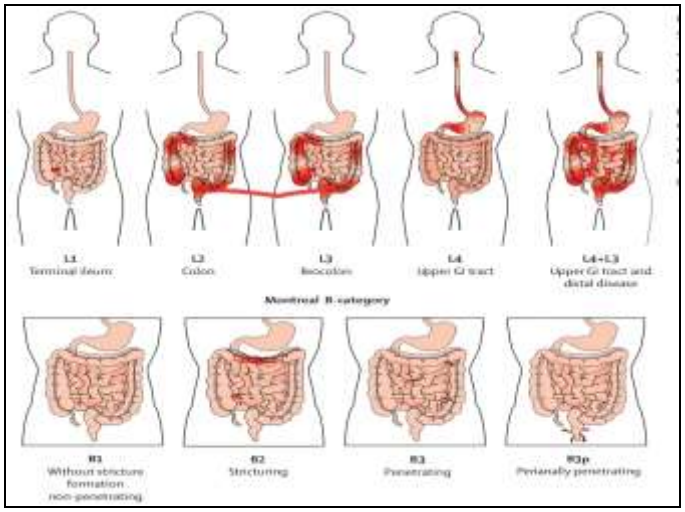


Figure 1: Phenotype Of Crohn's Disease

## VI. Dignostic Insrumentation

### *1. CT and MRI enterography or enteroclysis*

The requirement for using an intestinal tube to administer luminal contrast separates enteroclysis from enterography. In top centers, small intestinal fluoroscopy has been superseded by CTE, which offers the best spatial resolution. It is highly sensitive, capable of detecting inflammation that other techniques may miss, able to identify problems including fistulas, abscesses, and obstructions, and it may even be less expensive. High radiation exposure is its main drawback, albeit it can be decreased with complex mathematical picture processing and acquisition methods. A non-iodine-contrast, non-radiating substitute for CTE is MRE. It can produce videos to evaluate motility and in-depth imaging of the colon wall down to the mucosal level with the right techniques. For recurrent imaging, long-term monitoring, and the management of perianal fistula and abscess problems, it is the recommended option. (figure 2).[30]



Ram Kale, Pranjali Thakare, Sachin Pawar, Sudhanshu Sakharkar, Ajinkya Lodhe, Kunal Davhale, and Avinash Solanki, "An Overview Study of Crohn's Disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 13-17, 2024.

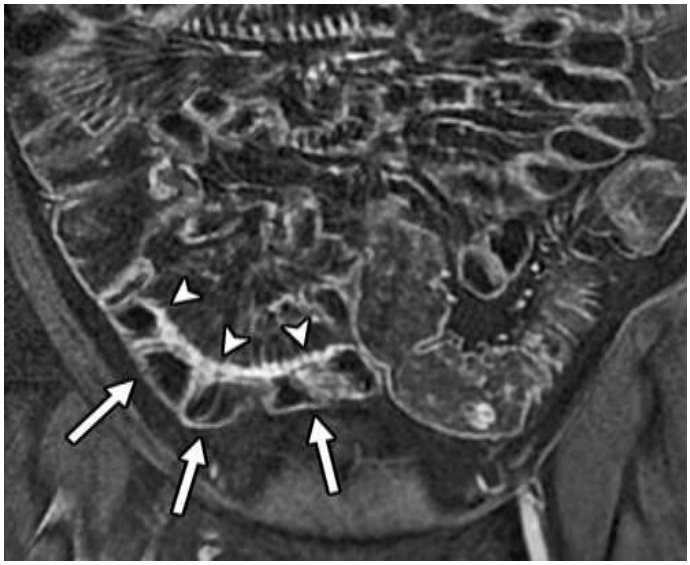

Figure 2: MR enterography of Crohn's disease restricted to the terminal ileum (Montreal category L1) with inflammatory stenosis.

*Ultrasound (sonography)*

Abdominal ultrasonography augmented by native and (gas or shell microbubble) contrast is a widely accessible non-invasive imaging modality whose overall sensitivity and specificity are similar to those of MRI and CT.[30] The initial diagnosis, evaluation of disease activity, identification of fistulas, stenoses, and abscesses, as well as a significant correlation with histopathology, laboratory results, validated disease activity indices, and endoscopy, have all been demonstrated to be aided by prospective research. In the event of perianal problems, transrectal and endoscopic ultrasonography can be helpful.

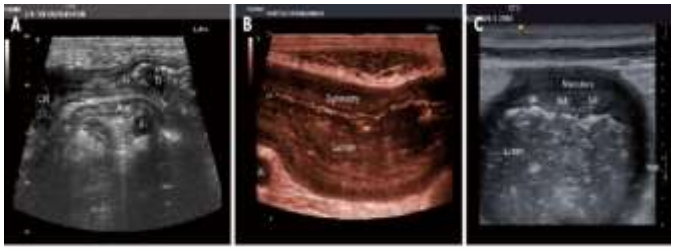

Figure 3: Ultrasound image of an intestinal stenosis in Crohn's disease. (A: The normal appendix is shown as well (APP) crossing the iliacal vessels; B: Crohn's disease of the terminal ileum. Note the symmetric thickening of the bowel wall. AI: Iliacal vessels; Crohn's disease of the sigmoid colon. Note the asymmetric and segmental thickening of the antimesenteric bowel wall mainly focussed on the submucosal layer (SM); C: Muscularispropria and the lumen are also indicated. TMR: Transmural reaction.)

## VII. Personalized Treatment In Crohn's Disease – Current Approaches

The optimal course of treatment should now be decided upon following a thorough evaluation of the patient's disease activity and overall severity. In the past, CD treatment plans were solely based on symptoms.[31-33] Growing research, however, indicates that symptom-controlling treatment plans frequently do not alter the disease's natural progression since underlying inflammation might continue to exist even in the absence of symptoms.[34,35] The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) program, created by the International Organization for the Study of Inflammatory Bowel Diseases (IOIBD), first introduced the "treat to target" strategy in 2015. As a result, the current approaches to CD treatment center around this approach.[36] To enhance long-term results and avoid complications connected to the disease, this was later updated in 2021 in STRIDE-II and developed evidence-based criteria for clinically relevant treatment targets in CD.[37] These goals center on remission of the disease, encompassing clinical, biochemical, and endoscopic remission. Many patients engaged in clinical trials failed to achieve biochemical or endoscopic remission, despite significant advancements in CD treatments. Additionally, even though the medicinal treatment of CD is the main emphasis of this review, surgical intervention is necessary for many complications that arise from the condition, including as strictures and fistulas, which cannot be treated with medication alone. As a result, discussing surgical options with patients is still crucial to their care. Finally, it is unlikely that clinical studies will result in recommendations on how to treat every clinical scenario in CD given the variety of clinical presentations, disease courses, and available therapeutic choices. However, by taking into account treatments that have the best likelihood of producing a clinical response as well as patient-specific considerations including therapy cost, patient adherence, safety, and patient preferences, doctors should strive to individualize treatment as much as feasible.

## VIII. Duration Of Therapy

Most medical professionals think that patients require long-term care because there is currently no cure that addresses the underlying genetic cause of this chronic condition. Experts differ on whether and when drug holidays should be implemented, though.[38,39,40] While prophylaxis, medication pauses, and prompt use of antimicrobials can effectively manage acute problems like infections, some specialists remain apprehensive about the long-term use of thiopurines and biological agents, especially when combined. There is little evidence available to establish the optimal length of therapy because most randomised controlled trials are created to comply with approval agency regulations and rarely offer information longer than a year. Although registry studies have obvious limitations, they offer extra information regarding the long-term safety of certain medical treatments.[41]

## IX. Management Of Disorders Commonly Associated With Crohn's Disease

*1. Anaemia*

A common cause of chronic anemia, which can manifest as a presenting symptom in Crohn's disease, is disrupted iron metabolism brought on by ongoing inflammation rather than intestinal blood loss. Erythropoietin plus intravenous iron substitution is necessary and sometimes helpful.[42]

*2. Arthropathy and Osteoporosis*



Ram Kale, Pranjali Thakare, Sachin Pawar, Sudhanshu Sakharkar, Ajinkya Lodhe, Kunal Davhale, and Avinash Solanki, "An Overview Study of Crohn's Disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 13-17, 2024.

In Crohn's disease, intestinal symptoms may be preceded by peripheral arthropathy (spondylitis and often solitary sacroiliitis) and axial arthropathy (pauciarticular and polyarticular arthritis). In contrast to polyarticular arthritis, which affects more joints—mostly small hand joints—and is unrelated to disease activity, pauciarticular arthritis, also known as oligoarthritis, typically affects fewer than five large joints, such as the ankles, knees, hips, wrists, elbows, and shoulder. It also correlates with disease activity and responds to optimizing medications. Nonsteroidal anti-inflammatory medications (ideally COX II inhibitors) and physical therapy are effective treatments for polyarticular and pauciarticular arthritis. Anti-TNF therapy is also effective for ankylosing spondylitis. Patients with Crohn's disease should take calcium and vitamin D supplements while taking steroids, or they should start receiving a bisphosphonate before starting such treatment, as they are at risk for osteoporosis due to steroid use and decreased vitamin and mineral absorption, as well as inflammation-induced bone loss.[43]

## X. Safety Profile

The majority of TNF inhibitor side effects are mild and don't necessitate stopping the medication. TNF inhibitors are well tolerated. Before starting the medicine, patients should be informed about these possible side effects as major adverse events have been documented. Increased risk of infection (especially reactivation of TB and Hepatitis B), melanoma skin cancer, lymphoma, demyelinating disorders, lupus-like reactions, and skin reactions are the primary side effects linked to TNF inhibitor use.[44-50] Before beginning TNF inhibitors, all patients should undergo screening for hepatitis B and tuberculosis. Patients using immunomodulators and TNF inhibitors have increased risks of infection and lymphoma.[51] All age-appropriate vaccines should be administered to patients after they begin therapy. Regardless of age, they should also get immunizations against shingles and pneumococcus. In other sophisticated medicines, we advise vaccines in a similar manner. They should also get routine dermatological examinations and, for women, gynecological care.

## References

1. Abraham C, Cho JH. Inflammatory bowel disease. N Engl JMed. 2009;361:2066–78.
2. Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidenceand prevalence of the inflammatory bowel diseases with time,based on systematic review. Gastroenterology.2012;142:46.e42–54.e42 [quiz e30].
3. Ng SC, Shi HY, Hamidi N, et al. Worldwide incidence andprevalence of inflammatory bowel disease in the 21st century: asystematic review of population-based studies. Lancet.2018;390:2769–78.
4. Ng SC, Tang W, Ching JY, et al. Incidence and phenotype ofinflammatory bowel disease based on results from the Asia-pacific Crohn's and colitis epidemiology study. Gastroenterol-ogy. 2013;145:158.e2–165.e2.
5. Kaplan GG, Jess T. The changing landscape of inflammatorybowel disease: east meets west. Gastroenterology.2016;150:24–6.
6. Asakura K, Nishiwaki Y, Inoue N, et al. Prevalence of ulcerativecolitis and Crohn's disease in Japan. J Gastroenterol.2009;44:659–65.
7. Ng SC, Leung WK, Shi HY, et al. Epidemiology of inflamma-tory bowel disease from 1981 to 2014: results from a territory-wide population-based registry in Hong Kong. Inflamm BowelDis. 2016;22:1954–60.
8. Yang SK, Yun S, Kim JH, et al. Epidemiology of inflammatorybowel disease in the Songpa-Kangdong district, Seoul, Korea,1986–2005: a KASID study. Inflamm Bowel Dis.2008;14:5429.
9. van der Valk ME, Mangen M-JJ, Leenders M, et al. Healthcarecosts of inflammatory bowel disease have shifted from hospi-talisation and surgery towards anti-TNFa therapy: results fromthe COIN study. Gut. 2014;63:72–9.
10. Peyrin-Biroulet L, Loftus EV Jr, Colombel J-F, et al. The naturalhistory of adult Crohn's disease in population-based cohorts.Am j gastroenterol. 2010;105:289.
11. Wolters FL, Russel MG, Sijbrandij J, et al. Phenotype at diag-nosis predicts recurrence rates in Crohn's disease. Gut.2006;55:1124–30.
12. Solberg IC, Vatn MH, Høie O, et al. Clinical course in Crohn'sdisease: results of a Norwegian population-based ten-year follow-up study. Clin Gastroenterol Hepatol. 2007;5:1430–8.
13. Lo B, Vester-Andersen M, Vind I, et al. Changes in diseasebehaviour and location in patients with Crohn's disease afterseven years of follow-up: a Danish population-based inceptioncohort. J Crohn's Colitis. 2018;12(3):265–272.
14. Shi HY, Levy AN, Trivedi HD, et al. Ethnicity influencesphenotype and outcomes in inflammatory bowel disease: asystematic review and meta-analysis of population-based stud-ies. Clin Gastroenterol Hepatol. 2018;16:190.e11–197e11.
15. Rungoe C, Langholz E, Andersson M, et al. Changes in medical treatment and surgery rates in inflammatory bowel disease: anationwide cohort study 1979–2011. Gut. 2014;63(10):1607–16
16. Annese V, Duricova D, Gower-Rousseau C, et al. Impact of new treatments on hospitalisation, surgery, infection, and mortality in ibd: a focus paper by the epidemiology committee of ECCO. J Crohns Colitis. 2016;10:216–25.
17. Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. Gastroenterology. 2012;142(1):46-54:e42; quiz e30.
18. Ng SC, Bernstein CN, Vatn MH, et al; Epidemiology and Natural History Task Force of the International Organization of Inflammatory Bowel Disease (IOIBD). Geographical variability and environmental risk factors in inflammatory bowel disease. Gut. 2013;62(4):630-649.
19. Loftus EV Jr. Clinical epidemiology of inflammatory bowel disease: incidence, prevalence, and environmental influences. Gastroenterology. 2004;126(6):1504-1517.
20. Cheifetz AS. Management of active Crohn disease. JAMA. 2013;309(20):2150-2158.
21. Lee SK, Kim BK, Kim TI, Kim WH. Differential diagnosis of intestinal Behçet's disease and Crohn's disease by colonoscopic findings. Endoscopy 2009; 41: 9–16.
22. Pawlowski SW, Warren CA, Guerrant R. Diagnosis and treatment of acute or persistent diarrhea. Gastroenterology 2009; 136: 1874–86.
23. Baumgart DC, Bernstein CN, Abbas Z, et al. IBD Around the world: comparing the epidemiology, diagnosis, and treatment: proceedings of the World Digestive Health Day 2010—Inflammatory Bowel Disease Task Force meeting. Inflamm Bowel Dis 2011; 17: 639–44.
24. Maartens G, Wilkinson RJ. Tuberculosis. Lancet 2007; 370: 2030–43.
25. Silverberg MS, Satsangi J, Ahmad T, et al. 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. Can J Gastroenterol 2005; 19 (suppl A): 5–36.
26. Vavricka SR, Brun L, Ballabeni P, et al. Frequency and risk factors for extraintestinal manifestations in the Swiss inflammatory bowel disease cohort. Am J Gastroenterol 2011; 106: 110–19.
27. Bernstein CN, Wajda A, Blanchard JF. The clustering of other chronic inflammatory diseases in inflammatory bowel disease: a population-based study. Gastroenterology 2005; 129: 827–36.
28. Peyrin-Biroulet L, Loftus EV Jr, Colombel JF, Sandborn WJ. The natural history of adult Crohn's disease in population-based cohorts. Am J Gastroenterol 2010; 105: 289–97.
29. Thia KT, Sandborn WJ, Harmsen WS, Zinsmeister AR,Loftus EV Jr. Risk factors associated with progression to intestinal complications of Crohn's disease in a population-based cohort. Gastroenterology 2010; 139: 1147–55.
30. Panés J, Bouzas R, Chaparro M, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal



Ram Kale, Pranjali Thakare, Sachin Pawar, Sudhanshu Sakharkar, Ajinkya Lodhe, Kunal Davhale, and Avinash Solanki, "An Overview Study of Crohn's Disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 13-17, 2024.

complications of Crohn's disease. Aliment Pharmacol Ther 2011;34: 125–45.
31. D'Haens GR, Sartor RB, Silverberg MS, Petersson J, Rutgeerts P. Future directions in inflammatory bowel disease management. J Crohns Colitis. 2014;8(8):726–734. doi:10.1016/j.crohns.2014.02.025
32. Palmela C, Torres J, Cravo M. New Trends in inflammatory bowel disease. GE Port J Gastroenterol. 2015;22(3):103–111. doi:10.1016/j.jpge.2015.03.009
33. Dignass A, Van Assche G, Lindsay JO, et al. The second European evidence-based consensus on the diagnosis and management of Crohn's disease: current management. J Crohns Colitis. 2010;4(1):28–62. doi:10.1016/j.crohns.2009.12.002
34. Bouguen G, Levesque BG, Pola S, Evans E, Sandborn WJ. Endoscopic assessment and treating to target increase the likelihood of mucosal healing in patients with Crohn's disease. Clin Gastroenterol Hepatol. 2014;12(6):978–985. doi:10.1016/j.cgh.2013.11.005
35. Colombel JF, Narula N, Peyrin-Biroulet L. Management strategies to improve outcomes of patients with inflammatory bowel diseases.
Gastroenterology. 2017;152(2):351–361 e5. doi:10.1053/j.gastro.2016.09.046
36. Peyrin-Biroulet L, Sandborn W, Sands BE, et al. Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE): determining therapeutic goals for treat-to-target. Am J Gastroenterol. 2015;110(9):1324–1338. doi:10.1038/ajg.2015.233
37. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: an update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD. Gastroenterology. 2021;160(5):1570–1583. doi:10.1053/j.gastro.2020.12.031
38. Talley NJ, Abreu MT, Achkar JP, et al, and the American College of Gastroenterology IBD Task Force. An evidence-based systematic review on medical therapies for inflammatory bowel disease.Am J Gastroenterol 2011; 106 (suppl 1): S2–25, quiz S26.
39. Dignass A, Van Assche G, Lindsay JO, et al, and the European Crohn's and Colitis Organisation (ECCO). The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: current management. J Crohn's Colitis 2010;4: 28–62.
40. Louis E, Mary JY, Vernier-Massouille G, et al. Maintenance of remission among patients with Crohn's disease on antimetabolite therapy after infliximab therapy is stopped. Gastroenterology 2012; 142: 63–70.
41. Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infections and mortality in association with therapies for Crohn's disease: TREAT registry. Clin Gastroenterol Hepatol 2006; 4: 621–30
42. Colombel JF, Adedokun OJ, Gasink C, et al. Combination therapy with infliximab and azathioprine improves infliximab pharmacokinetic features and efficacy: a post hoc analysis. Clin Gastroenterol Hepatol. 2019;17(8):1525–1532 e1. doi:10.1016/j.cgh.2018.09.033
43. Kopylov U, Al-Taweel T, Yaghoobi M, et al. Adalimumab monotherapy versus combination therapy with immunomodulators in patients with Crohn's disease: a systematic review and meta-analysis. J Crohns Colitis. 2014;8(12):1632–1641. doi:10.1016/j.crohns.2014.07.003
44. Burmester GR, Gordon KB, Rosenbaum JT, et al. Long-Term safety of adalimumab in 29,967 adult patients from global clinical trials across multiple indications: an updated analysis. Adv Ther. 2020;37(1):364–380. doi:10.1007/s12325-019-01145-8
45. Lichtenstein GR, Rutgeerts P, Sandborn WJ, et al. A pooled analysis of infections, malignancy, and mortality in infliximab- and immunomodulator-treated adult patients with inflammatory bowel disease. Am J Gastroenterol. 2012;107(7):1051–1063. doi:10.1038/ajg.2012.89
46. Grijalva CG, Chen L, Delzell E, et al. Initiation of tumor necrosis factor-alpha antagonists and the risk of hospitalization for infection in patients with autoimmune diseases. JAMA. 2011;306(21):2331–2339. doi:10.1001/jama.2011.1692
47. Mariette X, Matucci-Cerinic M, Pavelka K, et al. Malignancies associated with tumour necrosis factor inhibitors in registries and prospective observational studies: a systematic review and meta-analysis. Ann Rheum Dis. 2011;70(11):1895–1904. doi:10.1136/ard.2010.149419
48. Askling J, Fahrbach K, Nordstrom B, Ross S, Schmid CH, Symmons D. Cancer risk with tumor necrosis factor alpha (TNF) inhibitors: meta-analysis of randomized controlled trials of adalimumab, etanercept, and infliximab using patient level data. Pharmacoepidemiol Drug Saf. 2011;20(2):119–130. doi:10.1002/pds.2046
49. De Rycke L, Kruithof E, Van Damme N, et al. Antinuclear antibodies following infliximab treatment in patients with rheumatoid arthritis or spondylarthropathy. Arthritis Rheum. 2003;48(4):1015–1023. doi:10.1002/art.10876
50. Shin IS, Baer AN, Kwon HJ, Papadopoulos EJ, Siegel JN. Guillain-Barre and Miller Fisher syndromes occurring with tumor necrosis factor alpha antagonist therapy. Arthritis Rheum. 2006;54(5):1429–1434. doi:10.1002/art.21814
51. Chupin A, Perduca V, Meyer A, Bellanger C, Carbonnel F, Dong C. Systematic review with meta-analysis: comparative risk of lymphoma with anti-tumour necrosis factor agents and/or thiopurines in patients with inflammatory bowel disease. Aliment Pharmacol Ther. 2020;52 (8):1289–1297. doi:10.1111/apt.16050

*Author**
*Miss. Pranjali D Thakare*
*Email: thakarepd6@gmail.com*



Ram Kale, Pranjali Thakare, Sachin Pawar, Sudhanshu Sakharkar, Ajinkya Lodhe, Kunal Davhale, and Avinash Solanki, "An Overview Study of Crohn's Disease," *International Research Journal of Pharmacy and Medical Sciences (IRJPMS)*, Volume 7, Issue 2, pp. 13-17, 2024.