Research article

Utility of Geboes score for assessing histological activity in ulcerative colitis

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ABSTRACT

Introduction and Aim: Diagnosis of UC is challenging and calls for an integrated clinical, endoscopic, serological, and histological examination. Although inexpensive and non-invasive, endoscopic findings do not always correlate with disease activity, as demonstrated by traditional histopathological examination.

Materials and Methods: This retrospective study was conducted between January 2014 and December 2019. Specimens of patients diagnosed with UC that were received in the Department of Pathology were included. An experienced pathologist assessed the histological disease activity using the Geboes score. The Mayo endoscopic subscore was recorded for endoscopic activity. Results thus obtained were entered into MS Excel and analysis was done using SPSS version 25.0.

Results: Of the 123 cases of UC, (age, 14 to 74 years; males: 60.2%, females: 39.8%) majority had endoscopic findings of erythema and edema (n=20) with the least common finding being ileocolitis (n=1). Mayo subscore was available in 24 cases (ranging from 1 to 3; Mayo subscore of 1, 2, and 3 in 1, 14 and 9 cases respectively). Active colitis was noted in 78% (96/123) of the patients while the remaining 22% (27/123) of patients had inactive colitis. Only 24 cases had both Mayo subscore and Geboes score correlation. Fourteen cases had a Mayo subscore of 2 and a Geboes score ranging from 2A to 5.2; 9 cases had a Mayo subscore of 3 and a Geboes score ranging from 4.1 to 5.2.

Conclusion: Assessment of histological disease activity by Geboes score provides useful information in routine reporting of biopsy specimens of cases of Ulcerative colitis.

Keywords: Ulcerative colitis; Mayo; Geboes score.

INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic condition resulting from dysregulated mucosal immune response. This disorder is attributable to complex interactions among various genetic and environmental factors. IBD encompasses two specific diseases: Ulcerative Colitis (UC) and Crohn's Disease (CD) (1). Although widely prevalent in the developed world, there has been a dramatic rise in Asia over the past few decades, with a two-fold higher incidence of UC (1.2).

UC is characterized by mucosal inflammation, predominantly seen affecting the colo-rectum (3). The clinical presentation of UC is often myriad and ranges from mild symptoms such as abdominal cramping and diarrhea to a more fulminant presentation. With disease progression, there is exacerbation of weight loss and appetite, nutritional deficiencies, bleeding per rectum and anemia.

The diagnosis of UC is nonetheless challenging and calls for an integrated clinical, endoscopy, serological, and histological examination. Although inexpensive and non-invasive, endoscopic findings do not always correlate with disease activity, as demonstrated by traditional histopathological examination. Furthermore, a direct correlation of histological findings with clinical outcomes, including relapse rates and risk for cancer, has been established. Thus, in this context, there has been renewed interest in various facets of histological examination, complemented with clinical, endoscopy, and serological findings for accurate diagnosis of UC and its surveillance (4,5).

Of the many histological scores that have been proposed, the Geboes Score has enjoyed widespread popularity due to its excellent reproducibility and correlation with endoscopy grading of disease activity for UC (5). The Geboes Score has 6 grades with 4 subcategories (Fig. 1).

With the rising burden of UC being increasingly in younger individuals, and with the availability of effective treatments for the same, clinicians are frequently encountering various complications in patients with long-standing ulcerative colitis. Colorectal carcinoma is one such complication that adds substantially to morbidity and mortality in individuals living with this condition (7). This situation necessitates surveillance of UC and routine screening for neoplastic transformation. Pathologists, therefore, have a vital role in detecting disease activity. In this scenario, grading systems such as Geboes score may be utilized effectively for an objective assessment of the same.
MATERIALS AND METHODS

Study design and population
This study was conducted retrospectively in the Department of Pathology of a tertiary care center in South India, during January 2014 to December 2019. The Institutional Ethics Committee (IEC) clearance was obtained before the commencement of the study. The study included all small biopsies or resection specimens of patients diagnosed with UC that were received in the Department during the study period. Cases of CD and Indeterminate colitis, poorly fixed and processed tissue, and inadequate samples were excluded. The medical records of the selected cases were reviewed for demographic data, clinical history and examination findings, relevant laboratory and imaging investigations, and endoscopy findings.

Endoscopic and histological evaluation for disease activity
The hematoxylin and eosin (H&E) stained slides of the cases were studied under light microscopy after retrieving from the archives. An experienced pathologist assessed histological disease activity using the Geboes score. In cases of multiple biopsies showing various grades of activities, the biopsy showing the highest grade was considered. For grading of histological disease activity, the Geboes score ranged from 0 to 5.4. Severe inflammation was indicated by higher scores. A Geboes score of ≥3.1 will be considered as UC with active histological inflammation and a Geboes score of <3 will be considered an inactive disease.

Fig. 1: Geboes scores for assessing histological activity in ulcerative colitis (5)

The Mayo subscores were recorded for endoscopic activity: inactive disease and normal mucosa (score 0), mild disease (score 1), moderate disease (score 2), or severe disease (score 3). Mayo score of ≤1 will be considered as endoscopic remission.
Statistical analysis
The results thus obtained were entered into MS Excel and analysis was done using SPSS version 25.0. The descriptive statistics were done in terms of percentages, means, medians, etc.

RESULTS
Patient characteristics
The study included 123 cases of Ulcerative colitis. The age of the patients ranged from 14 to 74 years (mean age: 44.7 years) 74 were males (60.2%) and 49 were female (39.8%). The most common presenting complaints were blood in stools (n=41), followed by abdominal pain (n=19), diarrhea (n=10), and weight loss (n=6). The duration of symptoms ranged from 1 week to 20 years.

Endoscopic assessment
Endoscopic findings were available in 73 cases and the common findings included erythema and edema (n=20), bleeding and friability (n=9), left-sided colitis (n=6), procto-sigmoiditis (n=6), pancolitis (n=6), proctitis (n=4), pseudopolyps (n=2), deep ulcers (n=2) and ileocolitis (n=1). The Mayo subscore was available in 24 cases and ranged from 1 to 3. A Mayo subscore of 1 was noted in 1 case, a subscore of 2 was seen in 14 cases and 9 cases had a Mayo subscore of 3.

Table 1: Correlation between Geboes score and CRP levels

<table>
<thead>
<tr>
<th>Geboes Score</th>
<th>Elevated CRP</th>
<th>Normal CRP</th>
<th>Negative CRP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Grade 1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Grade 2A</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Grade 2B</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Grade 3</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Grade 4</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Grade 5</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>12</td>
</tr>
</tbody>
</table>

CRP levels were available only in 12 cases, of which 6 cases had elevated CRP levels ranging from 11.96 – 129 mg/ L, 4 cases had normal CRP levels and 2 cases were negative (Table 1). As per correlation with the Geboes score, only 22% (2/6 cases) of the cases with elevated CRP levels had active colitis (Geboes score >3) while the remaining 88% (4/6 cases) had inactive colitis (Geboes score <3). 100% (4/4 cases) of the cases with normal CRP levels had active colitis (Geboes score >3). Among the 2 cases negative for CRP, 1 case had active colitis (Geboes 5.1) while the other had inactive colitis (Geboes 2B.1). The sites of biopsy included the ascending, descending, and transverse colon, sigmoid colon, terminal ileum, and rectum.

Histological assessment of cases of active colitis
There were 96 cases of active colitis (Geboes score >3). All the cases of active colitis showed histological features of crypt disarray and mixed inflammation in the lamina propria. Additional histological findings included cryptitis (n=94), basal plasmacytosis (n=70), crypt abscesses (n=58) and crypt regeneration (n=37).

Geboes score in cases of active colitis
The Geboes score in cases of active colitis ranged from 3.1 to 5.2. Most cases of active colitis had a score of 3 or 4 (n=66), followed by a score of 5 (n=30). All cases with a Geboes score of 3 showed histological features of mixed inflammatory infiltrate in lamina propria and crypt disarray. In addition to these, most cases also showed other histological features including cryptitis (n=28) and basal plasmacytosis (n=23). Similarly, among the 36 cases with a Geboes score of 4, the histological features of cryptitis and crypt disarray were consistently seen. Other common findings included mixed inflammatory infiltrate in the lamina propria (n=36), crypt abscess (n=25), and basal plasmacytosis (n=22). In cases with a Geboes score of 5, all cases showed cryptitis, crypt disarray, and mixed inflammation in the lamina propria, followed by crypt abscess (n=22) and basal plasmacytosis (n=21).

Histological assessment of inactive colitis
In the present study, there were 27 cases of inactive colitis (Geboes score <3). The histological features in these cases of inactive colitis were crypt disarray (n=24), followed by mixed inflammation in lamina propria (n=19), eosinophils in lamina propria (n=16), basal plasmacytosis (n=9), eosinophilic cryptitis (n=6) and chronic inflammation in lamina propria (n=5) (Fig.2).

Correlation of Geboes score with Mayo endoscopic subscore
There were 24 cases where both Mayo subscore and Geboes score correlation was available, of which 14 cases had a Mayo subscore of 2, 9 cases had a Mayo subscore of 3 and 1 case had a Mayo subscore of 1 (Table 2). The corresponding Geboes score in these cases ranged from 4.1 to 5.2 for Mayo subscores of 3, 2A to 5.2 for Mayo subscores of 2 and 1.2 in the case with Mayo score of 1. All cases with Mayo subscore of 3 (n=9) showed cryptitis, crypt disarray, and mixed inflammatory infiltrate in the lamina propria. Additional findings included crypt abscess and basal plasmacytosis (n=8) (Table 3).
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**Fig 2**: A: Grade 1.2 moderately increased chronic inflammatory infiltrate in the lamina propria
B: Grade 2A.1 Mild but unequivocal increase of eosinophils in the lamina propria
C: Grade 3.2 Mild but unequivocal increase of neutrophils in the epithelium with <50% of crypt involvement
D: Grade 3.3- Marked presence of neutrophils in the epithelium with >50% of crypt involvement
E: Gr 5.2 Erosion; F: Basal plasmacytosis

**Table 2**: Correlation between Geboes score and Mayos endoscopic subscore (Refer Fig. 1)

<table>
<thead>
<tr>
<th>Geboes Score</th>
<th>Mayo 0</th>
<th>Mayo 1</th>
<th>Mayo 2</th>
<th>Mayo 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Grade 1</td>
<td>-</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>Grade 2A</td>
<td>-</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Grade 2B</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>Grade 3</td>
<td>-</td>
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<td>1</td>
<td>-</td>
<td>1</td>
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<tr>
<td>Grade 4</td>
<td>-</td>
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<td>1</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Grade 5</td>
<td>-</td>
<td>-</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>1</td>
<td>14</td>
<td>9</td>
<td>24</td>
</tr>
</tbody>
</table>

**Table 3**: Histological evidence of activity (Geboes score <3.1 and ≥3.1) as per the endoscopic activity (Mayo endoscopic subscore)

<table>
<thead>
<tr>
<th>Histological evidence of activity</th>
<th>Endoscopic activity (Mayo endoscopic subscore)</th>
<th>0 (Normal)</th>
<th>1 (mild)</th>
<th>2 (moderate)</th>
<th>3 (severe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geboes score &lt;3.1 Inactive disease</td>
<td></td>
<td>n=0</td>
<td>n=1</td>
<td>n=14</td>
<td>n=9</td>
</tr>
<tr>
<td>Geboes score &gt;3.1 Active disease</td>
<td></td>
<td>0</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

**Geboes score in cases of inactive colitis**

The Geboes score in cases of inactive colitis ranged from 1 to 2. Most of the inactive colitis showed a corresponding Geboes score of 2 (n=25). There were 2 cases with a score of 1.2, which showed only chronic inflammation and eosinophils in lamina propria. In cases with a Geboes score of 2, most cases showed histological features of crypt disarray (n=24), mixed inflammation in lamina propria (n=19), and eosinophils in lamina propria (n=16).

**Assessment of dysplasia**

High-grade dysplasia was absent in all the cases of active and inactive colitis in the present study, while 1 case of active colitis showed features of low-grade dysplasia. In this case, the patient was a female aged 64 years and had a history of UC for 5 years. In addition to low-grade dysplasia, the biopsies also showed cryptitis, mixed inflammation in lamina propria, crypt disarray, and basal plasmacytosis. The Geboes score was 5.1. There was one case of inactive colitis that was associated with low-grade dysplasia in a 37-year-old male with a Geboes score of 2 A. The histopathological features included crypt disarray, cryptitis, mixed inflammatory infiltrate in the lamina propria, and basal plasmacytosis. There were no cases of colorectal carcinomas in the present study.
DISCUSSION

With the steady rise in the incidence of ulcerative colitis, it is essential to apply appropriate diagnostic techniques to provide an accurate diagnosis and to reduce the associated morbidity and mortality. Histological assessment serves as a suitable marker of inflammation because disease activity detected on microscopy can persist even when there is lack of evidence of endoscopic disease activity (8).

The present study included 123 cases of UC in which the age of the patients ranged from 14 to 74 years with a mean age of 44.7 years, like the study done by Kim et al. who analyzed 154 specimens from 82 UC patients and found 47.5 years to be the mean age of the patients (5). In our study, 74 were males (60.2%) and 49 were female (39.8%). This contrasts with a study done by Jauregui-Amezaga et al., where females showed a slight predominance (51%; 6). In the present study, endoscopic findings were available in 73 cases. The most common findings included erythema and edema (n=20) followed by bleeding and friability (n=9), left-sided colitis (n=6), proctosigmoiditis (n=6), pancolitis (n=6), proctitis (n=4), pseudopolyps (n=2), deep ulcers (n=2), with the least common finding being ileocolitis (n=1). In contrast, left-sided colitis was the most common endoscopic finding in other studies conducted by Kim et al., Jauregui-Amezaga et al., and Simsek et al., (5,6,9).

Mayo subscore was available in 24 cases in the present study which ranged from 1 to 3. A Mayo subscore of 1 was noted in 1 case, and a subscore of 2 was seen in 14 cases. 9 cases had a Mayo subscore of 3. In concordance with our study, Mayo scoring was used also in studies done by Kim et al., Jauregui-Amezaga et al., and Narang et al., (5,6,10). In contrast to this, Rachmilewitz endoscopic scoring was used by Simsek et al., in their study (9).

In the present study, 96 cases of active colitis (Geboes score >3) were noted. All the cases of active colitis showed histological features of crypt disarray and mixed inflammation. Additional histological findings included cryptitis (n=94), basal plasmacytosis (n=70), crypt abscesses (n=58) and crypt regeneration (n=37). Alternative histopathological scoring methods like Harpaz HSS scoring which chiefly considers parameters like epithelial neutrophil infiltration, and the presence of ulcers or erosions were used by other authors like Simsek et al.,(9) Basal plasmacytosis which is considered an important parameter to assess activity in UC is not considered in Harpaz HSS scoring, although it was included in the present study because it has been identified previously as a variable capable of predicting relapse (6,11,12). Basal plasmacytosis predicted relapse in a multivariable analysis from patients with inactive UC(13). Simsek et al., in their study showed poor concordance between Rachmilewitz endoscopic activity index (EAI) and Harpaz histopathological activity scoring system (HSS).

Thus, the authors concluded that the management of patients with UC needs consideration of both histopathological and endoscopic results (9) which is like the present and other studies (6). In this study, most cases of active colitis had a Geboes score of 3 or 4 (n=66), followed by a score of 5 (n=30). Thus, crypt destruction and acute inflammation aid in predicting activity and relapse. These findings are like other studies (10,11).

In our study, there were a limited number of cases that had both Mayo subscore and Geboes score correlation (n=24). There was excellent reproducibility between endoscopic grading and Geboes scoring to assess disease activity in UC in the present study (Table 1). In contrast, Narang et al. studied Geboes score in patients who were in endoscopic remission (Mayo subscore ≤1) (10). Since in our study, there were no cases with a Mayo subscore of 0 and only 1 case with a Mayo subscore of 1 for correlation, we were unable to highlight the importance of the Geboes score in determining histological remission or activity in UC patients. Narang et al. in their study on 46 patients in remission endoscopically, observed histological remission in 67.3% of the patients, while the rest still showed features of histological activity. On follow-up for one year, most of the patients with histological remission were asymptomatic. However, it was noted that 12.9% of them had relapses whereas of the 15 histologically active patients, 46.6% were still in remission clinically, whereas 53.3% had relapsed. Thus, the study concluded that histological remission is a better tool to assess treatment efficacy and to ascertain sustained remission in patients with UC than endoscopic remission. These findings were like another study by Lobaton et al., (14).

In a review of colorectal cancer risk in Asian UC patients, Bopanna et al. analyzed the database of 31,287 patients with UC, in whom 293 cases were reported to have colorectal cancers. The overall prevalence was found to be 0.85%. The authors concluded that the risk of development of colorectal cancer in Asian patients with UC was like those in Europe and North America (7). In the present study, there were no cases of high-grade dysplasia or colorectal carcinomas.

CRP levels were available only in 12 cases, of which 6 cases had elevated CRP levels ranging from 11.96 – 129 mg/ L, 4 cases had normal CRP levels and 2 cases were negative. As per correlation with the Geboes score, only 22% (2/6 cases) of the cases with elevated CRP levels had active colitis (Geboes score >3) while the remaining 88% (4/6 cases) had inactive colitis (Geboes score<3). 100% (4/4 cases) of the cases with normal CRP levels had active colitis (Geboes score >3). Among the 2 cases negative for

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CRP, 1 case had active colitis (Geboes 5.1) while the other had inactive colitis (Geboes 2 B.1). Thus, there was no correlation between CRP levels and disease activity in the present study. On the contrary, Kim et al. concluded that patients with active disease had substantially higher CRP levels in comparison to those with inactive disease in their study. The authors thus concluded that assessing histological activity may be helpful in the evaluation of management outcomes and to plan patient follow-up (5). Rosenberg et al. believed that clinicians would be able to predict which patients may benefit from the assessment of endoscopic activity by taking into consideration the duration of remission and CRP level (15).

In the present study, 2 cases were showing additional findings of low-grade dysplasia. This stresses the importance of periodic surveillance by endoscopic examination along with targeted and random biopsies in detecting focal areas of dysplasia in patients with long-standing UC (16, 17).

The limitation in our study was a smaller number of cases having available Mayo scoring, only 1 case having low Mayo subscore (<1, endoscopic remission), thus limiting the results of correlation between Mayo subscores and Geboes scores, and the possibility of identifying histological remission/activity in patients who are in clinical and endoscopic remission. The major drawback with most endoscopic and histologic scoring systems is that they are not validated yet or are only partly validated. Hence more research in this regard is necessary as accurate timely diagnosis is crucial to direct treatment decisions in the future.

CONCLUSION
Assessment of histological disease activity by Geboes score provides useful information in routine reporting of biopsy specimens of cases of Ulcerative colitis. Geboes scoring along with endoscopic scoring together improve the diagnostic efficacy in Ulcerative colitis and can aid in better management of these cases.

CONFLICT OF INTEREST
The authors declare no conflicts of interest.

REFERENCES