Ulcerative Colitis and Its Histopathological Finding: An Assessment and Critical Appraisal

Priya Srivastava¹ & Rahul Pandey²
¹Asst. Professor Department of Pathology, Dr. M.C. Saxena Medical College, Lucknow
²Head of Physiotherapy Department, Javitri Hospital, Lucknow

ABSTRACT

Background- Ulcerative colitis is an idiopathic, chronic relapsing, progressive inflammatory bowel disease, in which inflammatory process is limited to the mucosa. The presence of intestinal and extra intestinal manifestations depends on the level of inflammatory process that is the activity of disease. The diagnosis of ulcerative colitis is established by means of clinical state analysis, endoscopic and histo-pathological findings. The histo-pathological analysis helps us to verify the phases of the disease – active, resolution, or the remission phase. Thus, the activity of inflammatory process can also be graded.

Objective- To grade and or to make a confirm diagnosis for ulcerative colitis.

Method- The biopsy tissue received after endoscopy of 34 patients was fixed in 10% formalin, processed and embedded in paraffin. Sections of 3-4 μ thickness were cut and stained with Haematoxylin and Eosin (H&E). Special stain for Mucin like Periodic Acid Schiff (PAS) was done, wherever required. H&E stained slides were examined for histopathological features of UC were analysed. Grading of these histopathological features was done to determine the histological activity using two grading systems, namely, Truelove’s histopathological grading system and simplified modification of Geobes’ histopathological grading system.

Conclusion- In the following study we found the most common and consistently observed histopathological features of ulcerative colitis are diffuse increase in lamina propria cellularity due to acute (neutrophil) and chronic (lymphoplasmacytic) inflammatory infiltrate, crypt distortion, cryptitis and basal plasmacytosis. If these features are present in the patient’s histopathological finding means patient having ulcerative colitis.

Key words- Endoscopic examination; geobes’ histopathological grading system; truelove’s histopathological grading system; ulcerative colitis.

Introduction- Ulcerative colitis is an idiopathic, chronic relapsing, progressive inflammatory bowel disease, in which inflammatory process is limited to the mucosa. The presence of intestinal and extra intestinal manifestations depends on the level of inflammatory process that is the activity of disease. The diagnosis of ulcerative colitis is established by means of clinical state analysis, endoscopic and patho-histological findings. The patho-histological analysis helps us to verify the phases of the disease – active, resolution, or the remission phase. Thus, the activity of inflammatory process can also be graded. It is important to differentiate ulcerative colitis from other forms of inflammatory bowel disease to make an accurate diagnosis of the disease and also equally important is to assess the disease activity. Assessment of disease activity is required for the purpose of optimal therapeutic approach in an individual patient. ¹, ²

Hence, the histo-pathological diagnosis of ulcerative colitis should be based on discriminating histopathological features which are sufficiently reproducible and can be easily used in routine biopsy specimens. It is also essential to determine histopathological features that have the highest discriminative power in distinguishing inflammatory bowel disease from the non-relapsing colitis as well as ulcerative colitis from Crohn’s disease. However, only a few histopathological criteria or scoring based on colonic biopsies have been established. ³, ⁴ The invention of the flexible, fibreoptic colonoscope has been a good achievement towards the diagnostic field. With the use of this facility, direct visualization of the site of biopsy, photographic visualization of the lesions and therapeutic induction is possible. Assessment of mucin depletion histologically is another important aspect of the disease. ⁵ The present study has been undertaken to study the histopathological features of ulcerative colitis and grade them histologically as well as endoscopically. Correlation between the histopathological grading and endoscopic score will also be studied, wherever possible.

Terminologies/definitions of histopathological features:
Terminologies/definitions of histopathological features used in the present study are \(^3,4,6-9\)

**Erosion:** Loss of surface epithelium with underlying inflammation; **Ulceration:** Damage to a greater thickness, extending to the muscularis mucosa with underlying granulation tissue; **Crypt distortion:** Non parallel arrangement of crypts along with crypt branching, crypt dilatation and tortuosity of crypts; **Cryptitis:** Presence or migration of PMN into crypt epithelium with focal lysis of epithelial cells; **Crypt abscess:** Presence of PMN in the crypt lumina or the chain of PMN extending from lamina propria through the crypt epithelium into the crypt lumen; **Crypt atrophy:** is defined as the increase gap between the base of crypt and muscularis mucosae and/or increased intercrypt distance; **Lamina propria cellularity:** Increase in lamina propria cellularity is defined as increase in mixed inflammatory infiltrate comprising of plasma cells, lymphocytes, eosinophils in the biopsy; **Lamina propria inflammation:** Presence of acute (neutrophilic) and/or chronic (lymphoplasmacytic) inflammation; **Lymphoid aggregates:** More than two lymphoid aggregates in basal part of lamina propria in a 2mm biopsy specimen are abnormal; **Basal plasmacytosis:** Chronic inflammation with predominance of plasma cells extending to mucosal base; **Mucin depletion in surface epithelium and crypts:** Unequivocal decrease in number of goblet cells or depletion of mucin within a cell in surface epithelium and crypt epithelium.

**Methodology:**

The present study is a cross-sectional study conducted at Gastroenterology department, Department of Medicine and Histopathology section, Department of Pathology respectively of K.L.E.S Dr. Prabhakar Kore Hospital and Medical Research Centre and J.N. Medical College, Belgaum. The period of study was four years, which included three years were retrospective study from January 2006 to December 2008 and one year is prospective from January 2009 to December 2009. The study was approved by J.N. Medical College Institutional Ethics Committee for Human Subjects Research. Informed consent was obtained from the participants. A pre-designed proforma was used to collect the relevant clinical details, investigation undergone including endoscopic examination. All cases of UC diagnosed on basis of histological and endoscopic findings were included in the study and the other inflammatory bowel diseases were excluded. 34 patient of UC diagnosed in the study period of 4 years, except 4 cases, which were excluded from the study as they were superficial biopsies and consequently, inadequate for assessing the histopathological features of UC.

Out of the total 57 cases diagnosed as UC, endoscopic findings were available in 34 cases. The endoscopic features such as loss of vascularity, granular nonfriable mucosa, friability on rubbing, and spontaneous bleeding and ulceration were noted. The severity of colitis endoscopically was graded according to Baron’s endoscopic grade. The biopsy tissue received after endoscopy was fixed in 10% formalin, processed and embedded in paraffin. Sections of 3-4 µ thickness were cut and stained with Haematoxylin and Eosin (H&E). Special stain for Mucin like Periodic Acid Schiff (PAS) was done, wherever required. H&E stained slides were examined for histopathological features of UC were analysed. Grading of these histopathological features was done to determine the histological activity using two grading systems, namely, Truelove’s histopathological grading system\(^10\) and simplified modification of Geobes’ histopathological grading system.

**Results:**

**Histopathological features of ulcerative colitis**

Eighteen reproducible histopathological features of UC were studied. The most consistently observed histopathological features were crypt distortion (98.24 %), cryptitis (92.98%), basal plasmacytosis (92.94%) villous/ irregular mucosal surface (85.96%), crypt abscess (85.96 % ) and crypt destruction ( 80.70%). Diffuse lamina propria inflammation was seen in all the biopsies with neutrophils (100%), eosinophils (96.49%), lymphocytes (100%) and plasma cells (100%). Most of the cases had mild to moderate increase of these cells. Acute inflammatory cell infiltration (neutrophil) was present in all cases, which was mild to moderate in most cases. Presence or increase in eosinophils was another consistent finding. Chronic inflammation (lymphoplasmacytic) was seen in all biopsies, but most of them having mild-moderate inflammation.
HISTOPATHOLOGICAL GRADING OF ULCERATIVE COLITIS

Truelove’s histopathological grading system:
According to this grading criteria, out of the 57 cases, histologically 91.22% patients had grade 3 severity of disease.

Geobes’ histopathological grading system: Out of 57 cases, majority (71.22% ) were noted in grade 6 according to modified Geobes’ histopathological grading system

Table no. 2: Histopathological grading of ulcerative colitis according to modified Geobes’ histopathological grading system
Ulcerative colitis is thought to be a rare chronic inflammatory bowel disease in developing countries but a changing trend is now being observed. In past couple of decades, studies from countries with low prevalence and incidence rates of UC have surfaced and redefined the whole epidemiology of UC world over. According to Iwashita et al the most important histological features on biopsy were dense mixed inflammatory infiltrate in the lamina propria and mucosal architectural abnormality. They also found that vascular change was also an important finding. However, it was not analysed in the present study.

In the present study, 49 out of 57 had mucosal surface abnormality. Out of these, 35.08% had either irregular or villous or both mucosal surface. This finding is similar to the finding of Berre et al. Ulceration in the present study was seen in 35.08% cases, which was also seen in 31% cases of Seldenrijk et al. Moreover, the present study confirms the finding of Seldenrijk et al, Berre et al and Bentley et al reporting crypt distortion in 92%, 95% and 91.66% cases respectively. In the present study, 98.24% cases had crypt distortion making it one of the most common feature seen in biopsies of UC. Cryptitis was seen in 92.98% cases in this study, in accordance to Berre et al (86%) and Jenkin et al (64-86%). However, there has been variation in defining cryptitis in most studies which can lead to the difference seen with Seldenrijk et al and Bentley et al. The present study adopted the definition used by Berre et al and Jenkin et al, which is presence or migration of PMN in crypt epithelium with focal lysis of epithelial cells. The same definition is used by Seldenrijk et al for describing ‘Basal neutrophilic cryptitis’ which is a non-reproducible and a separate feature than the reproducible feature ‘PMN in crypt epithelium’ in their study. Theodossi et al have also used the terminology of ‘crypt neutrophilia’, which has not been defined by the authors.

Most of the studies have defined ‘Crypt abscess’ as presence of PMN in the crypt lumina or the chain of PMN extending from lamina propria through the crypt epithelium into the crypt lumen. The same definition is adopted by this study and 83.33% cases showed crypt abscess which closely correlated with 83.33% cases in study by Bentley et al. However, other studies differed from this finding because these studies included only one of the features mentioned above in their definition of crypt abscess. Crypt atrophy in the present study is defined as the increased gap between the base of crypt and muscularis mucosae and/or increased intercrypt distance. The same has been used by other studies which reported this feature with a frequency ranging from 29 to 78%. In the present study crypt atrophy was seen in 47.36%, which closely correlated to the finding of Berre et al (43%).

<table>
<thead>
<tr>
<th>Modified Geobes' histopathological grades</th>
<th>Number</th>
<th>%</th>
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<tbody>
<tr>
<td>Grade 2</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Grade 3</td>
<td>3</td>
<td>5.26</td>
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<tr>
<td>Grade 4</td>
<td>3</td>
<td>5.26</td>
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<tr>
<td>Grade 5</td>
<td>10</td>
<td>17.54</td>
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<tr>
<td>Grade 6</td>
<td>41</td>
<td>71.92</td>
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Increase in lamina propria cellularity is seen in 100% cases, concordant with the findings of Jenkin et al and Iwashita et al. Increase in lamina propria cellularity is defined as increase in mixed inflammatory infiltrate comprising of plasma cells, lymphocytes, eosinophils in the biopsy. This inflammation was seen to be diffuse in 100% cases in the present study and in study by Bentley et al while none of the biopsies in the present study had focal inflammation. However, focal inflammation, a feature of CD, was seen in around 10% cases in studies done by Seldenrijk et al, Jenkin et al, Bentley et al. Presence of PMN in lamina propria is seen in 100% cases in this study, which is also consistent with the finding of Bentley et al (91.66%). Increased lymphoplasmacytic infiltration of lamina propria is seen in 100% cases in the present study, closely correlating to 92% and 93% finding of Seldenrijk et al and Berre et al respectively. Lymphoid aggregate is taken as nodular collection of lymphocytes without reactive centre in lamina propria (between crypts and muscularis mucosae) or submucosa. More than two lymphoid aggregates in basal part of lamina propria in a 2mm biopsy specimen is abnormal. Scattered aggregates do not constitute reliable evidence of active inflammation. In the present study, 75.43% cases had lymphoid aggregates, which is more than what reported by Jenkin et al (21%). This difference can be attributed to the difference in the definition used in both study. Jenkin et al has defined it as lymphoid aggregates in basal part of lamina propria not including submucosa.

Chronic inflammation with predominance of plasma cells extending to mucosal base was taken as ‘Basal plasmacytosis’ in the present study, as also by most of the previous studies. This feature was seen in 92.94% cases in the present study, in concordance with 92.4% and 100% of Konuma et al and Bentley et al. However, only 63% cases of Seldenrijk et al showed this finding. Presence of ulceration and fragmentation of biopsy can make it difficult to appreciate this feature. Diffuse mucin depletion was evident in 73.68% cases of this study, which included mucin depletion both in surface and crypt epithelium. Similar finding was seen by Bentley et al and Jenkin et al. While only 27% showed diffuse mucin depletion in study by Konuma et al. Thickened muscularis mucosae was analysed as a reproducible feature of UC by Theodossi et al and seen in 28% of cases of present study, close to around 25% cases of Theodossi et al.

**Conclusion-**
In conclusion, the present tertiary hospital based study confirms the existence of ulcerative colitis with a quite high relative frequency (20.5%) Belgaum district, North Karnataka. The most common and consistently observed histopathological features of ulcerative colitis in this study are diffuse increase in lamina propria cellularity due to acute (neutrophil) and chronic (lymphoplasmacytic) inflammatory infiltrate, crypt distortion, cryptitis and basal plasmacytosis. Grading of the disease to determine disease activity in ulcerative colitis revealed most patients being in high grade both on histology (91.22% and 71.92% on Truelove’s and Geobes’ system respectively).

**References-**


