

Importance of red blood cell distribution width (RDW) in patients with upper gastrointestinal haemorrhage

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Abstract

Objective: To explore the effect of red blood cell distribution width levels on the diagnosis and management of upper gastrointestinal haemorrhage.

Methods: The retrospective study was conducted at Ankara Numune Education and Research Hospital, Turkey, and comprised record of patients diagnosed with upper gastrointestinal haemorrhage from January 1, 2013, to December 31, 2013. Factors analysed were age, gender, red blood cell distribution width level, admission haemoglobin and haematocrit levels, endoscopy findings classified according to the Forrest system, comorbid diseases, use of medications, unhealthy habits like alcohol usage and smoking, and mortality rate.

Results: Of the 147 patients, 93(64%) were men. The overall median age of the sample was 60 years. Besides, 117(79.6%) patients had comorbid diseases, of which hypertension 56(38.4%) was the most common. A total of 24(16.8%) patients were using antiplatelet or anticoagulant drugs, while 30(20.5%) were on non-steroidal anti-inflammatory drugs. Peptic ulcer in 128(87.1%) patients was the most common cause of haemorrhage. The median red blood cell distribution width level of the study population was 15.25% which was significantly higher compared to the reference values ($p<0.05$). In contrast, haemoglobin 9.55% (3.7) and haematocrit 28.75% (10.8) were significantly lower ($p<0.05$). Mortality rates were significantly higher in patients with higher red blood cell distribution width values ($p<0.05$).

Conclusion: Red blood cell distribution width levels were higher during the acute phase of upper gastrointestinal haemorrhage.

Keywords: Gastrointestinal haemorrhage, Red blood cell distribution width, Emergency. (JPMA 66: 151; 2016)

Introduction

Upper gastrointestinal haemorrhage (UGIH) is an important cause of emergency admissions.¹ Peptic ulcer is the most common cause of UGIH with a prevalence of 52-170/100000 in different studies.² About 70-80% of UGIH is self-limited, but overall mortality is 7-10%, which makes UGIH a significant emergency condition.^{3,4}

Older age, comorbid diseases, medications and unhealthy habits like alcohol usage and smoking are common risk factors for UGIH.^{5,6}

In Turkey, endoscopy is usually difficult to reach in emergency units. Moreover, medical history and physical examination may sometimes not be useful to make the diagnosis and decide management approach, especially in debilitated patients due to the nature of the condition and because of the overcrowding in emergency

departments (EDs). These conditions together complicate the treatment of haemorrhagic patients and prolong hospitalisation time. For these reasons, there is a need for novel parameters to help clinicians diagnose UGIH in acute settings.¹

Red blood cell distribution width (RDW) is a marker that increases in emergency situations as acute myocardial infarction (AMI) and acute cerebrovascular events.⁷⁻⁹ As far as we know no study has yet investigated the relationship between UGIH and RDW. RDW, an anaemia parameter, is reportedly an independent risk factor for haemorrhage after AMI.^{10,11}

The current study was planned to determine the role of RDW levels in the diagnosis of UGIH.

Materials and Method

The retrospective study was conducted at Ankara Numune Education and Research Hospital, Turkey, and comprised record of patients diagnosed with UGIH from January 1, 2013, to December 31, 2013. After getting approval from the institutional ethics committee, patients records were retrieved from the hospital database. Age, gender, RDW level, admission haemoglobin (Hb) and haematocrit (Hct)

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levels, endoscopy findings classified according to Forrest system, comorbid diseases, medication use (antiplatelet/anticoagulant agents and non-steroidal anti-inflammatory drugs [NSAIDs]), unhealthy habits (alcohol usage and smoking), and mortality rate were investigated.

Data was analysed using SPSS 17. Descriptive statistics included frequency (n), percentage (%), median, and interquartile range (IQR). Normality of the study variables was tested with Kolmogorov-Smirnov test. Continuous variables were analysed using Mann-Whitney U test and Kruskal-Wallis test. RDW level of the patients and the upper limit of the normal for RDW were compared, as were the Hb and Hct levels of the patients and the lower limit of normal for Hb and Hct. Results were interpreted at a confidence interval (CI) of 95%. $P < 0.05$ was considered statistically significant.

Results

Of the 147 patients, 94(64%) were men. The overall median age of the sample was 60 years. Besides, 117(79.6%) patients had comorbid diseases, of which hypertension 56(38.4%) was the most common. A total of 24(16.8%) patients were using antiplatelet or anticoagulant drugs, while 30(20.5%) were on NSAIDs. Six (4.1%) patients were regularly consuming alcohol (Table-1).

Peptic ulcer in 128(87.1%) patients was the most common cause of haemorrhage (Table-2).

The median RDW level of the study population was 15.25%, which was significantly higher compared to the reference values ($p < 0.05$). In contrast, Hb 9.55% (3.7) and Hct 28.75% were significantly lower ($p < 0.05$) (Table-3).

Overall, 83(56.8) patients were at Forrest stage 3. No

Table-1: Demographic data.

		n	%
Gender	Male	93	63.7
	Female	53	36.3
Comorbid Disease	Hypertension	56	38.4
	Coronary artery disease	27	18.5
	Diabetes Mellitus	22	15.1
	Stroke	18	12.3
	Chronic Obstructive Pulmonary Disease (COPD)	15	10.3
	Cancer	13	8.9
	Chronic Liver Disease	7	4.9
	Other	35	24.0
Medications	Anticoagulant/Antiplatelet	24	16.8
	NSAID	30	20.5
Unhealthy Habits	Smoker	28	19.0
	Alcohol user	6	4.1

NSAID: Non-steroidal anti-inflammatory drugs.

Table-2: Endoscopic evaluation.

Endoscopy findings	n	%
Peptic Ulcer	128	87.1
Oesophagus Varices	13	8.8
Malignant Ulcer	5	3.4

Table-3: RDW, Hb and Hct levels.

Variable	UGIH	Reference	P*
RDW	15.25(3.5)	14.5	0.000
Hb	9.55(3.7)	14	0.000
Hct	28.75(10.8)	42	0.000

*Mann-Whitney U,
UGIH: Upper gastrointestinal haemorrhage
RDW: Red blood cell distribution width
Hb: Haemoglobin
Hct: Haematocrit

Table-4: Relation between Forrest Classification and RDW levels.

Stage	n (%)	RDW(Median-IQR)	P*
Stage 1a	12 (8.2)	17.45(6.2)	0.34
Stage 1b	16(11)	15.45 (4.8)	
Stage 2a	12 (8.2)	14.80 (3.1)	
Stage 2b	10 (6.8)	15.10(3.2)	
Stage 2c	13 (8.9)	15.60(4.1)	
Stage 3	83(56.8)	15.20(3.2)	

*Kruskal-Wallis, RDW: Red blood cell distribution width.

Table-5: Correlation between RDW and patient outcomes.

	N	RDW Median (IQR)	p*
Deceased	8	18.95(5.4)	0.02
Discharged	139	15.20(3.4)	

RDW: Red blood cell, IQR: Interquartile range.

statistically significant correlation existed between RDW levels and Forrest classification. ($p > 0.05$) (Table-4).

In our study 8(5.4%) patients died due to haemorrhage (Table-5). Mortality rates were significantly higher in patients with higher RDW values ($p < 0.05$) (Table-5). Forrest stage and higher age were significantly associated with higher mortality rates ($p < 0.05$ each). Gender, comorbid diseases, unhealthy habits and medication use did not affect mortality rate ($p > 0.05$).

Discussion

Management of UGIH has recently considerably improved

parallel to the developments in general healthcare. Despite these progresses, mortality rates have yet to get lowered significantly.¹² Older patients usually require intensive care unit (ICU) admissions due to medications and comorbid diseases.¹³

Literature suggests that most of the patients diagnosed with UGIH are 60 to 65 years old males, and our study demonstrated similar results with males constituting 63% of the sample, and the mean age was 63 years.^{1,6,14-16}

The prevalence of vascular pathologies and comorbid diseases increase with age. In addition, men consume more alcohol and smoke more than women. Unhealthy eating habits of male patients may also contribute UGIH aetiology. These facts can be the cause of higher prevalence of UGIH in older male group.

A study reported that 17% subjects with UGIH were using NSAIDs, 7% anticoagulants, 8.5% salicylate, and 1% clopidogrel. It also reported a high prevalence of alcohol consumption (38%).¹⁶ A study from Turkey indicated a rate of 31% for smoking and 6% for alcohol consumption. NSAIDs and anticoagulant use has been reported as high as 69% and 7%, respectively in Turkish population.¹⁴ Another domestic study reported NSAIDs, anticoagulant use, smoking, and alcohol consumption rates of 36%, 2%, 17% and 4%, respectively.¹² Unlike previous data, the prevalence of alcohol consumption is lower in Turkey (4%). We conclude that cultural influences on smoking and alcohol usage, especially aspirin, NSAID, anticoagulant and anti-platelet medications, affect the ratio of UGIH in different patient populations.

In addition to primary liver and kidney diseases, other comorbidities also increase the risk for UGIH.^{5,6} A study reported a rate of 4% for chronic kidney disease and 10% for liver disease,¹² while another study reported rates of 3.4% and 21%, respectively.¹⁴ The latter study also reported a malignancy rate of 8.4%. In our study the most common comorbid disease was hypertension; rates of malignancy, chronic liver and kidney disease were similar to those reported in literature.^{12,14}

Previous studies have reported that the most common cause of UGIH is peptic ulcer disease.^{14,17,18} A Turkish study indicated that mostly duodenal (52%) and gastric ulcers (29%) were encountered.¹⁹ Widespread NSAIDs use due to a high prevalence of coronary artery disease and rheumatological diseases in Turkey may be the basis of peptic ulcers as an aetiological factor.

One study reported that the rate of Forrest stage 3 ranged between 63-70%. We found similar results for re-haemorrhage risk to other studies from our country.¹

As far as we know, no study has yet compared the effect of RDW levels on UGIH. Several studies have identified RDW as an indicator of morbidity and mortality in acute coronary syndrome. Haemorrhagic processes stimulate erythropoietin (EPO) production. Higher EPO levels lead to a cascade that provokes anisocytosis. Inflammatory cytokines like tumour necrosis factor-alpha (TNF- α), Interleukin-1 (IL-1) and IL-6 affect bone marrow, desensitising erythrocyte progenitors,²⁰ which inhibit erythrocyte maturation and further add to anisocytosis.²⁰ Increased stress leads to neurohormonal activity and affects RDW levels.²¹ In our study we found that RDW levels are increased in UGIH patients. Stress, inflammatory process, and an acute drop in haemoglobin due to haemorrhage stimulate bone marrow to produce massive amounts of immature and deformed red blood cells (RBCs), increasing RDW levels. Our study found that Hb and Hct levels were as low as expected ($p < 0.005$). We encountered no study in literature that correlated RDW levels and Forrest stage. We found no significant correlation between them. As Forrest classification is used as a risk stratification tool for secondary haemorrhage but RDW levels increase in the acute phase, we conclude that this statistical insignificance was an expected finding.

Mortality rates reported in literature are 9.5%, 10.7%, 15% and 11% respectively.^{14,22-24} Our study found a relatively lower mortality rate, which may be explained by early medical interventions before an endoscopist takes over a patient. As most of the patients were diagnosed to be at Forrest stage 3 during endoscopy, we conclude that rapid and accurate medical interventions had positive effect on prognostic outcome.

Age is an independent risk factor for mortality in UGIH patients.^{14,21,25,26} A study reported age as the only risk factor for mortality among gender, smoking, NSAID, and anticoagulant usage.²⁷ We conclude that altered physiological functions by age and intolerance to hypovolaemia may be the cause of higher mortality in older population.

No studies have been conducted yet to explain the association between mortality caused by UGIH and RDW though such an association exists in different clinical circumstances such as AMI and pneumonia.²⁸⁻³⁰ We conclude that hypovolaemia due to massive haemorrhage before death leads to the secretion of a higher amount of EPO and stress factors. These factors in turn stimulate bone marrow to produce young RBCs. This cascade may be the cause of higher RDW levels in patients with higher mortality.

Conclusion

As far as we know, this is the first study in the literature

examining RDW levels during UGIH management. RDW can be used as a predictor for prognosis of UGIH patients. More studies are needed to show the role of higher RDW levels in association with the UGIH management. RDW levels were higher in UGIH, especially during the acute phase.

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