



Original Research Article

THE HIMALAYAN SHIFT: TRACING THE INFLAMMATORY BOWEL DISEASE IN THE KASHMIR VALLEY FROM A PATHOLOGIST'S LENS

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ABSTRACT

Background: The incidence of Inflammatory Bowel Disease (IBD) is rising globally, particularly in developing Asian countries such as India, where the epidemiological landscape is undergoing a significant transformation. This study aims to update the clinicopathological profile of IBD in the Kashmir Valley using recent 2025 data, with a focus on how genetic susceptibility and urbanization are contributing to these changes. **Objective:** To analyze the clinicopathological characteristics of IBD patients in the Kashmir Valley and examine the gross and microscopic findings of gastrointestinal biopsies over a one-year period in 2025.

Materials and Methods: A hospital-based prospective study was conducted over one year in 2025, evaluating 299 gastrointestinal biopsies. Biopsy samples were examined using standardized histopathological criteria, including the Nancy Histological Index (NHI) for grading inflammatory activity. Findings were also compared with global datasets to understand regional trends.

Results: Of the 299 biopsies, 174 (58.2%) met the diagnostic criteria for IBD. The male-to-female ratio was 1.17:1, with males comprising 54.0% (n=94) and females 46.0% (n=80). The mean age of patients was 39.14 years. The ileum was the most frequently biopsied anatomical site (40.2%). Crohn's Disease (CD) was the most common subtype, accounting for 42.5% (74 cases), followed by Ulcerative Colitis (UC) at 35.1% (61 cases), and Indeterminate Colitis (IBD-U) at 22.4% (39 cases).

Conclusion: This study highlights the evolving epidemiology of IBD in the Kashmir Valley, with a notable increase in the proportion of Crohn's Disease. These findings underscore the need for high clinical suspicion, routine ileoscopy, and multidisciplinary care to manage IBD effectively in this region.

Keywords: Inflammatory Bowel Disease, Crohn's Disease, Ulcerative Colitis, Indeterminate Colitis, Kashmir Valley, Epidemiology, Histopathology, Nancy Histological Index, Gastrointestinal Biopsies, Urbanization, Genetic Susceptibility.

INTRODUCTION

Inflammatory Bowel Disease (IBD) encompasses a group of chronic, relapsing, and remitting conditions that primarily affect the gastrointestinal tract, with

the most common forms being Ulcerative Colitis (UC) and Crohn's Disease (CD). The global incidence of IBD is rising steadily, and it has become a major public health concern worldwide. Traditionally, CD and UC were thought to primarily

affect Caucasian populations in North America, Western Europe, and Oceania,^[1] but the disease is now rapidly increasing in newly industrialized regions, particularly in Asia, marking a "Pivot to Asia" in its epidemiology.^[2] In India, the burden of IBD is rising faster than the global average, reflecting the adoption of Western lifestyles characterized by dietary shifts, urbanization, and altered environmental exposures, which are acting on a genetically susceptible population.^[3,4] According to the Global IBD Visualization of Epidemiology Studies in the 21st Century (GIVES-21) consortium, regions like Kashmir are within "Stage 2: Acceleration in Incidence," characterized by a sharp increase in new diagnoses driven by urbanization and changing diets.^[5] The rising incidence in South Asia has been accompanied by the emergence of a distinct "South Asian Phenotype" of IBD, with a male predominance and younger age of onset compared to White Europeans.^[6] A previous study from our center, conducted up to 2014, highlighted a predominant prevalence of UC (86.6%) compared to CD (12.38%) in the Kashmir Valley.^[7] This study aims to provide clinicopathological profile of IBD in the Kashmir Valley, analyzing the evolving trends and pathological characteristics of the disease to better understand the regional shift in disease patterns.

MATERIALS AND METHODS

This was a 1-year hospital-based prospective study conducted in 2025 at a tertiary care center in Kashmir. The cohort consisted of 299 consecutive patients who underwent gastrointestinal mucosal biopsies for the evaluation of chronic gastrointestinal symptoms. The study was approved by the institutional ethics committee, and informed consent was obtained from all patients prior to inclusion.

Inclusion and Exclusion Criteria

Patients with chronic gastrointestinal symptoms, including diarrhea, abdominal pain, weight loss, and rectal bleeding, were included. All patients underwent endoscopic evaluation, and gastrointestinal biopsies were obtained from those suspected to have IBD or other gastrointestinal conditions.

Exclusion criteria included

- Patients with a history of colorectal malignancy
- Known history of gastrointestinal tuberculosis, ischemic colitis, or other infectious diseases
- Patients who had received immunosuppressive therapy or antibiotics within the past 6 weeks prior to biopsy.

Histopathological Evaluation and Classification

All biopsy specimens were processed according to standardized protocols. Tissues were fixed in 10% neutral buffered formalin, processed for paraffin embedding, and sectioned at 4-5 microns. The sections were stained with Hematoxylin and Eosin (H&E) for routine examination.

The Nancy Histological Index (NHI) was used to grade the inflammatory activity of the biopsies.^[8] Given the high prevalence of infectious mimics in India, particularly gastrointestinal tuberculosis and amoebic colitis, a rigorous diagnostic algorithm was implemented. Special stains, including Ziehl-Neelsen for acid-fast bacilli and Periodic Acid-Schiff for fungi/mucin, were employed where clinically indicated.^[9]

Diagnostic Classification

Based on the histopathological features observed, the cases were classified into the following categories:

- **Ulcerative Colitis (UC):** Identified by continuous mucosal inflammation extending proximally from the rectum, crypt architectural distortion (branching, atrophy), basal plasmacytosis, and mucin depletion.
- **Crohn's Disease (CD):** Characterized by focal or patchy chronic inflammation, transmural involvement (where assessable), preservation of goblet cells, and the presence of non-caseating epithelioid granulomas.
- **IBD-Unclassified (IBD-U):** This category applied to cases exhibiting definitive features of chronic idiopathic inflammatory bowel disease (e.g., basal plasmacytosis, chronic architectural damage) but lacking sufficient specific features to differentiate between UC and CD. Given the need to rule out tuberculosis before diagnosing CD, this category was expanded in our study.
- **Infective Colitis (IC):** Diagnosed by features suggestive of acute self-limiting infection, such as neutrophilic infiltrate with preserved crypt architecture, or direct identification of pathogens using special stains.
- **Non-Specific Colitis (NSC):** Characterized by mild inflammation lacking the architectural chronicity features of IBD or the specificity of acute infection.

Statistical Analysis

The data were analyzed using SPSS software version 25. Descriptive statistics were used to summarize demographic and clinical characteristics. For comparisons between groups, the Chi-square test or Fisher's exact test was used, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

During the 1-year study period in 2025, a total of 299 gastrointestinal biopsies were evaluated. Of these, 174 patients met the diagnostic criteria for Inflammatory Bowel Disease (IBD), accounting for 58.2% of the total biopsies. The cohort exhibited a male predominance, with 94 males (54.0%) and 80 females (46.0%), resulting in a Male:Female ratio of 1.17:1 (Table 1). The mean age of the cohort was 39.14 ± 16.12 years, with a broad age range from 11 to 85 years. IBD patients in this cohort were significantly younger compared to those without

IBD, highlighting that the disease burden primarily affects the economically productive demographic. The detailed demographic profile of IBD patients is presented in Table 1.

The clinical presentation varied significantly between the two major IBD subtypes, as shown in Table 2. In Crohn's Disease (CD) patients (N=74), the most common symptoms were fatigue/pallor (91.9%, n=68), abdominal pain (86.5%, n=64), and tenesmus (67.6%, n=50). Aphthous ulcers were observed in 60.8% (n=45) of CD cases. Conversely, Ulcerative Colitis (UC) patients (N=61) predominantly presented with classic colitic symptoms, including abdominal pain (95.1%, n=58), tenesmus (88.5%, n=54), blood in stools (85.2%, n=52), and diarrhea (82.0%, n=50). Weight loss was more prevalent in UC patients (78.7%, n=48) compared to CD patients (10.8%, n=8). Recurrence of similar complaints was observed in 28.4% of CD patients and 19.7% of UC patients. The distribution of IBD subtypes showed a significant shift, with Crohn's Disease (CD) being the most common diagnosis, accounting for 42.5% (74 cases), followed by Ulcerative Colitis (UC) at 35.1% (61 cases), and Indeterminate Colitis (IBD-U) at 22.4% (39 cases) (Table 3). Histopathological evaluation of the biopsies showed chronic inflammation in 100% of both CD and UC cases. Lymphoid follicle formation was a distinguishing feature in CD, present in 94.6% (n=70) of biopsies, followed by fibrosis in 51.4% (n=38) and non-

caseating granulomas in 36.5% (n=27) (Table 4). In UC cases, the most prominent findings included crypt distortion (91.8%, n=56), crypt abscesses (90.2%, n=55), loss of plasma cell gradient (90.2%, n=55), and mucin depletion (82.0%, n=50). Dysplasia was observed in both groups, with a higher prevalence in UC (49.2%, n=30) compared to CD (31.1%, n=23). In UC cases (n=61), disease activity was graded using the Nancy Histological Index. The majority of patients (82.0%, n=50) were classified as having Grade 4 (Severe Chronic Active) disease, while a small proportion had lesser grades: Grade 3 (Moderate Chronic Active) in 8.2% (n=5), Grade 1 (Chronic Inactive) in 6.6% (n=4), and 1.6% (n=1) each for Grade 2 (Mild Chronic Active) and Grade 0 (No Activity). The ileum was the most frequently biopsied site, accounting for 40.2% of all diagnostic biopsies (Figure 1 and 2). This was particularly driven by the need to rule out ileocecal tuberculosis and the high prevalence of CD. Endoscopic findings revealed distinct morphological patterns. Skip lesions were the hallmark of CD, observed in 94.6% (n=70) of cases, followed by mucosal nodularity/cobblestoning (54.1%, n=40), and strictures (27.0%, n=20). In contrast, UC patients exhibited continuous mucosal damage, with ulcerations (82.0%, n=50), a diminished vascular pattern (80.3%, n=49), and spontaneous bleeding (44.3%, n=27) during endoscopy.

Table 1: Demographic Profile of IBD Patients

Parameter	Value
Total IBD Cases (n)	174
Mean Age (Years ± SD)	39.14 ± 16.12
Age Range (Years)	11 – 85
Gender Distribution	
Males (n, %)	94 (54.0%)
Females (n, %)	80 (46.0%)
Male: Female Ratio	1.17:1

Table 2: Clinical Presentation and Symptomatology in IBD Subtypes

Symptoms	Crohn's Disease (N=74)	Ulcerative Colitis (N=61)
Diarrhoea	30 (40.5%)	50 (82.0%)
Abdominal Pain	64 (86.5%)	58 (95.1%)
Tenesmus	50 (67.6%)	54 (88.5%)
Weight Loss	8 (10.8%)	48 (78.7%)
Blood in Stools	27 (36.5%)	52 (85.2%)
Fatigue/Pallor	68 (91.9%)	50 (82.0%)
Aphthous Ulcers	45 (60.8%)	6 (9.8%)
Family History	20 (27.0%)	13 (21.3%)
Similar Past Complaints (Recurrence)	21 (28.4%)	12 (19.7%)

Table 3: Subtype Distribution and Gender Ratio

Diagnosis	Total Cases (n, %)	Mean Age (Years)	Males (n)	Females (n)	Male: Female Ratio
Crohn's Disease (CD)	74 (42.5%)	41.05	41	33	1.24:1
Ulcerative Colitis (UC)	61 (35.1%)	37.85	36	25	1.44:1
Indeterminate Colitis (IBD-U)	39 (22.4%)	37.51	17	22	0.77:1

Table 4: Microscopic Findings in Crohn's Disease (CD) and Ulcerative Colitis (UC)

Histopathological Feature	Crohn's Disease (N=74)	Ulcerative Colitis (N=61)
Surface Epithelium		
Epithelial Damage with Surface Ulceration	44 (59.5%)	50 (82.0%)
Chronic Inflammation	74 (100%)	61 (100%)

Lymphoid Follicle Formation	70 (94.6%)	1 (1.6%)
Crypt Morphology & Architecture		
Crypt Abscess	10 (13.5%)	55 (90.2%)
Crypt Atrophy	11 (14.9%)	54 (88.5%)
Additional Findings		
Mucin Depletion	8 (10.8%)	50 (82.0%)
Granulomas	27 (36.5%)	0 (0%)
Dysplasia	23 (31.1%)	30 (49.2%)
Fibrosis	38 (51.4%)	0 (0%)

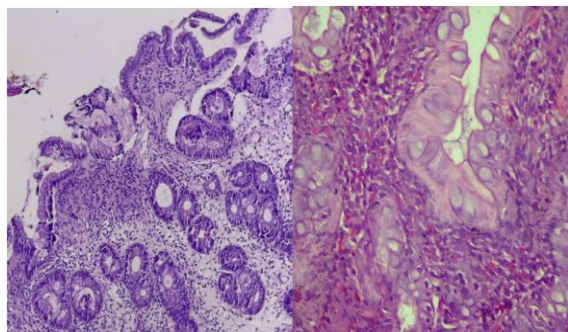


Figure 1: Photomicrograph of Crohn's disease showing dense chronic inflammatory infiltrate with basal plasma cell distortion. (a) Areas of vague granuloma formation and fibrosis is also noted. (b) Basal cell plasmacytosis at the base of crypts is also seen. [H&E stain ; (a)10x magnification, (b)40x magnification]

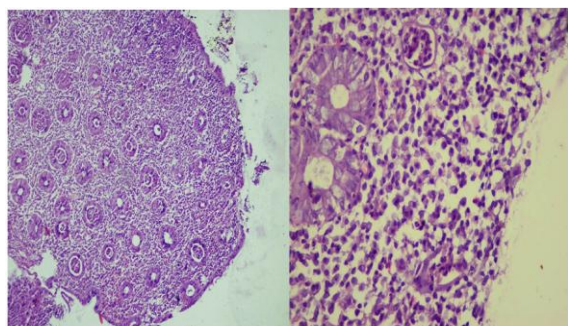


Figure 2: (a),(b) Photomicrograph of Ulcerative colitis showing crypt distortion and overt crypt abscess. [H&E stain ; (a)4x magnification, (b)40x magnification]

DISCUSSION

This 2025 update confirms the "Acceleration in Incidence" of Inflammatory Bowel Disease (IBD) in the Kashmir Valley, consistent with global trends that suggest an increasing burden of IBD in regions transitioning toward urbanization and dietary changes.^[10] The mean age of 39.14 years and the overall Male:Female ratio of 1.17:1 further validate the distinctive characteristics of the "South Asian Phenotype," where there is a male predominance and a younger age of onset compared to Western populations.^[11] A striking finding in this study is the high proportion of Crohn's disease (42.5%), surpassing Ulcerative Colitis (35.1%), a dramatic shift from the pre-2014 data from our center, where UC was predominantly observed (86.6%).^[12] This change could be attributed to several factors, including enhanced endoscopic evaluation, which allows for routine intubation of the terminal ileum, increased physician awareness, changing dietary

habits, and improved histopathological grading criteria.^[13] The rise in CD is in line with global epidemiological shifts where Crohn's disease is becoming more prevalent, especially in newly industrialized regions.^[7]

The substantial proportion of Indeterminate Colitis/IBD-Unclassified (IBD-U) cases (22.4%) highlights a significant diagnostic challenge in India, where distinguishing early-stage Crohn's Disease from Intestinal Tuberculosis (ITB) is difficult. Both conditions present with transmural inflammation and granulomas, which complicates the diagnosis.^[13] In our study, the high rate of IBD-U likely reflects a cautious approach to diagnosis, where physicians may refrain from definitively labeling a case as Crohn's disease to avoid misdiagnosing a treatable mycobacterial infection as a chronic, autoimmune condition.^[14] This cautious approach is crucial in regions like Kashmir, where the prevalence of tuberculosis is high. The clinical presentation of IBD in our cohort sharply illustrates the differing pathophysiological mechanisms between UC and CD. In UC, patients predominantly presented with classic colitic symptoms such as bloody stools (85.2%) and diarrhea (82.0%), leading to significant weight loss (78.7%) when compared to the CD cohort (10.8%). The clinical phenotype of UC appears to be more superficial, localized to the mucosal layer. In contrast, CD patients exhibited a more systemic and insidious clinical course, with fatigue and pallor (91.9%) being predominant symptoms, alongside extraintestinal manifestations like aphthous ulcers (60.8%). This pattern reflects the chronic, transmural nature of Crohn's disease, which often leads to systemic inflammation and malabsorption. Endoscopic and histopathological findings in this study correlate the established understanding of the distinct disease processes in UC and CD.^[15] Crohn's disease was associated with transmural inflammation, as evidenced endoscopically by skip lesions (94.6%) and cobblestoning, as well as histologically by lymphoid follicle formation (94.6%), fibrosis (51.4%), and non-caseating granulomas (36.5%). These features are hallmarks of CD, reflecting the inflammatory process that extends beyond the mucosal layer.

In contrast, UC patients exhibited continuous, superficial mucosal inflammation. Endoscopic findings included a diminished vascular pattern and spontaneous bleeding, typical of UC's more localized and superficial mucosal damage.^[7] Microscopically, UC was characterized by crypt distortion, crypt abscesses, and mucin depletion—features almost

universally present in our cohort. These findings are consistent with the literature, confirming that UC's pathology is primarily restricted to the mucosal layer with characteristic architectural changes, whereas CD affects the entire bowel wall.^[7] The application of the Nancy Histological Index (NHI) in UC cases revealed concerning results regarding disease severity. A significant proportion (82.0%) of UC patients had severe, active disease (Grade 4), characterized by extensive ulceration and neutrophilic infiltration. This suggests that the majority of patients present at an advanced stage of disease. The high proportion of severe disease could be indicative of delayed clinical presentation or diagnostic delays, which are common in resource-limited settings where gastrointestinal symptoms may initially be treated empirically. Furthermore, this finding may suggest an aggressive form of UC in the Kashmir Valley, which warrants further investigation into disease progression, treatment response, and the potential role of early biologic therapies in this population. The ileum was the most frequently biopsied anatomical site (40.2%), reflecting the high prevalence of ileocecal tuberculosis and Crohn's disease in this region. Endoscopic findings further support these observations, with CD patients showing characteristic skip lesions and strictures, while UC patients displayed continuous mucosal damage. These endoscopic and histopathological findings underscore the importance of thorough diagnostic workups, including endoscopic evaluation of the terminal ileum, especially in areas with high tuberculosis prevalence.

CONCLUSION

This study highlights a significant shift in the epidemiology of Inflammatory Bowel Disease (IBD) in the Kashmir Valley, with a notable increase in the proportion of Crohn's Disease cases, surpassing Ulcerative Colitis. The rising incidence of IBD in this region reflects broader global trends, driven by urbanization, dietary changes, and genetic susceptibility. The high rate of IBD-Unclassified cases underscores the diagnostic challenges, particularly in differentiating Crohn's Disease from Intestinal Tuberculosis. These findings emphasize the need for heightened clinical suspicion, improved diagnostic protocols, and a multidisciplinary approach to manage IBD effectively in this population.

Limitations

This study was conducted at a single tertiary care center, which may limit the generalizability of the

findings to other regions. Additionally, the reliance on histopathological criteria for diagnosis may have led to challenges in differentiating between IBD and infectious diseases like tuberculosis, requiring further validation in larger, multicenter studies.

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