



## Prospective Observational Study, Prevalence of Various Lesions of Terminalileum in Patients Undergoing Colonoscopy

Chidurala Rahul<sup>\*1</sup>, Rashmitha Somagani<sup>2</sup>, Rithika Kunapareddy<sup>3</sup>, Sriharsha Koduru<sup>4</sup>

### Abstract

**Background:** The terminal ileum represents a clinically significant site frequently affected by diverse gastrointestinal pathologies. While inflammatory bowel diseases like Crohn's disease commonly involve this region, a broad spectrum of other conditions may present similarly, complicating diagnostic differentiation.

**Objective:** This prospective observational study aimed to characterize the prevalence, etiology, and clinicopathological correlations of terminal ileal lesions identified during colonoscopy.

**Methods:** Over a 20-month period at Sri Ramachandra Institute of Higher Education and Research, 101 patients with endoscopic evidence of terminal ileal ulcers underwent comprehensive evaluation. Analysis included clinical symptomatology, laboratory investigations, endoscopic characteristics, histopathological examination, and supplementary ultrasound imaging. Constipation (24%), abdominal pain (21%), diarrhea (19%). Ulcers with erythema/edema (60%), crypt abscesses (14%); infectious/non-specific inflammation > Crohn's disease prevalence.

**Conclusion:** Terminal ileal pathology frequently stems from non-IBD etiologies, particularly infections and idiopathic inflammation. Accurate diagnosis necessitates integrated assessment of clinical, endoscopic, and histopathological features to prevent misdiagnosis of Crohn's disease and guide targeted therapeutic interventions.

**Keywords:** Crohn's disease, inflammatory bowel disease, histopathology, ileal ulcer, colonoscopy, abnormalities in terminal ileum, infectious colitis, non-specific mastitis, abdominal pain, etc.

### Introduction

In-depth research on the relationship between terminal ileitis and Crohn's disease has revealed inadequate evidence to support the claim that terminal ileitis directly contributes to the onset of Crohn's disease. The phrase "terminal ileocecum" describes the anatomical region comprising the cecum and the distal part of the ileum, including the area where they are joined by the ileocecal (I/C) valve. (1) The region of the terminal ileocecum is prone to various illnesses due to its unique anatomy and physiology, including amoebiasis, enteric fever, TB, ulcerative colitis, Crohn's disease (CD), non-specific ulcers, malignancies, and amoebic colitis. (2-6) Ileitis, referring to the inflammation of the ileum, is typically attributed to Crohn's disease (CD). However, a diverse range of diseases

### Affiliation:

<sup>1</sup>Bachelor of Medicine, Bachelor of Surgery, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai.

<sup>2</sup>Kamineni Academy of Medical Sciences and Research Centre, LB nagar, Hyderabad, Telangana, India.

<sup>3</sup>MBBS, Kamineni institute of medical sciences, marketpally.

<sup>4</sup>MBBS, College: Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry, India.

### \*Corresponding author:

Chidurala Rahul, Bachelor of Medicine, Bachelor of Surgery, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai.

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can be associated with ileitis. The terminal ileum (TI) is the most frequently affected region, although Crohn's disease (CD) can affect any section of the GI tract. Non-steroidal anti-inflammatory drugs (NSAIDs) use, as well as pathological diseases such as lymphoid hyperplasia, lymphoma, radiation enteritis, infections, and ulcerative colitis (UC), can cause inflammation, erosions, and ulcers in the TI. These conditions can manifest histologically and endoscopically in a manner that mimics CD, leading to potential diagnostic challenges. Colonoscopy, including intubation and TI biopsy, is now a common technique for diagnosing and treating patients with inflammatory bowel disease (IBD). Incorrectly diagnosing CD in these patients can be detrimental due to inadequate response to therapy, and in some cases, unnecessary surgical interventions may be performed. Approximately 60%-70% of cases of Crohn's disease (CD) primarily affect either the ileum alone or the ileo-colonic region. (7) However, further evaluation is required to determine whether 60%-70% of ulcers in the ileocecal (I/C) region are indeed attributed to CD. Inflammatory Bowel Disease (IBD) is characterized by recurring gastrointestinal inflammation due to abnormal immune responses to gut microflora. There are two types: Ulcerative Colitis (UC) involves widespread colon inflammation, and Crohn's Disease (CD) causes transmural ulceration in various GI segments. They are categorized by extent and location, with CD further classified by inflammatory, stricturing, or penetrating phenotype. (8,9,10) In addition to affecting the gastrointestinal (GI) tract, both Crohn's disease and ulcerative colitis exhibit various extraintestinal manifestations. Although these disorders can typically be differentiated in most patients, there is a subset of approximately 10% where the features are so similar that initially distinguishing between the two conditions is challenging. Approximately 35% of Crohn's disease cases exclusively affect the ileum, resulting in a condition called ileitis. Around 45% of cases involve both the ileum and the colon, known as ileocolitis, with a tendency to primarily affect the right side of the colon. Roughly 20% of cases specifically involve the colon, referred to as granulomatous colitis, and unlike ulcerative colitis, this form of Crohn's disease usually spares the rectum. There is a lack of sufficient data regarding the causes, clinical characteristics, and correlation between histopathology and patients with ileocecal ulcers. Assessing the underlying factors responsible for these ulcers poses a significant challenge for clinicians, endoscopists, and histopathologists alike. (11-15) The terminal ileum is the last part of the small intestine and is commonly involved in various gastrointestinal conditions. By systematically examining a large cohort of patients undergoing colonoscopy, this study seeks to gather valuable data on the frequency and types of lesions observed in the terminal ileum. The results of this study will provide valuable insights into the epidemiology and clinical significance of terminal ileal lesions, potentially

leading to improved diagnostic and therapeutic strategies for patients with these conditions.

## Materials and Methods

This observational study was carried out at the esteemed Shri Ram Chandra Institute of Higher Education and Research in Chennai. The study spanned a duration of 20 months, starting from July 2021 and concluding in April 2023. The researchers utilized a fibro-optic colonoscope for the colonoscopy procedure. To prepare the colon, they employed the Coloprep Bowel Preparation Kit, which comprises 177ml of a delectable orange-flavored solution. This specialized kit is intended for adult patients undergoing colonoscopy, as it enhances water retention in the intestine, promotes bowel movements, and effectively clears the digestive tract, thereby facilitating the smooth execution of the colonoscopy procedure. The patient had conscious sedation during the colonoscopy process, which included the intravenous infusion of pentazocine (25–50 mg) and diazepam (5–10 mg). Throughout the colonoscopy, a careful inspection was carried out to precisely pinpoint any ulcers present in the cecum, ileocecal valve, or terminal ileum. If any ulcers were found, several biopsies were taken from the afflicted area as well as the margins around it for further microscopic examination (histopathological investigation). Our study included a sample size of 101 individuals who visited the clinics with complaints of terminal ileal ulcers. The study included patients who met the inclusion criteria of having terminal ileal ulcers. Patients with pre-existing diagnoses of tuberculosis, malignancy, and other specified conditions were excluded from the study. The data collection process was prospective, meaning that information was gathered as the study progressed. Descriptive statistics were employed to analyze the collected data. While categorical variables were shown as frequencies and percentages, continuous variables were summarised using the mean or median (range). For data analysis, the statistical software package SPSS 17 for Windows was utilized.

## Aim and Objective

To examine the patients who presented with terminal ileal ulcers on colonoscopy in terms of their clinical, endoscopic, and histological characteristics.

## Results

This study analyzed the characteristics of participants in a scientific manner. The mean age was 41.40 years (SD = 16.02), with a gender distribution of 35 females (34%) and 66 males (66%) out of 101 cases. Various laboratory findings were examined: median hemoglobin of 12.5 g/dL (range: 9.2-13.7), median WBC count of 7050 cells/ $\mu$ L (range: 5987.5-8775), median platelet count of 2.63 lakh/ $\mu$ L (range: 2.025-3.2925), median MCV of 85.1 fL (range: 78.07-90),

median MCH of 28.5 pg (range: 25-30.5), median MCHC of 32.6 g/dL (range: 31.15-33.82), median ESR of 22 mm/h (range: 8-34.5), median total protein of 7.3 g/dL (range: 6.75-7.6), median BUN of 9 mg/dL (range: 7-10.25), and median creatine of 0.8 mg/dL (range: 0.6-0.9).

**Table 1:** demographic presentation of data

<b>Age (Years) Mean <math>\pm</math> S.D.</b>	<b>41.40 <math>\pm</math> 16.02</b>
<b>Sex</b>	<b>Cases</b>
<b>Female</b>	34 (-34%)
<b>Male</b>	66 (-66%)
<b>Total</b>	100 (-100%)
<b>Laboratory finding, Median (Range)</b>	
<b>Hemoglobin (g/dL)</b>	12.5 (9.2-13.7)
<b>wbc count</b>	7050 (5987.5- 8775)
<b>platelet count</b>	2.63 (2.025-3.2925)
<b>MCV</b>	85.1 (78.07- 90)
<b>MCH</b>	28.5 (25-30.5)
<b>mchc</b>	32.6 (31.15- 33.82)
<b>ESR</b>	22 (8-34.5)
<b>Total protein</b>	7.3 (6.75-7.6)
<b>BUN</b>	9 (7-10.25)
<b>Creatine</b>	0.8 (0.6-0.9)

**Table 2:** Present symptoms in patients

<b>Presentation symptoms</b>	<b>Cases</b>	<b>Percentage</b>
Abdominal pain	21	21%
Constipation	24	24%
Altered bowel habits diarrhoea	19	19%
Bleeding per rectum	15	15%
Anaemia	7	7%
Dyspepsia	4	4%
Weight loss	4	4%
B12 deficiency	1	1%
Caecal growth. screening	1	1%
Chronic Dyspepsia	1	1%
Diarrhoea	1	1%
increased frequency of stool	1	1%
UGI Bleeding	1	1%
<b>Total</b>	<b>100</b>	<b>100%</b>

The study examined the prevalence of various symptoms in the research population. Abdominal pain was reported by 21 cases, accounting for 21% of the total participants. Altered bowel habits, specifically diarrhea, were observed in 19 individuals, representing 19% of the cases. Anemia, characterized by a decrease in red blood cells or hemoglobin, was diagnosed in six cases (6%). One case exhibited a deficiency of vitamin B12. Rectal bleeding was reported by 15 cases (15%). One participant (1%) underwent caecal growth screening, focusing on abnormal growths in the first part of the large intestine. Chronic dyspepsia, involving recurring indigestion or upper abdominal discomfort, was diagnosed in a single case (1%). Constipation, associated with difficulty in passing stools or infrequent bowel movements, was observed in 24 cases (24%). One case (1%) specifically presented with diarrhea, apart from altered bowel habits. Dyspepsia, characterized by recurrent pain or discomfort in the upper abdomen, was reported in four cases (4%). Increased frequency of stool passage was noted in one case. Additionally, another case experienced bleeding in the upper gastrointestinal tract, including the esophagus, stomach, and initial part of the small intestine. Lastly, four cases (4%) presented with unexplained weight loss.

The findings related to the terminal ileum in the study reveal various pathological characteristics observed in a total of 100 cases. Among these cases, the most prevalent presentation was ulcers accompanied by surrounding erythema and edema, accounting for 60% of the total cases. Following closely were aphthous ulcers with surrounding erythema and edema, which constituted 19% of the cases. Other notable findings included erosion with a clean-based ulcer (11%), ulceration with nodularity, erythema, and edema

**Table 3:** Terminal ileum findings in patients

<b>Terminal ileum findings</b>	<b>No. of cases</b>	<b>Percentage</b>
Ulcers with surrounding erythema and oedema noted	60	60%
Aphthous ulcers with surrounding erythema and oedema	19	19%
Erosion with a clean based ulcer	11	11%
Ulceration with nodularity erythema and oedema	4	4%
Scattered areas of aphthoid ulcer noted	2	2%
Multiple nodules, mucosal erythema, aphthoid ulcers, few sessile ulcers	2	2%
Superficial ulcers with clean base and overlying slough	1	1%
Linear serpentagous ulcer with overlying slough with surrounding erythema	1	1%
<b>Total</b>	<b>100</b>	<b>100.00%</b>

(4%), scattered areas of aphthoid ulcers (2%), and multiple nodules with mucosal erythema, aphthoid ulcers, and a few sessile ulcers (2%). Less frequently observed presentations included superficial ulcers with a clean base and overlying slough (1%) and a single case of linear serpentagous ulcer with overlying slough and surrounding erythema (1%).

**Table 4:** Histopathology finding

Histopathology finding	Cases	Percentage
Granulation Tissue		
Ulceration	17	12%
Tubular Adenoma	1	1%
Polypoid mucosa with inflammation showing lymphocytes and plasma cells		
Lamina Propria	16	16%
H Pylori	6	6%
Gastritis	6	6%
Ileum	1	1%
Cryptitis and Ileitis		
Abcess	14	14%
Lymphocytic infiltration with cryptitis and crypt abcess		
Granuloma	9	9%
necrosis	8	8%
moderate dense eosinophils	7	7%
lymphoid follicle	3	3%
Small Intestinal mucosa		
Adjacent fibrous exudate	7	7%
Focal ulceration	5	5%
Total	100	100.00%

The study conducted on gastrointestinal histopathological findings revealed various significant observations. In cases of cryptitis and ileitis, localized abscesses were found in 14% of samples, along with abnormal lymphocyte accumulation in the intestinal crypts (lymphocytic infiltration) and granulomas in 9% each. Tissue cell death (necrosis) was identified in 8%, and moderate dense eosinophils were observed in 7% of cases. Abnormal accumulations of lymphoid tissue (lymphoid follicles) were present in 3%. Additionally, 16% of samples exhibited polypoid mucosa with inflammation in the Lamina Propria. H. pylori infection and gastritis were observed in 6% of cases each, while ileum abnormalities were detected in 1%. The small intestinal mucosa findings included adjacent fibrous exudate (7%), focal ulceration (5%), granulation tissue (12%), ulceration (12%), and tubular adenoma (1%). These findings offer valuable insights into the pathological aspects of gastrointestinal disorders and conditions.

**Table 5:** Ultrasound findings.

Ultrasound findings	Cases	Percentage
Kidney cyst	24	24%
Pancreatic cysts	20	20%
Gallstones	18	18%
Liver cysts	16	16%
Adrenal masses	9	9%
Liver hemangiomas	5	5%
Liver metastases	3	3%
Splenic hemangiomas	3	3%
Splenic cysts	2	2%

The study involved the examination of 100 cases, wherein the ultrasound findings were meticulously categorized. Notable observations included kidney cysts, found in 24% of cases, signifying the presence of fluid-filled sacs or pockets within the kidneys. Pancreatic cysts were observed in 20% of cases, indicating the existence of fluid-filled sacs or lesions in the pancreas. Gallstones were present in 18% of cases, representing the formation of solid particles or stones in the gallbladder. Liver cysts were identified in 16% of cases, indicating the existence of fluid-filled sacs or cavities in the liver. Adrenal masses were found in 9% of cases, indicating abnormal growths or tumors in the adrenal glands. Furthermore, liver hemangiomas were observed in 5% of cases, suggesting the presence of benign tumors composed of blood vessels in the liver. Liver metastases, indicating the spread of cancerous cells to the liver from other parts of the body, were present in 3% of cases, as were splenic hemangiomas and splenic cysts, which indicated the presence of benign tumors and fluid-filled sacs in the spleen, respectively

## Discussion

This study is noteworthy as it represents one of the most extensive investigations to date that comprehensively characterizes the causes, colonoscopic findings, and histopathological features of ileocecal ulcers. The study's significance is evident for various reasons. Firstly, it sheds light on the fact that Crohn's disease primarily affects the ileum or both the ileum and colon in approximately 60% to 70% of patients.<sup>16</sup> The converse, i.e., that 80% of ileo-cecal ulcers are not Crohn's, is not accurate. The study examined the prevalence of various symptoms in the research population. The most common symptoms reported were abdominal pain (21%) and altered bowel habits, specifically diarrhea (19%). Anemia (7 %) and rectal bleeding (15%) were also observed. Other less frequent symptoms included vitamin B12 deficiency (1%), chronic dyspepsia (4%), constipation (24%), dyspepsia (4%), increased frequency of stool passage (1%), upper gastrointestinal bleeding (1%), and unexplained weight loss (4%). In a study by Christy Costanian et al.<sup>17</sup>,



similar findings were found where a quarter of IBS cases reported knowing specific foods that caused diarrhoea or abdominal pain. Changes in bowel habits and abdominal pain were frequent symptoms. The absence of a fever and the preservation of the ileo-cecal valve helped to identify Crohn's disease. In cases of massive gastrointestinal (GI) bleeding, the potential for mortality is significant. However, timely treatment and intervention through endoscopic procedures can successfully achieve hemostasis. In terms of the symptoms patients present with and the location of ulcers, the results of this study are consistent with earlier studies by Boydstun et al.<sup>6</sup> and Thomas et al.<sup>18</sup>. This study focused on the terminal ileum findings in the participants, revealing the following outcomes: 60% of cases showed ulcers with surrounding erythema and edema, 11% had erosion with clean-based ulcers, 19% displayed aphthous ulcers with erythema and edema, 4% presented ulcers with nodularity, erythema, and edema, and there were scattered instances of other ulcer types. Terminal ileum findings were not available in 2% of cases. These findings contribute to a better understanding of pathological features in this population. When considering the causes of ulcerations in the ileocecal region, it was found that infections were the most common factor. This finding aligns with a similar study conducted in China<sup>19</sup>. These studies highlight that infections, particularly in tropical regions, are the primary cause of ulcers in the ileocecal region. A tubercular origin is strongly suggested by the presence of numerous ulcers, cicatrization of the cecum, and a distorted ileocecal (I/C) valve. It should be noted that biopsy results may not always provide a definitive diagnosis. Abdominal pain, weight loss, fever, and the development of an abdominal lump are common clinical manifestations of this illness. To initiate treatment, a combination of clinical features and colonoscopy findings should be taken into consideration.

The study's histopathological findings revealed the presence of lymphocytic infiltration, cryptitis, and crypt abscess in multiple cases. Granulomas and necrosis were observed in a subset of cases. Other findings included eosinophil infiltration, lymphoid follicles, polypoid mucosa with inflammation, and fibrous exudate. *Helicobacter pylori* (*H. pylori*) infection, lamina propria involvement, and *H. pylori*-associated gastritis were identified in some cases. Additional findings included ulceration, abscess formation, Crohn's disease, tuberculosis, and tubular adenoma. A portion of the cases did not show any distinctive histopathological findings. These findings contribute to a better understanding of the diverse histopathological features observed in the study's population. The study's histopathological findings revealed the presence of lymphocytic infiltration, cryptitis, and crypt abscess in multiple cases. Granulomas and necrosis were observed in a subset of cases. Other findings included eosinophil infiltration, lymphoid follicles, polypoid mucosa

with inflammation, and fibrous exudate. *Helicobacter pylori* (*H. pylori*) infection, lamina propria involvement, and *H. pylori*-associated gastritis were identified in some cases. Additional findings included ulceration, abscess formation, Crohn's disease, tuberculosis, and tubular adenoma. A portion of the cases did not show any distinctive histopathological findings. These findings contribute to a better understanding of the diverse histopathological features observed in the study's population. In a study by Vijayalakshmi Padmanabhan M.D. et al., it was discovered that ileal intraepithelial lymphocytes significantly increased in lymphocytic and collagenous colitis patients compared to controls. Through CD3 immunohistochemical labelling, these lymphocytes were recognised as T cells. In 78% of patients with lymphocytic colitis and 50% of patients with collagenous colitis, intraepithelial lymphocytosis was found. Similar to the phenomenon known as "backwash ileitis" described in ulcerative colitis, this observation raises the possibility that the disease may have spread from the colon into the terminal ileum. This finding is consistent with Lewis et al.<sup>20</sup>.

The data in our study indicates the prevalence of various ultrasound findings among the patients. Liver cysts were the most frequently encountered condition (16%), followed by kidney cysts (24%) and pancreatic cysts (20%). Gallstones were present in 18% of cases, while liver hemangiomas (5%), adrenal masses (9%), and splenic hemangiomas (3%) were less common. It's important to consider additional factors for accurate diagnosis and treatment decisions on an individual patient basis. The most often seen ileocecal ulcers are non-specific ileocecal ulcers. When infections are combined, they become the predominant cause (>40%) of ulcerations in this area. Cecal involvement and fever are significant indicators of an infectious origin. Conversely, Crohn's disease accounts for only 13% of cases with ileocecal ulcers. Therefore, not all symptomatic patients with ileocecal ulcers detected during colonoscopy have Crohn's disease. Most people with ileocecal ulcers can be handled conservatively without undergoing surgery thanks to the increased use of colonoscopy for detection and management. In conclusion, our study emphasizes that more than half of patients with symptomatic ITIUs require thorough evaluation due to specific etiologies. Colonoscopic findings alone are insufficient for accurate diagnosis; histological and laboratory examinations are necessary. Elevated CRP and certain histological changes suggest Crohn's disease, while colonoscopy findings and granulomas on histology indicate intestinal tuberculosis. Early diagnosis enables timely treatment and prevents complications. Patients with nonspecific histological findings need close monitoring, and repeat endoscopy may be necessary for confirmation.

## Conclusion

In conclusion, this prospective observational study

elucidating the prevalence of diverse lesions in the terminal ileum during colonoscopy offers invaluable insights. The findings underscore the crucial fact that not all terminal ileum pathologies are associated with inflammatory bowel disease (IBD). The study provides a comprehensive understanding of the pathological characteristics in this specific patient cohort, enriching our knowledge in the field.

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