Correlation between Clinical, Endoscopic, Biochemical and Histological Activity in Patients of Ulcerative Colitis

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ABSTRACT

Introduction: The correlation between clinical, endoscopic, biochemical and histological activity have been studied to see the severity of Ulcerative colitis. There are not many studies using these parameters in our country, so we planned a study to study correlation between these indices.

Material and methods: All consecutive patients of UC in age group 15-80 years attending GE Clinic in MM Hospital Mullana from April 2018 to April 2019,were enrolled. Diagnosis of UC was made by endoscopic picture and histopathology of colonic biopsies. Patients suffering from Crohn's colitis, TB colitis, allergic colitis and pseudomembranous colitis were excluded. Clinical activity was assessed with Partial Mayo Score (PMS) (activity ≥3), endoscopic activity with the Mayo Endoscopic Subscore (MESS) (activity ≥2) and histological activity by the Geboes Simplified Score (GSS) for UC (activity ≥3.1) and biochemical activity by CRP and ESR.

Results: UC cohort included 59 patients (M 28 [42.9%], median age 39 [15–75] years, median UC duration 1 year [0.02–20] years). Extent of disease was : pancolitis: 18(30.5%), left sided : 36(61%), proctitis : 5(8.5%) patients. Endoscopic activity was graded by MESS: (mild[15]; moderate[23]; severe[21]). In UC, microscopic activity (GSS ≥ 3.1) was observed in all patients. Highly significant correlation was observed between PMS vs. MESS ($r = 0.730$; $p < 0.001$); PMS vs. GSS ($r = 0.931$; $p < 0.001$) and MESS vs. GSS ($r=0.788$; $p < 0.001$). Highly significant correlation was observed between CRP and PMS ($r=0.725$, $p<0.001$); CRP vs. MES ($r=0.599$, $p < 0.001$) and CRP vs. Geboes Score ($r=0.764$, $p <0.001$). Moderately significant correlation was observed between ESR and PMS ($r=0.306$, $p =0.018$); ESR vs. Geboes Score ($r=0.270$, $p =0.038$). No significant correlation was observed between ESR and MES ($r=0.248$, $p=0.059$).

Conclusion: In this cross sectional study, significant correlation was observed between clinical, endoscopic, biochemical and histological activity in UC patients predicting the severity of disease.

Keywords: Ulcerative Colitis, Endoscopic Activity, Microscopic Activity, Histological Activity

INTRODUCTION

Diagnosis of UC is based on clinical, endoscopic and histo pathological findings. Mucosal assessment by colonoscopy is the best option in the diagnosis of ulcerative colitis.[1]

The erythrocyte sedimentation rate (ESR) and serum concentration of C-reactive protein (CRP) are potential laboratory surrogate markers for disease activity in ulcerative colitis (UC). Some studies have examined the relationship between CRP and another measure of disease activity such as clinical, endoscopic, or radiologic activity in patients with IBD.[2-6] No method has proven to be perfect in assessing disease activity. In addition, mucosal healing is proved to be related to sustained clinical remission, decreased admission in hospital, decreased need for surgical intervention and reduced risk of cancer.[7–10] However, endoscopic findings aren't according to histological activity and have a tendency to underestimate the degree of mucosal damage, relative to the histological findings.[11,12] Several studies have proved that histological improvements are related to better clinical outcomes, including reduced relapse rates and cancer risk, these studies refer to histological remission as a treatment goal in UC.[13–15] Amongst all these indices, the Geboes score shows decent reproducibility and moderate agreement with the endoscopic scoring system.[16]

It's important to workout the correlation between disease activity indices and to our knowledge, there is limited data available regarding these relationships; therefore this study was designed to investigate the relationship between clinical severity, endoscopic findings, histological findings & laboratory markers in patients of ulcerative colitis.

MATERIAL AND METHODS

This prospective study was conducted in the Department of Gastroenterology, MMIMSR, Mullana from May 2018-April 2019, with a sample size of 50 patients. Patients with a clinical diagnosis of ulcerative colitis, underwent colonoscopic examination and histologically confirmed cases of ulcerative colitis were included. Patients with Infectious enterocolitis, Colorectal cancer, Crohn's disease, Indeterminate colitis, Pregnancy, History of colorectal operation, NSAID or intake of aspirin (≥2 tablets/week) were excluded. Ethical clearance was taken from institutional committee of Maharishi Markandeshwar (deemed to be) university.

Assessment of disease activity: Detailed history about clinical

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presentation, duration of illness, past history, personal and family history, environmental and psychological factors prior to the onset of disease was obtained from the included patients. Hemoglobin, total leukocyte count, packed cell volume, ESR, and CRP levels were done. Laboratory test results outside the reference ranges were treated as abnormal. Disease severity was assessed using Partial Mayo Score (PMS) and were classified into mild, moderate and severe disease respectively. Endoscopic assessment and grading was done for all patients with the help of Mayo endoscopic subscore. The Mayo endoscopic subscore classified the disease as inactive disease and normal mucosa, mild disease, moderate disease, or severe disease.

Biopsies was taken as required and was sent for tissue diagnosis. The slides were graded using the Geboes grading system.[16]

Diagnosis of UC was made by combination of clinical findings, endoscopic appearance, blood investigations and histopathological examination. Only histopathologically confirmed cases during the study period were taken for this study.

STATISTICAL ANALYSIS

The statistical software package SPSS for windows version (SPSS Inc, Chicago III) was used to analyse the data. Mean and standard deviations were used to summarize data for continuous variables whereas percentages were used for categorical variables. Spearman's rank order correlation coefficient (r) was used to estimate correlation between variables. p values of <0.05 were considered significant.

RESULTS

Patient's characteristics: The baseline characteristics of the 82 patients are summarized in Table 1.

Highly significant correlation was observed between PMS vs. MES ($r = 0.730$; $p < 0.001$); PMS vs. Geboes score ($r = 0.931$; $p < 0.001$) and MES vs. Geboes score ($r=0.788$; $p < 0.001$). Correlation between Geboes score, Partial Mayo score (PMS) and Mayo Endoscopic Subscore (MES) summarized in table 2 and Figure1.

Highly significant correlation was observed between CRP and PMS ($r=0.725$, $p<0.001$); CRP vs. MES ($r=0.599$, $p < 0.001$) and CRP vs. Geboes Score ($r=0.764$, $p <0.001$). Moderately significant correlation was observed between ESR and PMS ($r=0.306$, $p =0.018$); ESR vs. Geboes Score ($r=0.270$, $p =0.038$). No significant correlation was observed between ESR and MES ($r=0.248$, $p=0.059$) [Table 3.]

Number of patients	**59**
Male (%)	28(47.5%)
Age (years, mean ± SD)	38.9 ±13.94
Duration of disease(years,mean ± SD)	3.20 ± 4.32
Extent of UC (%)	
Proctitis	5(8.5%)
Left sided colitis	36(61%)
Extensive colitis	18(30.5%)
Clinical disease severity (partial mayo score	
Mild	8(13.6%)
Moderate	28(47.5%)
Severe	25(39%)
Endoscopic disease severity (mayo endoscopic sub score)	
Mild	15 (25.4%)
Moderate	23(39%)
Severe	21(35.6%)
CRP (mean ± SD)	31.10 ± 49.11
ESR (mean ± SD)	48.60 ± 26.02

Table-1: Baseline patient characteristics

			Geboes score	**PMS**	**MES**
Spearman's rho	Geboes score	Correlation Coefficient	1	.931**	.788**
		Sig. (2-tailed)	.	<0.001	<0.001
		N	59	59	59
	PMS	Correlation Coefficient	.931**	1	.730**
		Sig. (2-tailed)	<0.001	.	<0.001
		N	59	59	59
	MES	Correlation Coefficient	.788**	.730**	1
		Sig.(2-tailed)	<0.001	<0.001	.
		N	59	59	59
**. Correlation is significant at the 0.01 level (2-tailed).					
PMS- Partial Mayo score. MES- Mayo Endoscopic Subscore. N- number of patients					

Table-2: Correlation between Geboes score, PMS and MES

			PMS	MES	Geboes score
Spearman's rho	CRP	Correlation Coefficient	.725**	.599**	.764**
		p value	<0.001	<0.001	<0.001
		N	59	59	59
	ESR	Correlation Coefficient	.306*	0.248	.270*
		p value	0.018	0.059	0.038
		N	59	59	59
PMS- partial Mayo score. MES- Mayo endoscopic subscore. N- number of patients					

Table-3: Correlations Correlation between lab parameters (CRP,ESR) and Geboes score, PMS and MES

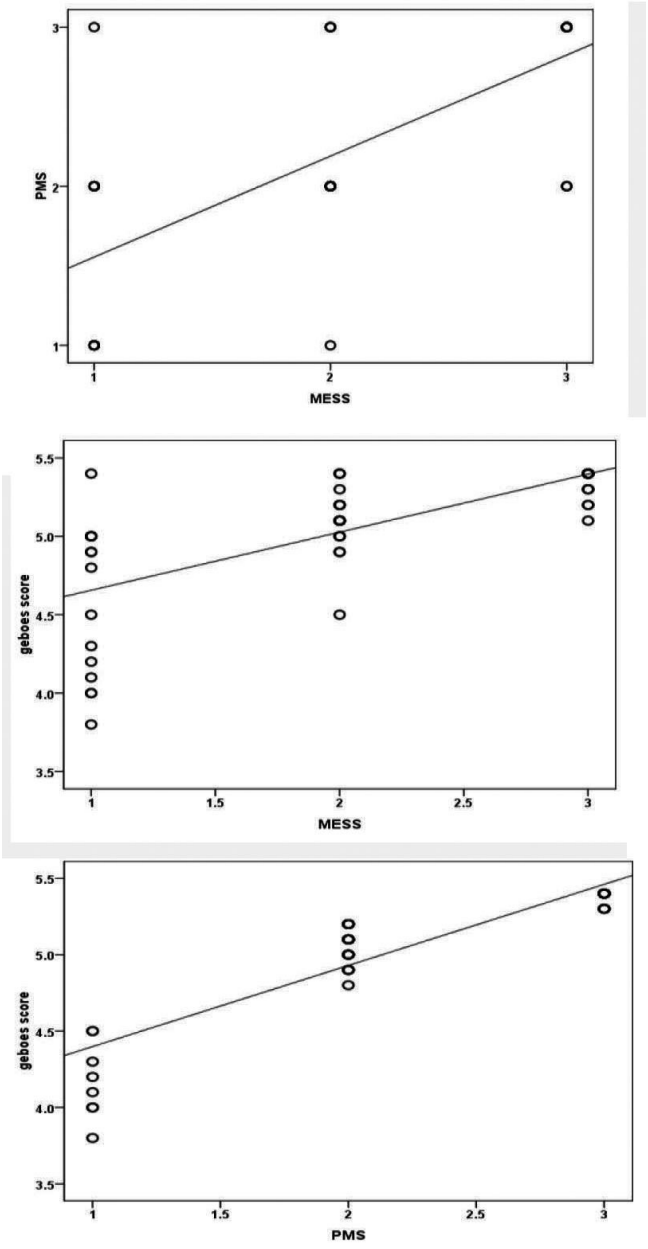

Figure-1:

DISCUSSION

In our study, age ranged from 15 -75 years with mean age of 39 years. The maximum number of patients were in the 4th decade.

In this study, females were affected slightly more than males, the ratio being 1.10:1. Another study by Tandon et al, Delhi, the male to female ratio was 1.5:1. The male-to-female ratio of about 1 : 1 was found in all age groups.[17]

In this study, 47.5% patients had disease duration from 1 to 5 years and 30.5% patients had less than 1 year disease duration. Mean duration of illness was 3.2 years.

On the basis of partial mayo score 47.5% patients had moderate disease severity and 39% had severe disease as per partial mayo score. 13.6% patients had mild disease.

61% patients had left sided colitis and 30.5% had pan colitis. Only 8.5% patients had disease limited to rectum.

In a study from India half of the patients had left sided colitis (47.5%), proctosigmoiditis in 25% and pancolitis in 27.5%.[18] Diarrhoea and rectal bleeding were the commonest clinical presentation. Patients having pancolitis had severe disease presentation clinically. 39% patients had moderate disease and 35.6% patients had severe disease, as per Mayo Endoscopic Subscore (MES).

Since all the patients who were enrolled for the study had active disease, minimum geboes score in our study was 3.8. And as per Kim et al[19], any score more than 3.1 was taken as active histological inflammation, so all our patients had histologically active disease.

In this study CRP had a positive correlation with the severity of the disease. Highly significant correlation was observed between CRP and clinical, endoscopic and microscopic activity. Moderately significant correlation was observed between ESR and PMS; ESR vs. Geboes Score. No significant correlation was observed between ESR and MES. Similar result was seen in another study from Rochester.[20]

CRP has been proven to be more useful in CD than in UC, as per previous studies likely because in CD the inflammation is transmural; compared to only mucosal inflammation in UC.[21] In UC patients, Yoon et al. found that CRP had a low sensitivity (53%) and specificity (71%) to detect endoscopic remission.[22] ESR was proven to be accurate biomarker to assess the endoscopic activity in UC but its sensitivity (52%) and specificity (79%) were also low proving it to be of very limited utility in IBD.[22,23] In a study by Solem et al, CRP had significant correlation with clinical disease activity and endoscopic activity but not histological activity.[20] Osada et al study concluded that ESR was relatively well correlated with both endoscopic and histological scores, with a higher degree of correlation than CRP, which was quite different compared to our study.[24]

In our study, highly significant correlation was observed between PMS vs. MES; PMS vs. Geboes score and MES vs. Geboes score.

Powell tuck et al found significant correlation between

clinical and endoscopic activity.[25] In study by Osada et al[24], endoscopic and histological activity correlated well with each other as well as with clinical activity. Correlation between clinical and histological activity was highly significant compared to clinical and endoscopic activity. In study by Fluxa et al[26], the Mayo Endoscopic Subscore correlated moderately with clinical and histologic scores. In this study, histologic activity had a moderate correlation with endoscopic activity and that both the Geboes Score and the basal plasmacytosis were predictive of endoscopic active disease. Study by Kim et al[19] included 82 patients, reported that Geboes Score was strongly correlated with Mayo Endoscopic Subscore ($r = 0.774$, $p<0.001$); and Geboes Score was moderately correlated with the Partial Mayo Subscore ($r = 0.403$, $p<0.001$). In contrast to our study, this study demonstrated weak correlation between partial mayo score and geboes score. The disparity between clinical activity with endoscopic and histological activity may be because of irritable bowel syndrome like symptoms[27], which was not the case in our study.

No major complications were encountered during this study. Recent colonoscopy is associated with a flare in UC.[17] The limitations of our study were that only symptomatic patients were enrolled in the study and underwent colonoscopy, so selection bias could have been there. Fecal calprotectin was not checked which is a promising biomarker of disease activity in Ulcerative Colitis. Our sample size was small and we used Geboes scoring system and Mayo scoring system for this study. Results could have changed if other indices were used.

CONCLUSION

A combination of clinical examinations, endoscopy, histology, and serology are required to monitor disease activity in patients with UC and it is essential to establish the relationship between the disease activity indices in managing ulcerative colitis patients. We also tried the same and obtained significant correlation between all the parameters using various indices.

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