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Otiginal Article

Red Cell Distribution Width Levels and Disease Activity in Ulcerative Colitis

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ABSTRACT

Background:
The amount of literature concerning the implication of the red cell distribution width (RDW) in the assessment of ulcerative colitis (UC) activity is rather limited. The aim of this study is to investigate the potential role of RDW in the evaluation of UC disease activity.

Materials and Methods:
A total of 96 patients with UC and 51 age and sex-matched healthy volunteers were included in a cross-sectional study. Clinical disease activity was defined using the numerical Disease Activity Index (DAI). In addition to RDW, serum C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), and platelet counts (PLT) were measured.

Results:
AThere were 47 (about 49%) patients with that had active UC. The RDW was significantly higher in patients with UC than in controls ($p=0.001$) and active versus patients in remission ($p<0.001$). RDW was significantly correlated with DAI scores, ESR, CRP and PLT in active patients. There was a significant correlation between RDW with DAI scores and CRP levels in patients who were in remission.

Conclusion:
RDW was elevated in UC patients in comparison with healthy controls and increased markedly in active disease. It was also strongly correlated with clinical disease activity scores and inflammatory parameters such as ESR and CRP. RDW, as a cost-effective tool, may be an additional parameter to assess disease activity in UC.

Keywords: Ulcerative colitis; Disease activity; RDW

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INTRODUCTION

Ulcerative Colitis (UC) is a form of chronic inflammatory bowel disease (IBD) of an unknown etiology that is characterized by recurring periods of remission and exacerbation (1). Recent studies suggest the number of UC patients that visit gastrointestinal clinics has been increasing gradually in Iran (2). Dysregulated immune responses (1,3) in addition to active participation of cellular systems such as platelets (4,5) play main role in the pathogenesis of UC. The

determination of disease activity in IBD patients relies on both noninvasive laboratory parameters and endoscopic procedures (6). However, endoscopic procedures are both expensive and invasive (7). Other assays used to determine inflammation in IBD patients that have been assessed in previous studies include alterations in the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), albumin, and hemoglobin (Hgb) levels, and platelet counts (PLT). However, the sensitivity and specificity of these tests for monitoring IBD disease activity are low (8-10). According to recent studies, fecal calprotectin, lactoferrin and polymorphonuclear neutrophil elastase tests are highly sensitive and specific, however are expensive and not available in many medical centers (11,12) Therefore, there is a need for a readily available, non-invasive, highly specific marker to evaluate disease activity in IBD.

The red cell distribution width (RDW) is a component of the complete blood count (CBC) and has been hypothesized to be associated with several disease processes including occult colon cancer, liver disease, heart failure and celiac disease (13-17) Recently, a few studies have pointed to a possible role of RDW in IBD as an additional inflammatory and disease activity marker (18-20). However the significance of this novel marker (RDW) in assessment of disease activity in patients with UC is still uncertain. This study carried out to assess the correlation of RDW with clinical disease activity and inflammatory parameters in UC patients.

MATERIALS AND METHODS

Patient population

A total of 96 patients with UC (47 active and 49 in remission) who were followed at the Department of Gastroenterology of the University Hospital and Outpatient Clinic of Tabriz, Iran were included in this cross-sectional observational study. All patients had a definitive diagnosis of UC confirmed by radiological, endoscopic, and histological studies. Furthermore, the clinical and laboratory parameters of these patients were reviewed to confirm the diagnosis. In addition to the UC patients, 51 healthy control subjects who were matched with the patients in terms of age and gender participated in the study. Subjects who took any medications were not included in the control group. The disease activity was classified according to the Disease Activity Index (DAI) criteria for UC as remission and active (21). The presence of renal failure, malignancy and connective tissue diseases were criteria for exclusion from the study. Informed consent was obtained from all patients and the study was approved by the local Ethics Committee.

Laboratory parameters

Hematological parameters that included Hgb (range: 14-18 g/dL for men, 12-16 g/dL for women), white blood cell count (WBC; range: 4,000-10,000/mm), PLT (range: 150,000-450,000/mm) and RDW (range: 11%-14%), were analyzed by standard methods. ESR and CRP were also measured.

Statistical evaluation

All continuous variables were presented as mean ± SD. Normal distribution of data was assessed by the one-sample Kolmogorov-Smirnov test. Comparisons of parametric data between study subjects and controls were performed by the independent t- and one-way ANOVA tests. Partial correlation analysis was used to analyze the relationship between RDW and ESR, CRP, WBC, PLT, and DAI. All statistical analyses were performed using SPSS 15.0 (SPSS Inc., Chicago, IL). p - values <0.05 were considered statistically significant.

RESULTS

Demographic and clinical characteristics of the

Table 1: Age distribution of 165 cases.

Characteristics	Control group (n=51)	UC (n=96)
Age (years)	36.16±11.52	35.26±12.41
Sex (F/M)[#]	24/27	42/54
Duration of disease (y) [£]	-	3 (1–8)
Distribution of disease	-	26
Proctitis	-	48
Left-side colitis	-	22
Pancolitis	-	
Disease activity (DAI)		
Active	-	47
Remission	-	49

[#]: Number of females/males
[£]: median (P25 – P75)

controls and UC patients are shown in Table 1. No significant differences were found between the UC patients in the study compared with the control group in terms of age and gender.

Laboratory test findings from patients with UC compared to those from the control group are presented in Table 2. RDW was significantly higher in patients compared to controls (p=0.001). The RDW percentage in active UC patients (16.23±3.28) was significantly higher than in UC patients in remission (13.74±1.55; $p<0.001$).

CRP and ESR levels in patients with active UC were found to be significantly higher than those from UC patients in remission. Similar results were observed in patients with UC versus the control group. No statistically significant differences were found between the PLT counts of UC patients in remission and the control group ($p=0.531$).

RDW was significantly correlated with inflammatory markers (Table 3) as well as DAI scores (Figure 1). As anemia may lead to misevaluation of RDW, (17) we used partial correlation to exclude hemoglobin as a confounding factor.

Correlation analysis showed that increased inflammatory parameters such as ESR, CRP and PLT were significantly correlated with elevated RDW levels in patients in the active phase of their disease. In addition, the inflammatory parameters themselves were significantly correlated. Among patients in remission, there was only a meaningful relation between RDW and CRP levels. Clinical disease activity scores were well correlated with RDW percentages in both the active ($p=0.007$) and remission phases ($p=0.01$).

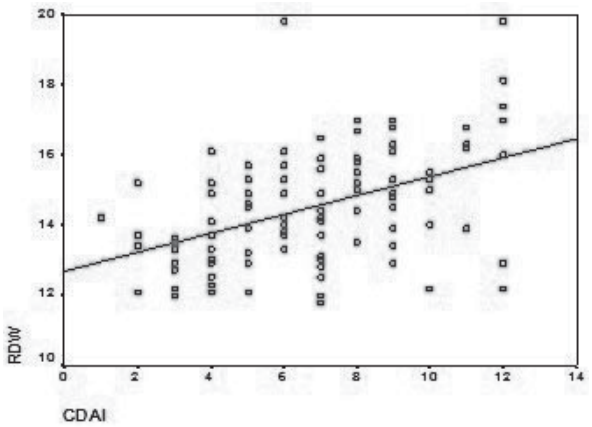

Fig.1: Correlation between RDW levels and clinical disease activity index (DAI) scores.

DISCUSSION

The induction of remission and its maintenance are two major purposes in UC treatment. Thus identification of non invasive, easy to perform and available tests for assessment of disease activity seems necessary. In the present study, the potential association of RDW with clinical disease activity and inflammatory markers has been evaluated. Significant increases in RDW, ESR, and CRP were observed in the UC groups compared to the control group. We also observed a significant increase in RDW, ESR and CRP in the active disease periods of the UC group compared to patients in remission. Our findings have also demonstrated a correlation between ESR, CRP, clinical disease activity and RDW in UC.

The RDW is derived from pulse height analysis and is the width of the red cell size distribution curve in fL at the 20% level of the peak. RDW can also be expressed as the CV% of the measurements of the red cell volume. It is a quantitative measurement of variation in red cell size and is equivalent to anisocytosis seen on the examination of a stained blood film (22).

In recent years, many studies have investigated alterations in RDW in association with cardiac (especially heart failure) and noncardiac deaths. These studies have reported a correlation of RDW with ESR and CRP such that RDW increases during inflammation, similar to the increase seen in other inflammatory parameters, and have suggested that RDW might increase due to chronic inflammation (16, 23). Lee et al. have investigated the potential correlation of RDW with ESR and CRP in patients with rheumatoid arthritis, an inflammatory disease, and found a correlation between RDW and CRP in both the anemic and nonanemic groups (24). Lippi et al. conducted a large-scale cohort study on 3845 subjects and investigated the correlation of RDW with ESR and CRP. They concluded that RDW increased during inflammation, similar to the increase seen in other inflammatory parameters (25).

The amount of literature concerning the implication of RDW in the field of IBD is rather limited. In a study conducted by Cakal et al. the correlation between IBD disease activation state and RDW was investigated (18). This study included a total of 96 patients (74 UC patients and 22 Crohn's disease patients). The researchers observed that RDW significantly increased during active disease in both UC and CD patients compared to RDW in patients in remission and the control group. Similarly we found a significant increase in RDW compared to the control group and active patients versus those in remission. In addition, a correlation between elevated RDW levels and CRP and ESR levels was

Table 2: **Comparison of laboratory parameters between ulcerative colitis (UC) patients and controls.**

Parameters	Control group	UC group		*p*-value*
		Active (n=47)	Remission(n=49)	
RDW (%)	12.5±0.8	16.23±3.28	13.74±1.55	<0.001
Hgb (g/dL)	14.02±0.84	10.79±2.83	14.02±1.95	0.006
WBC (×103 /µL)	7.11±1.43	8.70±4.23	14.02±1.95	0.040
PLT (×10 3/µL)	289.31±131.22	294.47±143.96	303.73±126.11	0.231
ESR (mm/hr)	7.31±1.7	21.4±10.1	10.5±5.9	<0.001
CRP (mg/dL)	0.32±0.13	1.23±0.94	0.51±0.22	0.002

WBC: White blood cell; Hgb: Hemoglobin; PLT: Platelet count; RDW: Red blood cell distribution width; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein.
*One-way ANOVA test (between control and UC groups)

Table 3: **Correlation between RDW and other inflammatory markers in ulcerative colitis (UC).**

Variables	Active				Remission			
	R_+	$R_‡$	p	p_{adj}	R_+	$R_‡$	p	p_{adj}
PLT (×10^3/µL)	0.331	0.263	0.020	0.041	0.201	0.127	0.132	0.342
ESR (mm/hr	0.460	0.311	<0.001	0.006	0.271	0.269	0.064	0.082
CRP (mg/dL)	0.403	0.289	<0.001	0.008	0.381	0.270	0.003	0.012

$_+$: Pearson correlation
$_‡$: Partial correlation (adjusted for Hgb)

found. Sensitivity and specificity analysis for the RDW test showed 75% sensitivity and 86% specificity in UC patients and a 63% sensitivity and 92% specificity observed in CD patients. Thus, it was concluded that RDW was significantly higher in active IBD patients and that an increase in RDW was the most sensitive and specific test for the determination of active disease in UC patients. Recently, Yesil et al. (20) demonstrated elevated levels of RDW in IBD patients compared to healthy controls. Their findings indicated a strong correlation between RDW and CRP, ESR and PLT counts. According to Receiver operating characteristic (ROC) analysis, ESR was an important marker of active UC, while RDW was a sensitive and specific marker for determining active CD. These data have suggested that RDW levels increase in the presence of inflammation in a similar fashion to other inflammatory parameters; thus, RDW can be considered to be an indicator of active inflammation.

Clarke et al. (19) observed a significant difference in RDW values between CD and UC groups, however did not categorize patients according to disease status. In their study RDW was used to distinguish between CD and UC. When the RDW cutoff value was set at 14%, RDW could be used as a specific indicator for determining the disease activity in UC and CD patients.

Shen et al. (26) have shown that PLT counts were higher in CD and UC patients than healthy controls, which contrasted our study results. However they determined significant associations of PLT and PDW with disease activity only in patients with active UC. Similarly we found a direct relation between PLT with DAI, but not RDW.

Thus, similar to other parameters such as CRP and ESR, the determination of RDW will also help clinicians to determine the presence of active disease. Nutritional deficiencies and related anemia are frequently observed in the IBD patient group. In addition, due to replacement therapies and transfusions, elevated RDW levels are also frequently present (20). Although simple hematologic tests are routinely performed in most patients, sufficient attention is not often paid to RDW, except for its use in the evaluation of anemia.

In conclusion, our study has demonstrated elevated RDW results in UC patients compared to healthy controls and in active patients versus those in remission. RDW

was well correlated with clinical disease activity and inflammatory markers (ESR and CRP) in patients with active disease. As RDW is a routine CBC parameter that can be determined using an automatic blood counting device, it is an easy, accessible and affordable test to evaluate early stage disease response to treatment and clinical follow-up. Further studies are needed to better understand the importance of the increased RDW observed in UC patients with active disease.

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