Ulcerative colitis
An endoscopic and histopathological Comparison study

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Abstract

Background:

Ulcerative colitis is an idiopathic chronic inflammatory colonic disease characterized by relapses and remissions. It is common in Iraq.

Patients and methods:

A total of 116 patients with ulcerative colitis were evaluated endoscopically and histopathologically to determine the histological activity index according to Truelove's scale and the simplified modification of Geboes' scale. The latter was adopted in our center.

Results:

Our results showed that 24.1% of our patients had proctitis, 45.7% had proctosigmoiditis, 22.4% had subtotal colitis, and 7.8% had total colitis. The study showed that higher endoscopic grade was significantly associated with more extensive disease and higher histopathological activity index by Truelove's and modified Geboes' histological scales. Both the Truelove's and modified Geboes' histological grades systems were well correlated to each other, although the latter by its sharper criteria was easier to apply, and thus more reproducible. Higher mean eosinophilic count and inflammatory pseudopolypi were associated with more extensive disease. Goblet cell depletion showed statistically significant association with histological activity grade. Pseudopolypi, paneth cell metaplasia, and mean eosiniphilic count also correlated to the histological activity grade but the association was statistically not significant.

Conclusion:

The histological grade of colitis was strongly correlated to disease extension , endoscopic severity, and both Truelove's and modified Geboes' system. The latter was easier to apply by its sharper criteria and is expected to produce less inter-observer variation.

Introduction:

Ulcerative colitis (UC) is a chronic inflammatory condition of the colonic mucosa characterized by episodes of diarrhea with blood, abdominal pain, rectal urgency, and tenesmus. This idiopathic disease always involves the rectum and may extend proximally to involve the entire colon but not the small intestine [1]. Combined information from medical history, physical examination, endoscopic examination of the rectum and colon, and histopathological findings from colonic biopsy specimens are essential to make a correct diagnosis [1] . Based on the extent of colorectal involvement, four types of disease distribution are recognized; (1) ulcerative proctitis (2) proctosigmoiditis (3) subtotal colitis & (4) pancolitis[2]. Jewell's endoscopic disease severity grades include; (0) normal (1) loss of vascular pattern (2) granular, non-friable, mucosa (3) friability on rubbing (4) spontaneous bleeding and ulceration [3]. Microscopically; the changes are limited to the mucosa and superficial layer of the submucosa and it is characterized by inflammatory cell infiltration; in active phase, neutrophil infiltration of the crypt is commonly (crypt abscesses), together with crypt destruction, regeneration, and goblet cell depletion[4].

Original Article

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Patients and Methods:

A review of 116 patients diagnosed as having ulcerative colitis(UC)through combined clinical, endoscopic, and histopathological criteria in the center of gastrointestinal and liver diseases from Jan.1996 to the end of Dec.2001. A re-evaluation of those patients was done though subjecting them to colonoscopy or sigmoidoscopy. The severity of colitis was graded according to modified Jewell's grading system[3]. The extent of disease was recorded and biopsies were taken from diseased and normal areas. The histopathological findings of all these patients were reviewed. The determination of histological activity was according to Truelove's histological activity index[5]. We did a simplified modification of the scale proposed by Geboes [6] in order to be easier to apply, and as follows:

(0) Normal mucosa. (I) Architectural changes, focal or diffuse. (II) Expansion of lamina propria by chronic inflammatory cells. (III) Granulocytes infiltration of the lamina propria (eosinophils and neutrophils). (IV) Neutrophils in epithelium (cryptitis and crypt (1) abscess formation). (V) Crypt destruction. (VI) Erosion or ulceration of surface epithelium.

In addition, the histological assessment included evaluation of the average number of eosinophils /10HPF, presence of goblet cell depletion, paneth cell metaplasia , pseudopolypi, and dysplasia.

Statistical analysis was done performed through the help of SPSS version 7.5 computer software (statistical package for social science) in association with Excel version 5. For statistical comparison the Spearman Rank correlation coefficient test was used. The r-value when equal or more than 0.3 was considered statistically significant.

Results:

Our results showed that higher endoscopic severity grade of the patients with ulcerative colitis was associated with more extensive disease. Table [1]

Table 1: Correlation between endoscopic extension and severity grade of colitis in ulcerative colitis Patients. r–value=0.55(significant).**

Endoscopic severity grade	Proctitis	Procto-sigmoiditis	Subtotal colitis	Pancolitis	Total
GI	17 60.7%	7 13.2%	1 3.8%	0 0%	25
GII	8 28.6%	13 24.5%	7 26.9%	4 44.4%	32
GIII	3 10.7%	25 47.2%	10 38.5%	5 55.6%	43
GIV	0 0%	8 15.10%	8 30.8%	0 0%	16
Total	28 100%	53 100%	26 100%	9 100%	116

The severity of colitis endoscopically is compared to the Truelove's histological grade system in UC patients in table [2]. A significant correlation existed between Truelove's hitological grade and endoscopic grade of colitis.

Table 2: Correlation between endoscopic severity grade with Truelove's histopathological grade of colitis in ulcerative colitis patients. r-value=0.77 (significant).**

Endoscopic severity grade	Truelove's GI	Truelove's GII		Truelove's GIII
		Mild	Moderate	
GI No 27	15	8	4	0
GII No 31	0	14	9	8
GIII No 46	0	7	8	31
GIV No 12	0	0	1	11
Total No 116	15	29	22	50

The modified Geboes' histological grading system also showed a statistically significant correlation to the endoscopic severity of colitis, table [3].

Table 3: Correlation between endoscopic severity grade with modified Geboes' histopathological grade of colitis in ulcerative colitis patients . r-value=0.72 (significant).**

Endoscopic Sevirity grade	Modified Geboes' GI	Modified Geboes' GII	Modified Geboes' GIII	Modified Geboes' GIV	Modified Geboes' GV	Modified Geboes' GIV
GI No 27	12	5	6	4	0	0
GII No 31	0	1	12	10	3	5
GIII No 46	0	1	4	14	7	20
GIV No 12	0	0	0	1	0	11
Total No 116	12	7	22	29	10	36

The degree of mucosal infiltration by eosinophils, presence of pseudopolypi, and dysplasia in various endoscopic grades of UC patients is shown in table [4]. Generally pseudopolypi is associated with high grade of colitis, while dysplasia was diagnosed in one patient only. Mean eosinophilic infiltration count was higher in more severe cases of colitis.

Table 4: Correlation between endoscopic severity grade of colitis with eosinophilic count, psudopolypi, and dysplasia in ulcerative colitis patients. r-value=0.18(not significant) for eosinophilic count, r-value=0.1(not significant) for pseudopolypi.

Endoscopic severity grade	Eosinophils count /10HPF		Pseudopolypi	Dysplasia
	Range	Mean		
GI No 27	1-150	75	0	0
GII No 31	7-225	116	2	0
GIII No 46	10-500	225	4	0
GIV No 12	10-395	202	2	1

Table [5] shows the incidence of variable histological features including eosinophilic infiltration, paneth cell metaplasia, goblet cell depletion, pseudopolypi, and dysplasia in different activity grade of UC in the modified Geboes' activity scale. A statistically significant correlation was observed for goblet cell depletion with increasing histological grade, while not significant for pseudopolypi, paneth cell metaplasia, and eosinophilic count. Dysplasia was uncommon.

Table 5:Correlation between modified Geboes' histopathological grade of colitis with eosinophils count, paneth cell metaplasia ,psudopolypi, and dysplasia in ulcerative colitis patients.
r-value=0.86**(significant) for goblet cell depletion
r-value=0.23(not significant) for pseudoplypi.
r-value=0.01(not significant) for paneth cell metaplasia.
r-value=0.2(not significant) for eosinophils count.

Modified Geboes' grade	Eosinophils count /10HPF		Paneth cell metaplasia	Goblet cell depletion	Dysplasia	Pseudo polyp
	Range	Mean				
GI No 12	9-48	28	1	1	0	0
GII No 7	18-150	84	0	1	0	0
GIII No 22	7-200	103	3	16	0	0
GIV No 29	1-500	250	6	29	0	0
GV No 10	10-225	117	3	10	0	0
GVI No 36	10-401	205	4	36	1	8

When the various histological parameters were correlated to the histological grade of inflammation in Truelove's activity scale, Table [6], a positive correlation was observed between goblet cell depletion and grade of inflammation in UC patients. A non-significant correlation was observed between grade of inflammation and pseudopolypi, paneth cell metaplasia,and mean eosinophilic count.

Table6: Correlation between Truelove's histopathological grade of colitis with eosinophils count , paneth cell metaplasia ,psudopolypi, and dysplasia in ulcerative colitis patients.
r-value=0.82(significant) for goblet cell depletion.**
r-value=0.19(not significant) for pseudopoylpi.
r-value=0.03(not significant) for paneth cell metaplasia..
r-value=0.25(not significant) for eosinophilic count.

Truelove's grade	Eosinophils count /10HPF		Paneth cell metaplasia	Goblet cell depletion	Dysplasia	pseudopolyp
	Range	mean				
GI No 15	8-120	64	1	1	0	0
GII-mild. No29	7-200	103	5	20	0	0
GII-moderate No 22	1-500	250	6	22	0	0
GIII-severe No 50	4-410	207	5	50	1	8

The Geboes' system for grading of inflammation with its sharply defined criteria is compared to Truelove's grading system with its more or less descriptive criteria for patients with ulcerative colitis in table [7], both systems revealed an excellent statistically significant correlation with each other.

Table 7:Correlation between modified Geboes' histopathological grade of colitis with truelove's histopathological grade in patients with ulcerative colitis. r-value=0.92(significant).**

Truelove's Grade	Modified Geboes' GI	Modified Geboes' GII	Modified Geboes' GIII	Modified Geboes' GIV	Modified Geboes' GV	Modified Geboes' GVI
GI No 15	12	3	0	0	0	0
GII-mild. No 29	0	4	19	6	0	0
GII-moderate No 22	0	0	3	18	1	0
GIII-severe No 50	0	0	0	5	9	36

The endoscopic extent of inflammation in UC patients was compared to histological activity grade by modified Geboes' & Truelove's system (table [8] & [9] respectively). In both, more extensive disease was associated with a higher grade of inflammation (statistically significant).

Table 8: Correlation between modified Geboes' histopathological grade of colitis with endoscopic extension of disease in patients with ulcerative colitis. r-value=0.37* (significant).

Endoscopic extension of disease	Modified Geboes' GI	Modified Geboes' GII	Modified Geboes' GIII	Modified Geboes' GIV	Modified Geboes' GV	Modified Geboes' GVI
Proctits No 28	7	3	8	7	2	1
Procto-sigmoiditis No 53	4	4	7	15	5	18
Subtotal colitis No 26	1	0	4	5	3	13
Pancolitis No 9	0	0	3	2	0	4

Table 9: correlation between Truelove's histopathological grade of colitis with endoscopic extension of disease in patients with ulcerative colitis. r-value=0.37* (significant).

Endoscopic extention of disease	Truelove's GI	Truelove's GII		Truelove's GIII
		Mild.	Mod.	
Proctits No 28	9	10	6	3
Proctosigmoiditis No 53	5	11	10	27
Subtotal No 26	1	5	4	16
Pancolitis No 9	0	3	2	4

Discussion:

Ulcerative colitis is relatively a common disease in Iraq. It is a chronic relapsing disease, and accurate assessment of disease activity is essential for evaluation of the effect of treatment and for prediction of prognosis. A number of clinical activity indices have been described for patients with inflammatory bowel disease however, it is thought that the emphasis placed on them in clinical trials is misplaced [7] and it seems that colonoscopic and histopathological evaluations are best for assessing therapeutic benefit [7].

The extent of UC in this study was different from that reported by AL-Akashi & Shubbar [8] . In our study proctitis formed 24.1% of cases, proctosigmoiditis 45.7%, subtotal colitis 22.4%, pancolitis 7.8%. The corresponding figures by AL-Akashi & Shubbar were 31.7%, 15.6%, 23%, & 30%.

The use of colonoscopy in detection of mucosal disease, its severity, and extent is well-established [9] . Moreover, an endoscopic severity index is used commonly and well agreed upon [10] . However, grading of histological activity is of limited value and its grades have not agreed upon.

Different histological scoring systems have been designed for measurement of disease activity in ulcerative colitis [11] . Usually they combine chronic and acute changes, and epithelial as well as inflammatory features. Microscopic activity is based on the presence of neutrophils and is defined as unequivocal damage of surface and crypt epithelium in conjunction with neutrophils. The latter appear to be the effector cell causing epithelial damage [12].

In this study two systems were evaluated to determine disease activity in ulcerative colitis patients. An older system proposed by Truelove in 1955 [5] which is a three grade system, simple yet subjective. The second is our simplified modification of a newer system proposed by Geboes et at in 2000 that defined six grades [6].

The use of both these histological grading systems showed generally good correlation with endoscopic grading and to each other but we expect the modified Geboes' by its sharp criteria to produce less inter-observer variation and more reproducible results.

Healthy & James (1978) [13] have found that increased eosinophilic count in mucosa of UC patients correlates with better response to therapy. In this study it was found that the mean eosinophil count was higher with increasing grade of activity. However, assessment of their relationship to prognosis and response to therapy requires pre-treatment and post-treatment evaluation.

Inflammatory polyps were found in 7% of patients in this study and generally associated with more severe disease. It is generally accepted that these pseudopolypi are the consequence of severe mucosal damage, occurring in 10-20% of cases [14]; most commonly following severe total colitis, and have a positive correlation with toxic dilatation of the colon, but with no relationship to the chronicity of the disease [15].

Goblet cell depletion is a typical feature of UC, but it can be seen in any form of colitis. Its severity is related to the amount of inflammation present [16] . In this study goblet cell depletion was more severe with increasing histological activity grade both in modified Geboes' and Truelove's grading system.

Paneth cell metaplasia is rarely seen distal to ascending colon normally. Increasing number of paneth cell is a recognized features of UC, but it is not a specific feature [16] , and should not be considered a reliable diagnostic criteria. Mild paneth cell metaplasia was seen in 14.7% of UC patients. However, in this study presence of paneth cell metaplasia did not correlate with disease activity grade or duration of the disease.

A significant correlation of disease activity grade both endoscopically and histologically with the extent of disease was seen in this study.

The extent of colonic involvement in UC positively correlates to clinical severity of the disease and with poor long term prognosis [17] . Histological evaluation has been shown to be a more sensitive tool than endoscopy alone for determination of disease activity, thus colonoscopy with multiple biopsies has come to be recommended routine investigation for diagnosis and follow up of UC patients.

Conclusion:

The histological grade of colitis was strongly correlated to disease extension and endoscopic severity. Both Truelove's and modified Geboes' system were of practical value in this regard. However, the latter was easier to apply due to its sharper criteria, and it is expected to produce less inter-observer variation.

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