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Red Blood Cell Distribution Width as a Predictor of Clinical Outcome in Acute Ischemic Stroke Patients

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Abstract **Background:** High red cell distribution width (RDW) has been demonstrated as a powerful predictor of mortality in patients with heart failure, myocardial infarction, and peripheral artery disease, as well as in the general population. The aim of this study was to evaluate the role of RDW as a predictor of stroke severity and functional outcome of acute ischemic stroke patients. **Patients and methods:** From August 2016 to October 2017, 150 consecutive acute ischemic stroke patients and 150 non stroke patients were enrolled to this analytical case- control study. The prognostic value of RDW was assessed using logistic regression model and receiver operating characteristic (ROC) curve analysis. **Results:** Mean RDW level in the patients group was 15.4±1.8 and in the control group was 13.66±1.41 and this difference was of high statistical significance (p <0.001). RDW values higher than 14.6 increased the risk of stroke several folds (odds ratio 4.38; p value < 0.001). Multivariate analysis revealed that, higher RDW was associated with a significant poor functional outcome in patients with acute cerebral infarction. **Conclusion:** RDW values can predict the occurrence, severity and functional outcome of acute ischemic stroke.

Keywords: *acute ischemic stroke; stroke severity; functional outcome; red cell distribution width*

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1. Introduction

Stroke is one of the leading causes of mortality and disability. The early detection and reliable predictors of functional decline after stroke are valuable perspectives for both accurate diagnostic and therapeutic management [1]. Red cell distribution width (RDW) can measure the size variability of the circulating erythrocytes and is considered as the electronic equivalent to the anisocytosis judged from a peripheral blood smear. It represents the coefficient of variation of the red blood cell (RBCs) volume percentage and thereby expresses the width of the volume curve [2].

High RDW has been demonstrated as a powerful predictor of mortality in patients with heart failure [3,4], myocardial infarction [5], and peripheral artery disease [6], as well as in the general population [7]. Several studies have asserted that RDW is a strong independent stroke outcome predictor [8,9,10], with a statistically significant correlation with the National Institutes of Health Stroke Scale (NIHSS) scores.

2. The Aim of the Study

The aim of the study was to evaluate the role of RDW as a predictor of stroke severity and functional outcome in acute ischemic stroke patients.

3. Patients and Methods

3.1. Study Design and Setting

This was a case-control study conducted in the intensive care and stroke units, Neurology Department, Zagazig University Hospitals, Sharqia Governorate, Egypt in the period from August 2016 to October 2017.

3.2. Study Populations

One hundred and fifty patients with acute ischemic stroke (AIS) whom were admitted within 24 hours from stroke onset were included in this study and 150 patients were presented to the emergency department with different complaints and diagnosed as having disorders other than acute ischemic stroke, confirmed by clinical findings, laboratory tests, and imaging studies as a control group. They were matched with the patients group regarding, age, sex and risk factors. Patients with cerebrovascular damage due to head trauma, brain tumors or CNS infections were excluded from the study. Also, those with recent myocardial infarction, known immunological disorders all types of anemia, those with current use of iron, folic acid, vitamin B12 supplements or stroke with an

uncompensated system failure or metabolic emergencies were excluded.

3.3. Clinical and Laboratory Analysis

Patients with cerebrovascular disease suspicion were admitted to the emergency care unit. Detailed data were collected for each patient including demographics, thorough medical history, and vascular risk factors.

3.4. Laboratory Assessment of RDW

A venous blood sample of Three milliliters was collected from all stroke patients and controls using standard venipuncture techniques within the first 24 hours of stroke onset into vacutainer tubes containing EDTA as an anticoagulant (K3-EDTA 40 µL, 0.37 mol/L per tube). The blood sample was sent to the hospital clinical pathology laboratory for complete blood cell count analysis, including RDW where it was analyzed in an automated blood cell counter. (SYSMEX K1000 hematology analyzer; TOA Medical Electronics, Kobe, Japan). RDW is expressed as a percentage coefficient of variation (CV) and is calculated by dividing the standard deviation (SD) of the RBC volume by the mean corpuscular volume (MCV). The result was multiplied by 100 to be expressed as a percentage [11]. Normal RDW range 11.6 -14.6 % [12]

Assessment of the level of consciousness, stroke severity and short-term outcome:

At the time of the presentation, the patients underwent a physical examination, neurological examination, and scoring. The level of consciousness was assessed using the Glasgow coma scale (GCS) and its severity was rated as mild (GCS, 14-15), moderate (GCS, 9-13) and sever (GCs, 3-8) [13]. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) score and was graded into mild (NIHSS was ≤ 8), moderate (NIHSS, 9-15) and severe (NIHSS was ≥ 16) [14]**.** The primary outcome of this study was the functional outcome at one month from stroke onset. The functional outcome was assessed using the modified Rankin scale (mRS) score. The good outcome was defined as mRS level ≤2 and a poor outcome as mRs>2 [14].

3.5. Radiological Assessment

All patients were subjected to computed tomography (CT) brain at admission to exclude those with stroke mimics or primary intracerebral hemorrhage (ICH). A second CT brain scan for volumetric analysis was performed at 5 to 7 days, to minimize the "fogging" effect seen in the second to third weeks after ischemic stroke. Ischemic stroke volumes were measured using the "abc method" which is reproducible, accurate, and provides the best simple geometric estimate of infarction volume [15]. The "abc method" uses the Formula (a x b x c)/2, in which *a* and *b* are the largest perpendicular diameters measured on CT and *c* is the number of 10 mm slices containing infarction. Ischemic stroke was classified according to its volume into [16]: Small; when volume < 1.5 cm^3, Medium; when volume range from 1.5 cm^3 to 3 cm^3, Large; when volume > 3 cm^3.

4. Sample Size

The sample size of this study was calculated using the mean RDW among the patients group was 14.7 and among the control group was 13.6 which was reported in a study of RDW and neurological scoring system in acute stroke patients [11]. A sample size of 292 (146 for each group) was found to achieve a power of 80% at a 95% confidence interval. We recruited 150 patients to increase the power of our study. The calculation was performed using Epi Info 7 (CDC, 2015).

5. Statistical Analysis

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 22 [17]. Qualitative data were represented as frequencies and relative percentages. Chi square test was used to calculate difference between qualitative variables. Quantitative data were expressed as mean ± SD (Standard deviation). Independent T test and Mann Whitney was used to calculate difference between quantitative. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of different parameters with maximum sensitivity and specificity for prediction of the outcome. Reliability data were calculated using Sensitivity, Specificity, PV+, PV- and Accuracy. The significance Level for all above mentioned statistical tests done. As follow P value of >0.05 indicates non-significant results, P value of <0.05 indicates significant results and P value of <0.01 indicates highly significant results.

6. Results

The present study is a case-control study involving 150 ischemic stroke patients and 150 age and sex-matched controls. A total of 150 patients with acute cerebral infarction met the inclusion criteria. The patients group included 65 men and 85 women, and the control group included 82 men and 68 women. The mean age of the patients group was 66.76±11.18 years while the control group mean age was 64.53±11.07years. Apart from the absence of a past history of cerebrovascular accidents in the controls group, there were no other significant differences between the groups regarding the co-morbidities (Table 1). Hematological and inflammatory parameters in both groups are shown in the Table 2. The mean for RDW in the patients group was 15.4±1.8 and in the controls group, 13.66±1.41 and this statistical difference was highly significant (p =<0.001). When all the patients were categorized into two groups based on RDW values of >14.6 and ≤14.6 respectively, it was found that the participants in the former group were several times more likely to have a stroke than the other group (odds ratio= 4.38; p-value <0.001) (Table 3). Among our patients, a total of 95 patients had a severe stroke (63.3 %) and 140 patients (93.3 %) had a poor functional outcome at one month after stroke onset. On univariate analysis, RDW was one of the parameters correlated significantly with the short-term outcomes (p=0.02), as well as, stroke size, GCS and

NIHSS. Even after adjustment of other factors, increased RDW was an independent factor which correlated with poor functional outcome (Table 5). The RDW predictive value for diagnosis of stroke using the ROC curve was 0.76 (95% CI, 0.71-0.81) (Figure 1).

Table 1. Demographic and clinical characteristics of the studied patients.

Characteristics	Ischemic stroke (n =150)		control (n=150)		P
Age (years) [a]	66.76±11.18		64.53±11.07		0.08
Sex, male [b]	65	43.3%	82	54.7%	0.06
Female [b]	85	56.7%	68	45.3%	
Hypertension [b]	100	66.7%	90	60.0%	0.23
Diabetes mellitus [b]	66	44%	54	36%	0.16
Dyslipidemia [b]	41	27.3%	44	29.3%	0.7
Atrial fibrillation [b]	61	40.7%	49	32.7%	0.15
Smoking [b]	26	17.3%	21	14%	0.43
Previous stroke [b]	41	27.3%			
Previous TIA [b]	15	10.0%			
GCS [a]	11.27±1.8 (7-15)				
NIHSS [a] (admission)	19.6±9.6 (3-38)				
mRS [a]	4.29±1.3 (1-6)				
Stroke size [a]	17.8±15.4 (1.2-48)				

[a] mean (±SD), [b] number (%),GCS; Glasgow coma scale , mRS; modified rankin scale, NIHSS; National Institutes of Health Stroke Scale TIA; transient ischemic attack.

Table 2. Hematological and inflammatory parameters in stroke and control patients

	Patients	Control	P
CRP at admission	32.8±36.2	14.04±9.1	0.002**
HB	13.26±2.02	13.29±1.79	0.909
WBCs	9.16±4.24	8.92±2.9	0.48
MCV	81.71±8.28	81.13±8.3	0.54
RDW	15.4±1.8	13.66±1.41	<0.001**
Platelet count	205.46±63.85	208.33±55.17	0.68

CRP; C-reactive protein, HB; Hemoglobin, MCV; Mean corpuscular volume, RDW; Red cell distribution width, WBCs; White blood cells.

Table 3. RDW and stroke

	Patients	Control	X^2	P	OR (CI 95)
RDW >14.6	103 (68.7%)	50 (33.3%)			
RDW≤14.6	47 (31.3%)	100 (66.7%)	37.47	<0.001**	4.38 (2.70-7.11)

RDW; red cell distribution width.

Table 4. Clinical data and discharge status of patients classified according to RDW levels

Characteristics	RDW>14.6 N=103	RDW≤14.6 N= 47	P
Age	67.3±10.6	65.6±12.4	0.41
CRP	35.9±33.78	31.36±37.36	0.02*
Hb	13.18±2.1	13.4±1.8	0.5
WBCs	8.6±4.1	10.1±4.2	0.03*
MCV	80.7±9.2	83.9±4.8	0.03*
GCS	11.1±2	11.5±1.1	0.27
NIHSS	20.83±10.7	16.9±5.8	0.12
mRs	4.7±1.4	3.3±0.67	<0.001**
stroke size	19.4±15.8	14.5±13.9	0.04*

CRP; C-reactive protein, HB; Hemoglobin, WBCs; White blood cells, MCV; Mean corpuscular volume, RDW; Red cell distribution width, mRS; modified rankin scale, NIHSS; National Institutes of Health Stroke Scale

Table 5. Ordinal logistic regression analysis to identify independent factors of mRS scores in patients with AIS

Independent variable	Univariate analysis		Multivariate analysis	
	OR	P	OR	P
Age.>60	2.46(1.79-5.30)	0.04*	2.33(0.64-5.19)	0.15 NS
Large Stroke size>3cm	13 (3.22-52.54)	<0.001**	9.1 (3.12-23.45)	<0.001**
Sever GCS ≤ 8	12(2.96-51.6)	<0.001**	8.67(2.53-20.19)	<0.001**
RDW>14.6	3.33(2.14-8.49)	0.02*	2.94(2.01-7.65)	0.03*
Sever NIHSS≥16	2.8 (1.75-9.52)	0.03*	2.65(1.43-8.94)	0.04*

cm; centimeter GCS; Glasgow coma scale, RDW; red cell distribution width, NIHSS; National Institutes of Health Stroke Scale.

Table 6. Diagnostic value of RDW level for stroke

	Cutoff	AUC	Sensitivity (%)	Specificity (%)
RDW	13.8	0.764	75.3	63.3

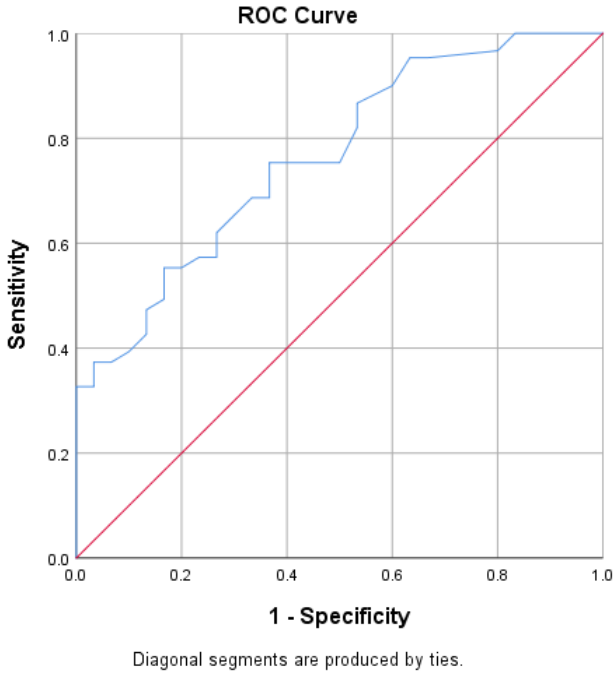

Figure 1. ROC curve

7. Discussion

Stroke is the second most common cause of death worldwide. It is also one of the common causes of disability and impairment [18]**.** Red cell distribution width (RDW) is an erythrocyte parameter, which is measured by automated cell counters and is a marker of anisocytosis. RDW has been used for the differential diagnosis of anaemia [19]. Many studies have shown that this simple test represents a strong predictor of mortality in a variety of serious human ailments including cardiovascular disease [20,21]. Rrecently, there is growing evidence that RDW is associated with prognosis in patients with stroke [22]**.** This study was designed to evaluate the role of RDW as a predictor of stroke severity and functional outcome in acute ischemic stroke patients.

We found that the mean RDW values in the patients group were significantly higher than that of the control group (p <0.00). We also noted that RDW values higher

than 14.6 increased the stroke risk several folds (odds ratio 5.18; p-value 0.00) Table 3. Jia et al [23] studied 392 patients with ischemic stroke. They have found higher levels of RDW in these patients than those without strokes. In a case-control study by Ramírez-Moreno and his colleges [10], they included 224 stroke patients and an equal number of age and sex-matched controls. They reported that RDW was a powerful predictor of stroke. Also, they observed that higher RDW was associated with higher stroke risk suggesting a level response gradient.

The studied patients were divided into a normal-RDW-level group (n= 47) and a high-RDW-level group (n=103) by the standard reference value. We found that there were significant differences between the two groups regarding the studied CBC parameters (WBC count, MCV) and CRP at admission. This finding was in agreement with that of Lippi et al [24] who reported that, RDW is associated with higher inflammatory parameters, such as CRP. In a large cohort of unselected outpatients, kim et al [9] found that RDW was significantly higher in patients with high CRP, high creatinine, low hemoglobin, low total cholesterol, lower low-density lipoprotein (LDL)-cholesterol, low albumin and low serum glucose, while Riedl et al [25] and Vaya´ et al [26] did not find a correlation between RDW and the several inflammatory and laboratory parameters analyzed, such as leukocyte, neutrophil counts, and CRP. This difference between our study and others may be due to different sample sizes and different types of study and may be the time of blood sample collection since the stroke onset.

On univariate analysis, RDW was significantly correlated with the functional outcome (p=0.02). After adjustment for other multiple study factors, increased RDW was still associated significantly with poor functional outcome in patients with acute cerebral infarction. This was agreed with Turcato et al, [1] who reported that in multivariate analysis, RDW (p=0.005**) and NIHSS (p = 0.001**) were found to be independent predictors for poor outcome. Also, Fan et al, [27] stated that RDW is associated with poor short and long term outcome of patients with ischemic stroke. However, Ntiaos et al, [28] concluded that RDW does not predict severity or functional outcome in patients with acute ischemic stroke. Also, Lappegård et al [29] had found that elevated RDW levels did not predict any increased risk of death after stroke.

Although several mechanisms explaining the association between RDW and poor clinical outcome, the exact biological mechanism between RDW and ischaemic stroke remains unclear. Inflammation and oxidative stress (OS) are examples of these mechanisms playing an important role in RDW in ischaemic stroke [11]. Inflammation is one of the suggested mechanisms as it can inhibit erythrocytes production, enhance their damage or decrease responses to erythropoietin. Some studies considered that RDW is an inflammatory marker similar to interleukin-6 (IL-6), tumor necrosis factor receptor and CRP [30]. Others proved a strong association between these cytokines and RDW [20-31].

Another suggested mechanism is high oxidative stress and low antioxidant levels association with the RDW [32,33]. Oxidative stress may induce RBC membranes damage and increase RBCs fragility and might be a key link between increased RDW and poor clinical outcome. Another explanation is that the higher RDW is considered a marker of the pro-coagulant state as it increases RBCs aggregation and platelet recruitment [9]. Another theory explained the association between RDW and ischemic stroke is the renin-angiotensin system activation resulting in a prothrombotic state [34] and increases erythropoiesis [35] leading to raised RDW. Although many studies theorized that RDW might be a biomarker or a predictor of outcome and mortality in ischaemic stroke, few trials proposed that RDW could predict the severity of the stroke and the functional outcome in patients with early acute ischemic stroke.

8. Conclusion

High RDW values can predict the occurrence, severity and functional outcome in patients with acute ischemic stroke.

List of Abbreviations

RDW; Red cell distribution width, **CRP**; C-reactive protein, **HB**; Hemoglobin, **WBCs**; White blood cells, **MCV**; Mean corpuscular volume, **NIHSS**; National Institutes of Health Stroke Scale, **GCS**; Glasgow coma scale, **mRS**; modified rankin scale, **LDL**; low-density lipoprotein, **IL-6**; inter-leukin-6, **CV** ; coefficient of variation, **TIA**; transient ischemic attack.

Conflict of Interest

The authors declare that they have no conflict of interests.

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Ethics Approval and Consent to Participate

The study was approved from the investigational review boards of the Faculty of Medicine, Zagazig University (ZU-IRB#3457- 26-2-2017). Written informed consent was obtained from all study participants after explaining the details and benefits as well as risks to them. Surrogate consent from the patient's legal guardian or designated health proxy was permitted in cases where the patient did not have decision-making capacity.

References

[1] Turcato G, Cervellin G , Cappellari M , et al. Early function decline after ischemic stroke can be predicted by a nomogram based on age, use of thrombolysis, RDW and NIHSS score at admission. J Thromb Thrombolysis 2017; 43:394-400.

[2] Sadaka F, O'Brien J and Prakash S. Red cell distribution width and outcome in patients with septic shock. J Intensive Care Med 2013; 28(5):307-313.

[3] Pascual-Figal DA, Bonaque JC, Redondo B, et al. Red blood cell distribution width predicts long-term outcome regardless of anaemia status in acute heart failure patients. Eur J Heart Fail 2009; 11: 840-846.

[4] Al-Najjar Y, Goode KM, Zhang J, et al. Red cell distribution width: an inexpensive and powerful prognostic marker in heart failure. Eur J Heart Fail 2009; 11: 1155-1162.

[5] Dabbah S, Hammerman H, Markiewicz W, et al. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. Am J Cardiol 2010; 105: 312-317.

[6] Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol 2011; 107: 1241-1245.

[7] Perlstein TS, Weuve J, Pfeffer MA, et al. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med 2009; 169: 588-594.

[8] Ani C and Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. J Neurol Sci 2009; 277(1-2):103-108.

[9] Kim J, Kim YD, Song TJ, et al. Red blood cell distribution width is associated with poor clinical outcome in acute cerebral infarction. Thromb Haemost 2012; 108(2):349-356.

[10] Ramírez-Moreno JM, Gonzalez-Gomez M, Ollero-Ortiz A, et al. Relation between red blood cell distribution width and ischemic stroke:a case-control study. Int J Stroke 2013; 8(6): E36.

[11] Kara H, Degirmenci S, Bayir A, et al. Red cell distribution width and neurological scoring systems in acute stroke patients. Neuropsychiatr Dis Treat 2015; 11: 733.

[12] Vajpayee N, Graham SS, Bem S. Basic Examination of Blood and Bone Marrow. Henry's Clinical Diagnosis and Management by Laboratory Methods. 22nd ed. Philadelphia, PA: Elsevier/Saunders; 2011, Chap 30.

[13] Mena JH[1], Sanchez AI, Rubiano AM, Peitzman AB, Sperry JL, Gutierrez MI, Puyana JC. Effect of the modified Glasgow Coma Scale score criteria for mild traumatic brain injury on mortality prediction: comparing classic and modified Glasgow Coma Scale score model scores of 13.

[14] Muchada M, Rubiera M, Rodriguez-Luna D, Pagola J, Flores A,Kallas J, Sanjuan E, et al. Baseline National Institutes of Health stroke scale-adjusted time window for intravenous tissue-type plasminogen activator in acute ischemic stroke. Stroke. 2014; 45(4):1059-1063.

[15] Sims J, Gharai LR, Schaefer P, et al. ABC/2 for Rapid Clinical Estimate of Infarct, Perfusion and Mismatch Volumes. Neurology. 2009;72(24):2104-2110.

[16] Kiers L, Davis SM, Larkins R et al., (1992): Stroke topography and outcome in relation to hyperglycaemia and diabetes. Journal of Neurology, Neurosurgery & Psychiatry; 55: 263-70.

[17] IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp

[18] Go AS, Mozaffarian D, Roger VL, et al. (2014): Executive Summary: Heart Disease and Stroke Statistics—2014 Update: A Report From the American Heart Association. Circulation; 127(1): 143-52.

[19] Ntaios G, Chatzinikolaou A. Red cell distribution width in iron deficiency anemia and beta-thalassemia minor. Am J Clin Pathol; 2008: 130: 313.

[20] Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol 2011; 107:1241-1245.

[21] Tonelli M, Sacks F, Arnold M, et al. Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People With Coronary Disease. Circulation 2008; 117: 163-168.

[22] Ani C and Ovbiagele B. (2009). Elevated red blood cell distribution width predicts mortality in persons with known stroke. J Neurol Sci.; 277(1-2):103-108.

[23] Jia H, Li H, Zhang Y, et al. Association between red blood cell distribution width (RDW) and carotid artery atherosclerosis (CAS) in patients with primary ischemic stroke. Arch Gerontol Geriatr 2015; 61:72-5.

[24] Lippi G, Targher G, Montagnana M, et al. (2009): Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med; 133:628-32.

[25] Riedl J, Posch F, Marosi C , et al., (2014). Red Cell Distribution Width and Other Red Blood Cell Parameters in Patients with Cancer: Association with Risk of Venous Thrombo embolism and Mortality. PLOS ON (9) 1-14.

[26] Vaya A´, Hern`andez V, Rivera L,, Bautista D, et al. (2014). Red Blood Cell Distribution Width in Patients With Cryptogenic Stroke.Clinical and Applied Thrombosis/Hemostasis. 1-5.

[27] Fan L, Gui L, Qing Chai E, Wei C. Routine hematological parameters are associated with short-and long-term prognosis of patients with ischemic stroke. J Clin Lab Anal. 2018; 32: e22244.

[28] Ntaios G[1], Gurer O, Faouzi M, Aubert C, Michel P. Red cell distribution width does not predict stroke severity or functional outcome. Int J Stroke. 2012 Jan; 7(1): 2-6.

[29] Lappegørd J, Ellingsen TS, Skjelbakken T, et al. Red cell distribution width is associated with future risk of incident stroke. The Tromsø Study. Thromb Haemost 2016; 115: 126-34.

[30] Macdougall IC, Cooper A. The inflammatory response and epoetin sensitivity. Nephrol Dial Transplant 2002; 17(Suppl 1): 48-52.

[31] Feng G-H, Li H-P, Li Q-L, Fu Y, Huang R-p. Red blood cell distribution width and ischaemic stroke. Stroke and Vascular Neurology 2017; 2: e00007.

[32] Semba RD, Patel KV, Ferrucci L, et al. Serum antioxidants and inflammation predict red cell distribution width in older women: the Women's Health and Aging Study I. Clin Nutr 2010; 29: 600-604.

[33] Tauler P, Aguilo A, Gimeno I, et al. Influence of vitamin C diet supplementation on endogenous antioxidant defences during exhaustive exercise. P flugers Arch 2003; 446: 658-664.

[34] Remkova A, Remko M. The role of renin-angiotensin system in prothrombotic state in essential hypertension. Physiol Res 2010; 59: 13-23.

[35] Park TS, Zambidis ET. A role for the renin-angiotensin system in hematopoiesis. Haematologica 2009; 94: 745-747.