

Predictive value of epithelial lesion heterogeneity in the etiological diagnosis of chronic inflammatory bowel disease

Habsatou ABDOULAYE BIYOU

habsatou.abdoulayebiyou@usmba.ac.ma

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Meryem Zaryouhi

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Imane FADLALLAH

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Hind BOURKHIME

Sidi Mohamed Ben Abdallah University

Sanae MOQRAN

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Souhaila EL-YAAGOUBI

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Mounia EL YOUSSEFI

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Layla TAHIRI ELOUSROUTI

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

NAWAL Hammas

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Laila CHBANI

CHU HASSAN II, Sidi Mohamed Ben Abdallah University

Research Article

Keywords: Crohn's disease, Ulcerative Colitis, Predictive Value, Heterogeneity

Posted Date: April 19th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-9304837/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.
[Read Full License](#)

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at BMC Gastroenterology on August 29th, 2026. See the published version at <https://doi.org/10.1186/s12876-026-05285-4>.

Abstract

Introduction: Chronic inflammatory bowel diseases (IBD) are characterized by chronic, intermittent, and continuous inflammation of a part of the digestive tract, with an increased risk of dysplasia and colorectal cancer (CRC). They typically include Crohn's disease (CD) and ulcerative colitis (UC). The diagnosis of IBD is multidisciplinary. One biopsies are essential for establishing a diagnosis, monitoring treatment, and/or identifying complications. This study evaluates the predictive value of the heterogeneity of epithelial abnormalities in the etiological diagnosis of IBD.

Materials and Methods: This is a retrospective study involving 81 cases of IBD diagnosed at the Department of Pathological Anatomy and Cytology of the Hassan II University Hospital in FES from 2021 to 2023. The diagnosis was established after histological examination. The homogeneous or heterogeneous nature of the lesions between different biopsies was categorized into two groups.

Correlations were made between the presence of homogeneous or heterogeneous characteristics of the lesions and the various epithelial abnormalities, as well as the clinical diagnosis of CD and UC. The positive and negative predictive values were assessed.

Results: Our study included 81 cases of IBD. The average age of the patients was 40 years with a standard deviation of 14. All patients underwent colonic biopsy. These 81 cases were distributed as follows based on the final clinical diagnosis: 19 cases of CD, 59 cases of UC, and 3 cases of IBD on histological examination. When endoscopic and histopathological data were correlated, heterogeneous lesions were found in 44% of patients with CD compared to 16% with homogeneous characteristics. In UC, homogeneous lesions were found in 84% of patients compared to 56% with heterogeneous characteristics ($P = 0.009$).

Conclusion: Our study demonstrated that the homogeneous nature of epithelial abnormalities was more commonly observed in UC than in Crohn's disease. This could serve as a discriminatory histological criterion for better categorizing IBD.

Introduction

Inflammatory Bowel Diseases (IBD) are characterized by chronic, intermittent, or continuous inflammation of a portion of the digestive tract with an increased risk of dysplasia and colorectal cancer (CRC). They are relatively common, often starting between the ages of 15 and 30, and affecting both men and women equally. The first description of IBD dates back to 1932 when Burrill Bernard Crohn published his article "Regional ileitis: A pathologic and clinical entity [1, 2].

Histopathology plays a crucial role in the diagnosis, and histological examination is typically based on biopsy samples, which involve only the mucosa and the superficial part of the submucosa.

The radiological signs of Crohn's disease include thickening of the intestinal wall, especially in the terminal ileum, ulcers, fistulas, and the presence of skip lesions (areas of intestinal lesions interspersed

with healthy segments) [3]. Histologically, this disease is characterized by discontinuous lesions, which may appear as affected segments with areas of healthy mucosa in between. Crohn's disease can affect any part of the gastrointestinal tract, from the mouth to the anus, and may also involve areas other than the colon, such as the terminal ileum. Histological features include transmural inflammation, spanning the entire intestinal wall, and the presence of granulomas, often located in the submucosa, making their detection difficult on superficial biopsies [1].

Ulcerative colitis (UC) is radiologically characterized by thickening of the colon and rectum walls, accompanied by ulcers and superficial wounds [3]. In UC, inflammation affects the rectocolonic mucosa continuously, without interruptions, and is generally limited to the colon and rectum, although it may start in the rectum and gradually spread to the colon. This condition is characterized by continuous and superficial inflammation of the colonic mucosa, without involvement of all layers of the intestinal wall. Unlike Crohn's disease, granulomas are not observed in UC, which is a significant distinction between the two conditions [1].

In both subtypes of IBD, the infiltrate is primarily mononuclear, with a predominance of lymphocytes and plasma cells. The presence of neutrophils indicates an active disease [1].

The continuous development of colonoscopy technology has allowed clinicians to have a better view of the colon, providing pathologists with more material [3]. The diagnosis of IBD and other inflammatory conditions of the colon cannot be established when only one or a few features are present, given the lack of specific histological signs [4]. Most abnormal biopsies of the colonic mucosa do not provide a specific etiological diagnosis but rather show a pattern of injury. An essential part of the diagnosis is the distribution pattern of the disease.

Ulcerative Colitis (UC) is characterized by continuous, homogeneous lesions without any intervening healthy mucosa. On the other hand, focal lesions are more indicative of Crohn's disease (CD) but can also be observed in ischemic colitis and UC [5]. However, normal endoscopic results do not necessarily reflect normal histology.

The correlation between endoscopy and histology is weak, and up to one-third of patients with CD and ulcerative colitis in endoscopic remission may show signs of persistent histological activity [1, 6, 7]. An accurate assessment of microscopic disease activity using respective scoring indices is, therefore, necessary.

The aim of our study is to correlate the final diagnosis based on clinical and endoscopic data with the heterogeneity of epithelial lesions in the etiological diagnosis of IBD. We also aim to evaluate the positive predictive value and negative predictive value of heterogeneity in diagnosing CD and UC.

Materials and Methods

This is a retrospective study involving 81 cases of IBD diagnosed at the Department of Pathological Anatomy and Cytology of Hassan II University Hospital in FES. The diagnosis was established based on fragments of endoscopic colonic biopsy fixed in 10% formalin, processed using conventional methods, and embedded in paraffin blocks. Sections of these blocks were stained with hematoxylin and eosin saffron (HES) following standard procedures.

The inclusion criteria included an ileo-colonic biopsy, availability of endoscopic and clinical data, and the presence of sufficient histological criteria for diagnosis. Exclusion criteria were the unavailability of endoscopic data and insufficient histological criteria to confirm the diagnosis. Biopsies were obtained without orientation. Biopsied segments included the rectum in 23 cases, the ileocecal valve in 4 cases, and in 54 cases, the pathological colon without precise localization. In Crohn's disease, biopsies of the terminal ileum were performed in 4 cases. Slides were annotated by two experienced gastrointestinal pathologists.

After an initial histological study, a review of HES slides was conducted by a second experienced gastrointestinal pathologist to thoroughly analyze the various epithelial abnormalities and lesion heterogeneity.

The heterogeneity of lesions was categorized into two groups: homogeneous or heterogeneous.

A degree of heterogeneity of lesions was observed within a single biopsy, which was classified into two groups: homogeneous and heterogeneous.

Definition of terms:

In the context of inflammatory bowel diseases (IBD), lesion heterogeneity refers to the diversity of observed tissue alterations, including their location, type, depth, and histological appearance. This variability can have significant implications for the diagnosis, treatment, and prognosis of patients with these inflammatory intestinal conditions.

A lesion is considered homogeneous when the entire or the majority of the sample exhibits a uniform appearance upon examination. This means that the entirety or most of the examined area is abnormal. A lesion is termed heterogeneous when an irregular or varied appearance is present upon examination, indicating that a portion of the sample (or fragment) is entirely normal while another part is abnormal.

Correlations were made between the presence of homogeneous or heterogeneous characteristics of the lesions and various epithelial abnormalities, as well as the clinical diagnosis of CD and UC. Positive and negative predictive values were also evaluated.

Various epithelial abnormalities included architectural anomalies such as loss of crypt parallelism, bifurcation, branching, cystic change, atrophy, dedifferentiated gland appearance, as well as surface villi appearance and dysplastic lesions. The type of inflammatory infiltrate was also examined.

Statistical analysis was performed using SPSS software version 26, and a correlation was considered significant if $p < 0.05$. The tests conducted included Pearson's chi-square test, Fischer's exact test, and the student's t-test (T-test).

Descriptive statistics such as mean, standard deviation, and percentages were calculated to characterize the studied sample. A Pearson correlation analysis was used to assess the presence of homogeneous or heterogeneous lesion characteristics with various epithelial anomalies and the clinical diagnosis of CD and UC. Fischer's t-test and the Student's t-test were used to compare epithelial anomalies between CD and UC.

Results

Our study included 81 cases of IBD over a two-year period.

The average age of the patients was 40 years with a standard deviation of 14. The gender ratio was male to female: 1.53.

All patients underwent colonic biopsy.

These 81 cases were distributed as follows based on the final clinical diagnosis: 19 cases of CD, 59 cases of UC, and 3 cases of IBD that clinicians were unable to classify. All these cases presented epithelial abnormalities on histology.

When endoscopic and histopathological data were correlated: Among patients with UC, the endoscopic extent of the disease was histologically confirmed to be a homogeneous lesion (image 1), pancolitis, in 42 patients. Among CD patients, the heterogeneous nature of lesions (image 2) after histological study was found in 11 out of 19 CD patients ($P = 0.009$); the details of this correlation are documented in Fig. 1.

Histological architectural changes were more pronounced in UC than in CD. The details of these modifications are presented in Fig. 2 and image 3 (A et B).

On the histological level, dysplastic foci were not observed in any of the cases. In UC, the inflammatory infiltrate predominates, as shown in Fig. 3, especially cryptic abscesses (Fig. 3 and image 3 C) in 86% of cases ($p = 0.02$).

Furthermore, in both diseases, there are coexisting architectural abnormalities and inflammatory infiltrates in particular basal plasmacytosis.

Moreover, no granulomas were detected in the 19 cases of Crohn's disease.

The extent and duration of the disease and the treatments administered to patients are recorded in Table 1.

The predictive values of heterogeneity in diagnosing UC in an IBD population have a sensitivity of 25% and a specificity of 42.1%. The positive predictive value (PPV) is 56%, and the negative predictive value (NPV) is 16%.

Regarding the predictive values of heterogeneity in diagnosing Crohn's disease in an IBD population, there is a sensitivity of 57.9% and a specificity of 75%. The positive predictive value (PPV) is 44%, and the negative predictive value (NPV) is 84%.

Image 1: Image of homogeneous lesion

Image 2: Image of heterogeneous lesion

Image 3: HES (Haematoxicilin eosin saffron) x 200: A-B: Architectural abnormalities (bifurcation, cystization, dedifferentiated appearance of glands), C-Cryptic abscess and basal plasmacytosis.

Table 1: Summary table of patient data on disease extent, follow-up duration, and treatments

IBD TYPE		CD	RCH
Disease extent	Homogenous(continuous)	16%	84%
	Heterogeneous (discontinuous)	44%	56%
Disease duration		14mois	18mois
Treatment: all patients were treated with:		-Decreasing corticosteroid therapy -Anti-inflammatory (pentaza) -Immunosuppressant (imurel)	-Anti-inflammatory (pentaza) -Immunosuppressant (imurel) -Decreasing corticosteroid therapy -Iron supplementation -Anti-TNF: infliximab (only one patient was treated with this product after failure of conventional treatments)

Discussion

In Crohn's disease (CD), the homogeneous character of lesions was found in an the heterogeneous character of lesions was observed in approximately 58% of patients (11 out of 19). The presence of heterogeneity was also noted in both CD and UC.

Our results indicate that the homogeneous character of lesions is strongly associated with UC, while the heterogeneous character is more common in CD. This would constitute a discriminating histological criterion for better classification of inflammatory bowel diseases (IBD) and is also explained by the continuous nature of lesions in endoscopy.

These results are comparable to those in the literature. Thereby reinforcing the validity and reproducibility of our conclusions [5].

Histological evaluation of biopsy samples is crucial for establishing a specific diagnosis of IBD. This approach is essential for guiding therapeutic choices, taking into account significant differences in surgical treatment and long-term prognosis between UC and CD [8].

However, in about 10 to 20% of cases, it is difficult to make a clinical and histological distinction between UC and CD. In these situations, the diagnosis of Indeterminate Bowel Disease (IBD-U) is made, highlighting the complexity of diagnosing these diseases [8].

For the diagnosis of UC, the heterogeneity of lesions has a positive predictive value (PPV) of 56% and a relatively low negative predictive value (NPV) of 16%. For the diagnosis of CD, the heterogeneity of lesions shows a PPV of 44% and a higher NPV at 84%.

Predictive values add an important dimension to understanding the clinical relevance of these histological features. This distinction can play an essential role in diagnostic and therapeutic decision-making, contributing to better management of patients with IBD.

Most abnormal colonic mucosa biopsies do not provide a specific etiological diagnosis but rather show a pattern of lesion [5].

An important part of the diagnosis is the disease distribution pattern. Although UC is characterized by diffuse and continuous inflammation limited to the mucosa, discontinuous and focal forms can also be observed, emphasizing the complexity of the diagnosis [5, 10].

There is no specific histological characteristic of UC that is not observed in CD, highlighting the need for a thorough clinical evaluation and contextual interpretation of histological results [5, 9, 10].

Epithelial abnormalities predominantly occur in UC, consistent with medical literature [8, 11]. These abnormalities can be crucial in the diagnosis of IBD.

Similarly, inflammatory infiltrate predominates in UC in our series. It is important to note that the presence of activity has no impact on disease categorization and has no diagnostic value as it can be observed in many forms of colitis. For example, cryptic abscesses can be observed in UC, CD, or infection [5]. Basal plasmacytosis is also a fairly constant and reproducible sign in the diagnosis of IBD [12].

In our series, basal plasmacytosis was present in both UC (76%) and CD (24%).

No granulomas were detected in our series. Detecting granulomas in biopsies can be challenging due to their deep location within the intestinal wall, random sampling of biopsies, variability in granuloma presence among patients and disease stages, and the technique used for sample collection. It is crucial to carefully interpret histological findings and consider other diagnostic criteria, including clinical and radiological data, to achieve an accurate diagnosis and develop an appropriate treatment plan for patients with inflammatory bowel diseases.

Differential diagnosis is important, especially during the initial onset of symptoms. Conditions to consider include ischemic colitis, occurring most often in the elderly, microscopic colitis (collagenous and lymphocytic) occurring preferentially in the young, drug-induced enterocolitis (especially non-steroidal anti-inflammatory drugs), radiation-induced digestive tract disorders, celiac disease, and its complications.

Conclusion

The homogeneous character of epithelial abnormalities is a discriminating histological criterion, with a predominant observation in ulcerative colitis (UC) compared to Crohn's disease (CD). This suggests that this characteristic can play an important role in the classification of chronic inflammatory bowel diseases (IBD).

Most biopsies from patients with colitis do not present pathognomonic histological characteristics. It is crucial to interpret them considering clinical, endoscopic, and biological data to reach an accurate diagnosis.

The histopathology report is based on the description of histological patterns rather than a definitive diagnosis. This report offers a preliminary differential diagnosis and provides the gastroenterologist other arguments for more accurate diagnosis.

Declarations

Ethics approval and consent to participate

This retrospective study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision). Ethical approval was obtained from the Ethics Committee of the Centre Hospitalier Universitaire Hassan II de Fès (Ref: CE-CHUH2-2024-015; Date of approval: 15 March 2024).

Due to the retrospective nature of the study and the use of fully anonymized patient data, the requirement for informed consent was waived by the Ethics Committee.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The authors received no specific funding for this work.

Authors' contributions

SE, ME and SM designed the study

LT, NH and LC supervised the work.

HAB collected the data and wrote the manuscript.

HB, ZM and FI analyzed the data.

All authors reviewed and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Ondrej Fabian et Lukas Bajer. Histopathological Evaluation of Microscopic Activity in Inflammatory Bowel Diseases, *World journal of gastroenterology*, 28th September 2022. 10.3748/wjg.v28.i36.5300 PMC9521520, PMID: 36185628.
2. CROHN BB, OPPENHEIMER GINZBURGL. GD. Regional ileitis; a pathologic and clinical entity. *Am J Med*. 1952;13(5):583 – 90. 10.1016/0002-9343(52)90025-9. PMID: 12996536.
3. SCENIC. International Consensus Statement on Surveillance and Management of Dysplasia in IBD. *Gastrointest Endosc*. 2015;148(3):639–651.e28. 10.1053/j.gastro.2015.01.031. PMID: 25702852.
4. Rath I, Ahmed S, Biligi DS. (2020). Diagnostic Dilemma of Inflammatory Bowel Disease: A Study from a Tertiary Hospital in Southern India. *Int J Sci Study*, 8(3).
5. Haboubi N. Reporting Colonic Biopsies in Patients With Inflammatory Bowel Disease; a Practical Approach. *Inflamm Bowel Dis*. 2019;25(4):679–684. 10.1093/ibd/izy288. PMID: 30256953.
6. Peyrin-Biroulet L, Bressenot A, Kampman W. Histologic remission: the ultimate therapeutic goal in ulcerative colitis? *Clin Gastroenterol Hepatol*. 2014;12(6):929 – 34.e2. 10.1016/j.cgh.2013.07.022. Epub 2013 Aug 1. PMID: 23911875.
7. Molander P, Sipponen T, Kemppainen H, Jussila A, Blomster T, Koskela R, Nissinen M, Rautiainen H, Kuisma J, Kolho KL, Färkkilä M. Achievement of Deep Remission during Scheduled Maintenance Therapy with TNF α -Blocking Agents in IBD. *J Crohns Colitis*. 2013;7:730–5. [PubMed] [Google Scholar].
8. Chbani L, Hammas N, El Fakir S, Nejari C, Amarti A. Interobserver variability and value of histological examination in the diagnosis of inflammatory bowel disease (experience of Hassan II University

Hospital Fez). J Africain d'Hépatogastroentérologie. 2012;6:288–91.

9. Schumacher G, Kollberg B, Sandstedt B. A prospective study of first attacks of inflammatory bowel disease and infectious colitis. Histologic course during the 1st year after presentation. *Scand J Gastroenterol*. 1994;29(4):318 – 32. 10.3109/00365529409094843. PMID: 8047806.
10. Odze. and Goldblum: Surgical Pathology of the Gastrointestinal Tract, Liver, Biliary Tract, and Pancreas. 3rd ed. Philadelphia, PA: Saunders; 2014.
11. enkins D, Balsitis M, Gallivan S, Dixon MF, Gilmour HM, Shepherd NA, Theodossi A, Williams GT. Guidelines for the initial biopsy diagnosis of suspected chronic idiopathic inflammatory bowel disease. The British Society of Gastroenterology Initiative. *J Clin Pathol*. 1997;50(2):93–105. PMID: 9155688; PMCID: PMC499731.
12. Allison MC, Hamilton-Dutoit SJ, Dhillon AP, Pounder RE. (1987) The Value of Rectal Biopsy in Distinguishing Self-limited Colitis from Early Inflammatory Bowel Disease. *QJ7Med* 65: 985–95.

Figures

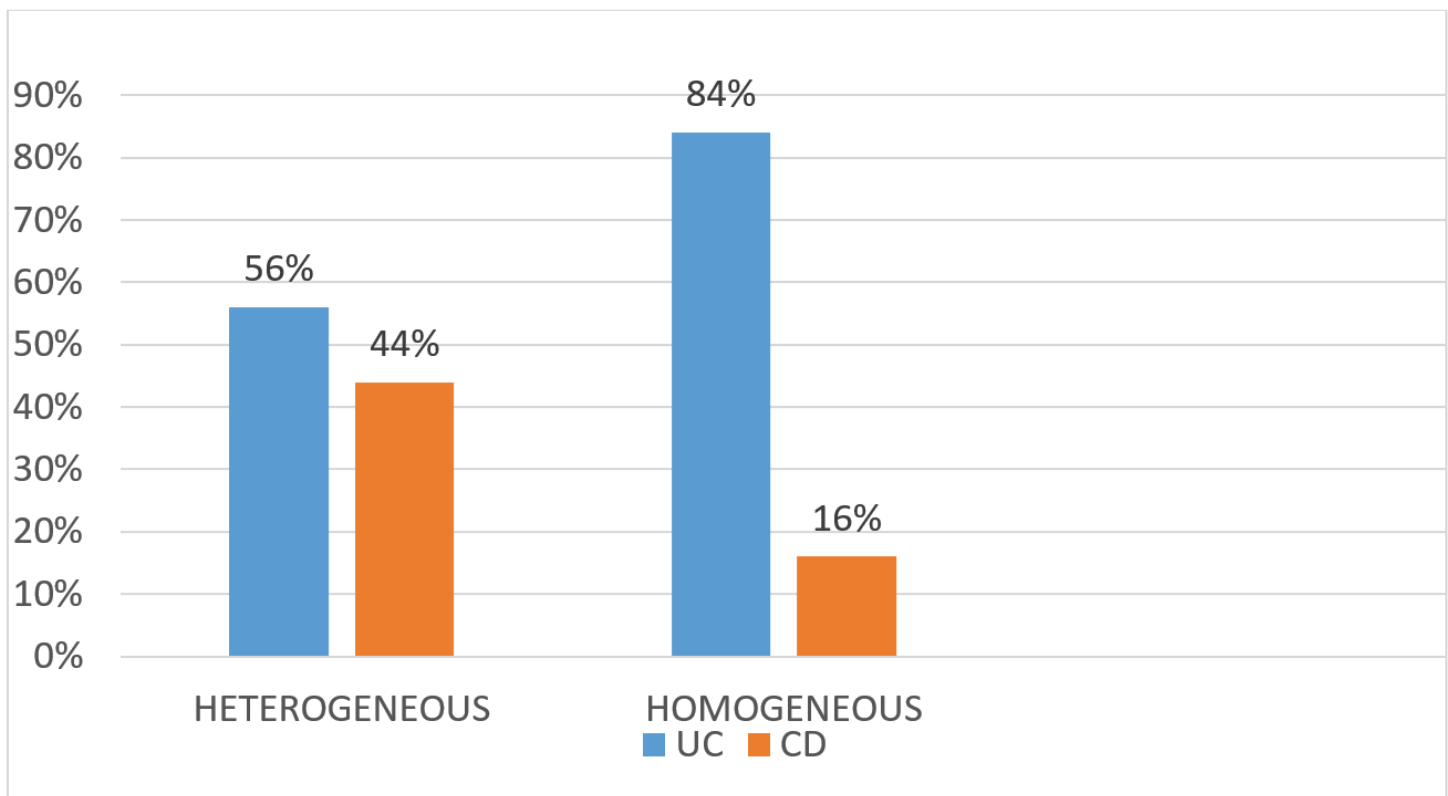


Figure 1

Distribution of heterogeneity of epithelial abnormalities in UC and CD

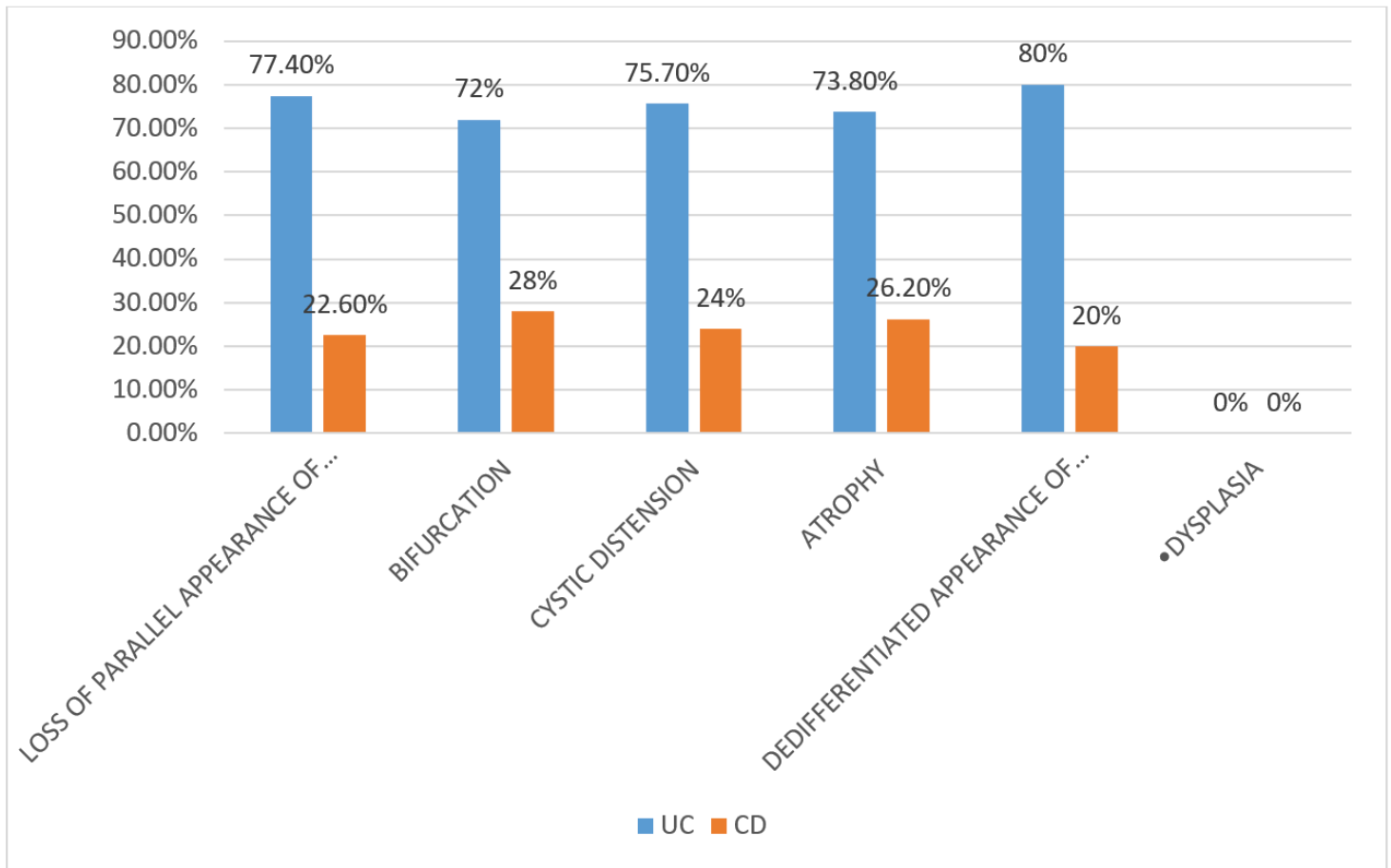


Figure 2

Significant histological architectural changes in UC.

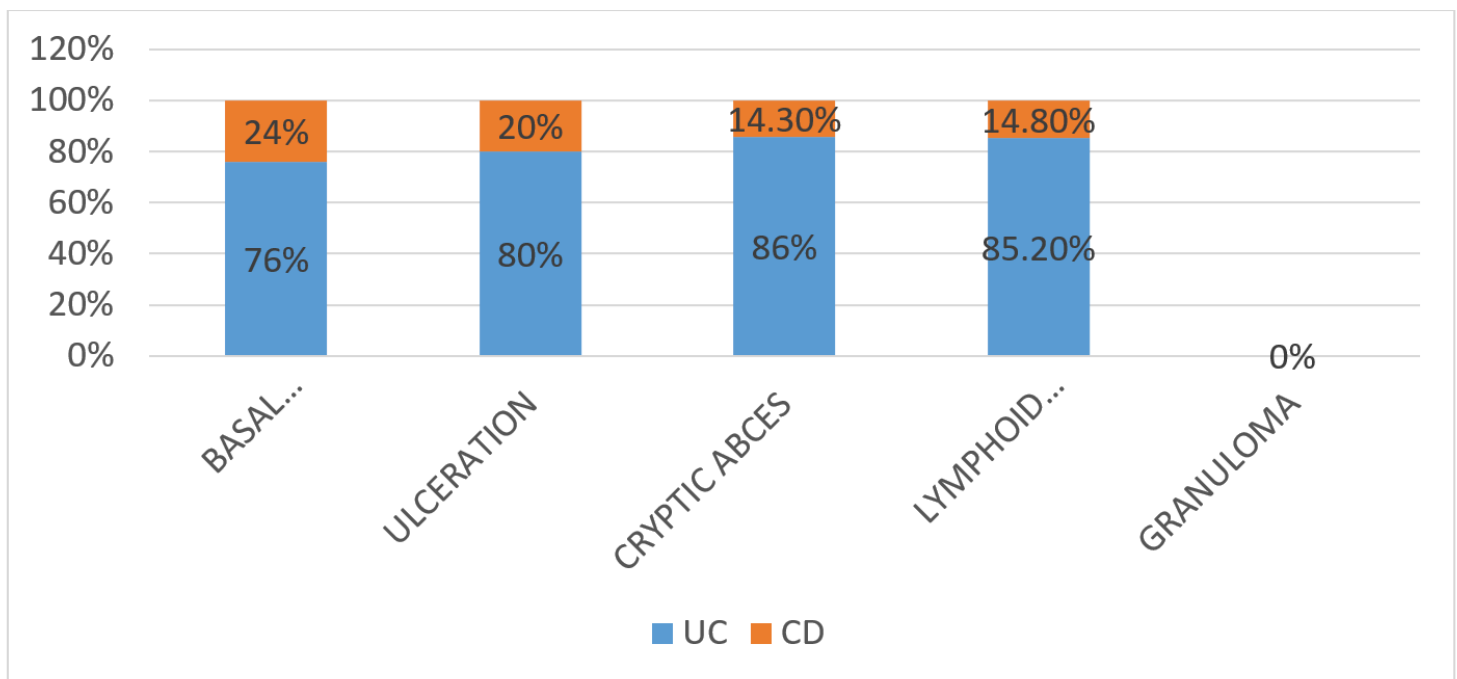


Figure 3

Distribution of inflammatoire changes in both CD and UC

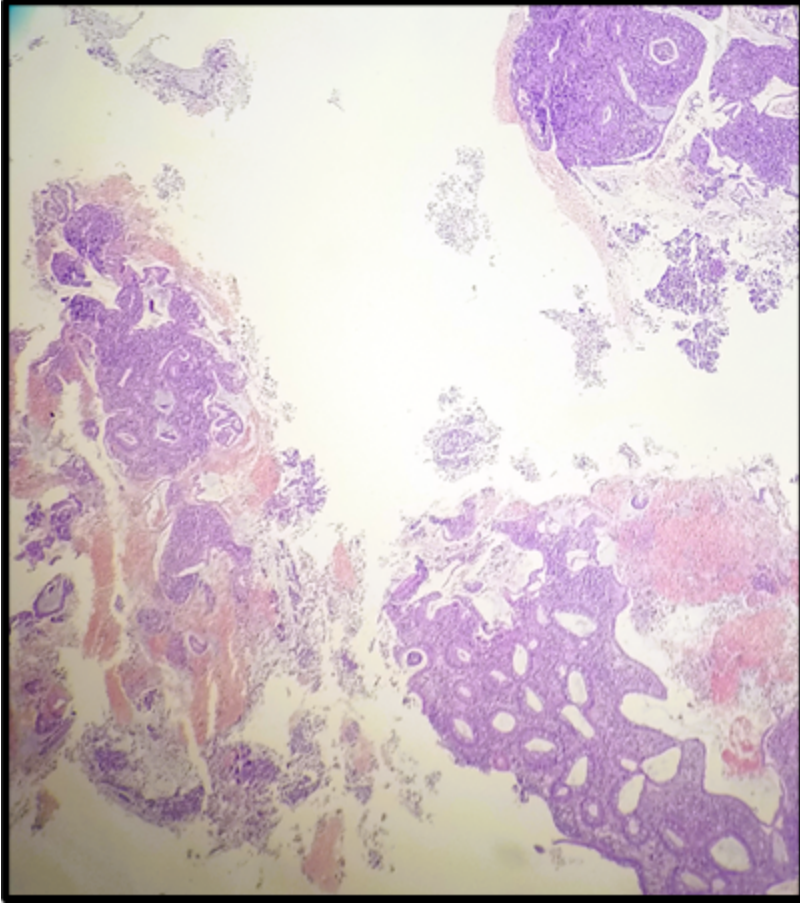


Figure 4

Image 1: Image of homogeneous lesion

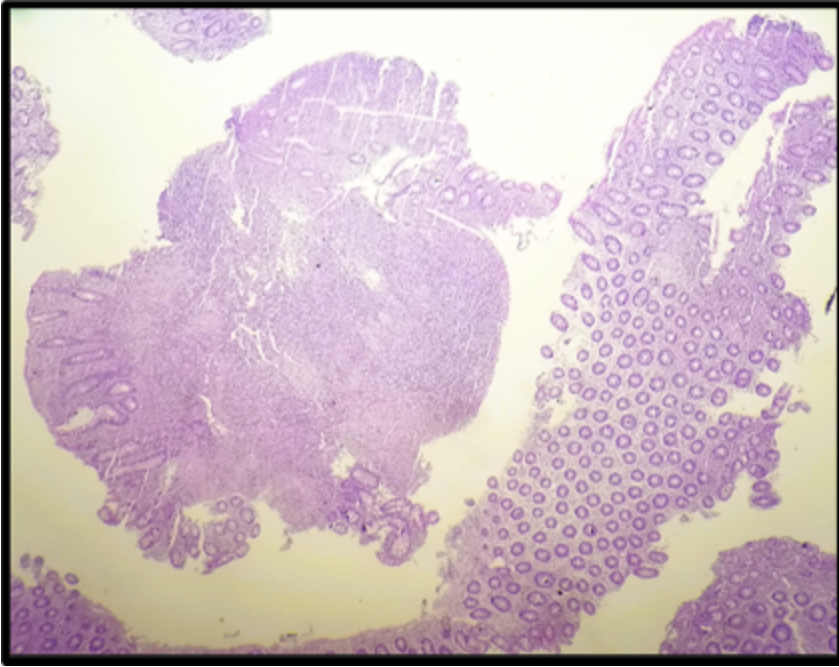


Figure 5

Image 2: Image of heterogeneous lesion

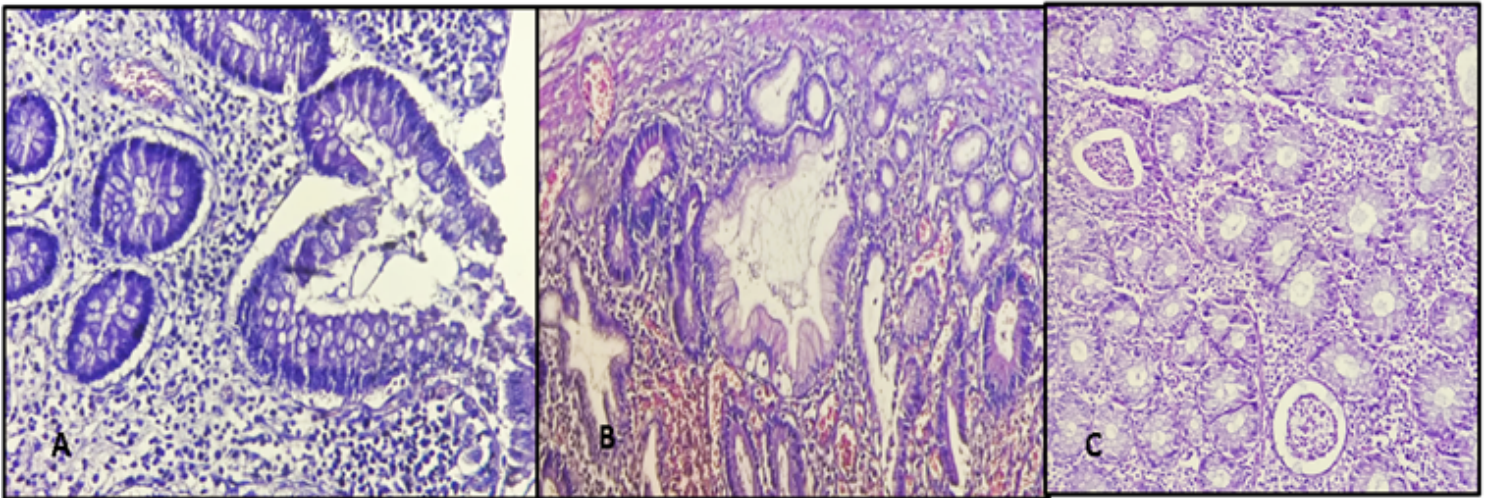


Figure 6

Image 3: HES (Haematoxylin eosin saffron) x 200: A-B: Architectural abnormalities (bifurcation, cystization, dedifferentiated appearance of glands), C-Cryptic abscess and basal plasmacytosis.