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ORIGINAL ARTICLE – OPEN ACCESS

Red Blood Cell Distribution Width Value as a Predictor for Mortality in Stroke Patients

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ABSTRACT

Objective: Acute ischemic stroke (AIS) is a clinical condition that generally arises from non-traumatic brain vascular disorders. In this regard, red blood cell width distribution (RDW) is considered as a biochemical factor that could be used for stroke diagnosis. The main purpose of this study is regarding the use of red cell width distribution (RDW) in predicting of stroke patients for optimal use of facilities.

Materials and Methods: In the current study, about 500 patients were included with a definitive diagnosis of cerebrovascular events that were referred to the emergency department of Emam-Reza hospital in 2015. Patients were randomly selected in the morning, evening and night shifts. The related analyses were performed according to the prepared checklist, including patient demographic information, outcomes and routine laboratory tests.

Results: Based on our results, there is not a significant difference between RDW and gender, stroke type and diabetes occurrence, while a direct relationship between patient clinical appearance, age and numbers of WBC was observed. In fact, the mean of WBC count was 8331 in patients with complete remission, 9736 in partial remission and 9640 in expired subjects (p=0.001). We also found that RDW changed according to patients' outcomes.

Conclusion: Together, we conclude that WBC and age are able to affect the RDW significantly, which correlated with the outcome and mortality of stroke patients. By measuring these parameters early in stroke patients, further outcomes and disabilities in stroke patients can be predicted by on time interventions to prevent stroke-related complications and mortality.

Keywords: Acute ischemic stroke (AIS), red cell width distribution (RDW), patients with stroke

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INTRODUCTION

Stroke is one of the main causes of mortality and morbidity worldwide, with a heavy burden on health systems (1, 2). The incidence of stroke is increasing in most countries, particularly by the growing elderly population (3, 4). This causes a need for a better diagnosis, treatment and management of stroke patients (5, 6). Recently, much progress has been made regarding the prevention and treatment of stroke patients. However, until now, no easy, reliable and economically feasible indicator exists to predict the outcome and prognosis of stroke in developing countries, where much of the basic medical instruments maybe not available (7–9). This is important as a prediction of outcome, which helps clinicians to make better decisions for patients' therapeutic schedules. Red blood cell distribution width (RDW) known as a surrogate factor introduced to predict the patients' outcome under multiple clinical conditions (10–13). RDW increases in multiple human pathologies and has been used as a predictor in multiple chronic and acute conditions, including traumatic brain injury, sepsis and septic shock, malignancies and undetermined causes of fever (14–17). Recent studies have suggested that the same may occur in stroke, but contradictory evidence exists within no approved guideline (18). In this study, the authors aim to evaluate the RDW effect in predicting mortality in stroke patients (19).

MATERIALS and METHODS

Patients Selection

The patients with stroke symptoms, who were admitted to the emergency department of Imam Reza medical center from January 2017 until January 2018, were included in this study. All included patients were initially visited by an expert neurologist, and the stroke diagnosis was confirmed by further neuro-imaging techniques.

Questioner Design

Questioners were precisely designed to gather proper data regarding the demographic characteristics, types of stroke, total blood parameters (in first visit), and patients' outcome (which was obtained retrospectively from the hospital registration systems).

Table 1. Cross-tabulation of gender, type of stroke, and past medical history with short-term outcome (full remission, partial remission, death) of 458 patients with stroke

Variable	Full remission		Partial remission		Death		p*
	n	%	n	%	n	%	
Gender							
Male	67	27.7	131	54.1	44	18.2	=0.754
Female	66	30.6	110	50.9	40	18.5	
Type of CVA							
Ischemic	130	37.9	177	51.6	36	10.5	<0.001
Hemorrhagic	3	2.6	64	55.7	48	41.7	
History of hypertension							
Positive	4	2.5	98	62.0	56	35.5	<0.001
Negative	129	43.0	143	47.7	28	9.3	
History of diabetes mellitus							
Positive	3	6.0	37	74.0	10	20.0	<0.001
Negative	130	31.9	204	50.0	74	18.1	
History of stroke							
Positive	0	0.0	11	55.0	9	45.0	=0.001
Negative	133	30.4	230	52.5	75	17.1	
History of ischemic heart disease							
Positive	1	2.3	30	68.2	13	29.5	<0.001
Negative	132	31.9	211	51.0	71	17.1	
RDW							
>14%	31	20.8	74	49.7	44	29.5	<0.001
≤14%	102	33.0	167	54.0	40	12.9	

*: Chi-square test; CVA: Cerebrovascular accident; RDW: Reticulocyte distribution width

Ethical Considerations

This study was approved by the ethics board of Tabriz University of Medical Sciences (IR.TBZMED.REC.1398.944). All of the patients being included in this study had signed the informed consent forms. Additionally, this study was conducted in accordance with the Helsinki declaration.

Statistical Analysis

SPSS (version 22- IBM, USA) was used to carry out the analysis. Data were reported using frequency, distributions, mean and standard deviation. Chi-square test was used to investigate the associations between different categorical variables. Independent t-test or ANOVA was used to compare results between different stroke types and short term outcomes. Logistic regression was used to investigate the predictors of mortality in the patients. P-value less than 0.05 was considered statistically significant and the power of the study was set at 80 percent.

RESULTS

Demographic Determination in Stroke Patients

We included 458 patients aged 23 to 96 years, among whom 242 (52.8%) were male and 216 (47.2%) female. 343 (74.9%) patients had an ischemic stroke, and 115 (25.1%) had hemorrhagic form. 133 patients (29.0%) fully remitted, while 241 (52.7%) patients showed partial remission and 84 (18.3%) died. Twenty patients (4.4%) had a history of stroke, 50 (10.9%) patients had diabetes mellitus (DM), 158 (34.5%) patients had hypertension (HTN), and 44 (9.6%) patients had a previous history of ischemic heart disease (IHD). Three patients (0.7%) had a positive history for all four medical conditions, whereas 276 (60.3%) patients had no past medical histories.

Relationship Between Gender, Type of Stroke, and Past Medical History with Short-term Outcome

As shown in Table 1, the short-term outcome did not correlate with gender (p-value=0.754), while it was significantly associated with stroke type, history of hypertension, DM, IHD, and stroke (p-value=0.001). One hundred thirty patients (37.9%) with ischemic stroke fully remitted compared with three (2.6%) of patients with hemorrhagic stroke. 36 (10.5%) and 48 (41.7%) patients died of ischemic and hemorrhagic stroke, respectively. Four (2.5%) patients with hypertension fully remitted compared with 129 (43.0%) patients without any history of hypertension. 56 (35.5%) and 28 (9.3%) of patients with and without hypertension died, respectively. Three (6.0%) of diabetic patients fully remitted compared with 130 (31.9%) patients without any history of DM. Respectively, 37 (74.0%) with and 204 (50.0%) of patients without DM

Table 2. Analysis of the age and routine blood tests in different groups of short-term outcome of patients with stroke

Variable (unit)	Full remission	Partial remission	Death	p*
Age (year)	65.05±14.56	67.24±14.99	72.90±11.51	<0.001
WBC (×10³/microliter)	8.28±3.01	9.60±4.04	9.78±3.60	0.002
Platelet (×10³/microliter)	219.02±75.37	237.11±82.14	216.21±77.80	0.036
RBC (×10⁶/microliter)	4.64±0.61	4.63±0.76	4.74±0.90	0.471
RDW (%)	13.56±1.37	13.87±1.51	14.86±3.09	<0.001
Hemoglobin (g/dL)	13.20±1.91	13.12±2.28	13.21±2.58	0.918
Hematocrit (%)	41.18±4.90	40.62±6.12	41.95±8.87	0.250

*: ANOVA test; RBC: Red blood cell; RDW: Reticulocyte distribution width; WBC: White blood cell

showed partial remission. One (2.3%) of patients with IHD history fully remitted compared with 132 (31.9%) patients without any history of IHD. 13 (29.5%) and 71 (17.1%) of patients with and without a history of IHD died, respectively. Of 438 patients presenting their first stroke event, 363 (82.9%) patients survived, and 133 (30.4%) patients fully remitted, while none of 20 patients with history of stroke showed full remission (0.0%). Seventy-five (17.1%) of the patients died of their first stroke compared with nine (45.0%) patients with a history of stroke. Among one hundred forty-nine (32.5%) who had high RDW (>14%), 31 (20.8%) fully remitted compared with 102 (33.0%) patients with RDW ≤14%. 44 (29.5%) and 40 (12.9%) of patients with RDW >14% and ≤14% died, respectively.

Relationship Between Gender, Short-term Outcome, and Past Medical History with Type of Stroke

Supplementary 1 Table demonstrates cross-tabulation of gender, short-term outcome, and past medical history with type of stroke. There is no correlation between gender and type of stroke (p-value=0.281), history of stroke (p-value=0.620), DM (p-value=0.058), IHD (p-value=0.282), and high RDW (p-value=0.924). Forty-eight (57.1%) of dead patients had hemorrhagic stroke, compared with 67 (17.9%) remitted subjects (p-value<0.001); 61 (38.6%) patients with hypertension (HTN) yielded hemorrhagic stroke, compared with 54 (18.0%) patients without HTN (p<0.001).

Relationship Between Age and Hematologic Parameters with Short-term Outcome

Based on the obtained data from Table 2, in total population, average age, WBC count, platelet count, RBC count, hemoglobin concentration, hematocrit, and RDW was 67.64 years old (±14.51), 9.25×10³/microliter (±3.73), 228.02×10³/microliter (±79.85), 4.65×10⁶/microliter (±0.75), 13.16 g/dL (±2.23), 41.02% (±6.42), and 13.96% (±1.92), respectively. Table 2 compares age and routine blood tests among three groups of short-term outcomes. Regarding age, the dead (72.90±11.51 years) was older than patients fully (65.05±14.56 years) or partially (67.24±14.99 years) remitted (p<0.001). WBC count was higher in the dead (9.78±3.60×10³/microliter) compared with patients fully (8.28±3.01) or partially (9.60±4.04) remitted (p-value=0.002). Platelet count significantly differed (p-value=0.036) among three outcome groups (full remission, partial remission, and death), while RDW was significantly higher in the dead (14.86±3.09%) compared with fully (13.56±1.37) or partially (13.87±1.51) remitted patients (p<0.001).

Table 3. Univariate logistic regressions with m data of 458 patients with stroke

Variable (unit)	OR	95% CI for OR	p
Age (year)	1.036	1.016–1.056	<0.001
Hemorrhagic CVA	6.109	3.681–10.139	<0.001
RDW (%)	1.286	1.136–1.455	<0.001
High RDW[a]	2.818	1.737–4.572	<0.001
Past medical history (0–4)[b]	1.928	1.496–2.485	<0.001
History of hypertension	5.333	3.211–8.860	<0.001
History of ischemic heart disease	2.026	1.010–4.064	0.047
History of stroke	3.960	1.586–9.891	0.003

CI: Confidence interval; CVA: Cerebrovascular accident; OR: Odds ratio; RDW: Reticulocyte distribution width; a: RDW >14%; b: From 0 (negative medical history) to 4 (positive history of stroke, diabetes mellitus, ischemic heart disease, and hypertension)

Correlation of Age and Hematologic Parameters with Stroke Different Types

Results of supplementary 2 show the differences in patient's age and general blood tests between two types of stroke. There is no significant difference between age and ischemic or hemorrhagic strokes (68.24±14.29; 65.84±15.04 years; p-value=0.125). Among routine blood tests parameters, only WBC count was significantly higher in hemorrhagic (10.27±3.8×10³/microliter) stroke in comparison with ischemic (8.91±3.65×10³/microliter) stroke (p-value=0.001). Additionally, RDW was not different between ischemic (13.97±1.95%) and hemorrhagic (13.96±1.82%) stroke (p-value=0.990).

Evaluation of Univariate Logistic Regressions with Mortality

As shown in Table 3, age (OR=1.036, 95% CI: 1.016–1.056), hemorrhagic stroke (OR=6.109, 95% CI: 3.681–10.139), RDW (OR=1.286, 95% CI: 1.136–1.455), HTN (OR=5.333, 95% CI: 3.211–8.860) (p<0.001), history of stroke (OR=3.960, 95% CI: 1.586–9.891), and IHD (OR=2.026, 95% CI: 1.010–4.064) were significantly univariate predictors of the mortality (p<0.05).

Table 4. Multivariate logistic model for prediction of "death" in 115 patients with hemorrhagic stroke

Variable	OR	95% CI for OR	p
Female gender	2.296	0.897–5.878	0.083
Age decade	1.734	1.198–2.510	0.004
History of hypertension	3.771	1.459–9.746	0.006
History of diabetes mellitus	0.072	0.007–0.723	0.025
High RDW[a]	2.982	1.105–8.047	0.031
Constant	0.029	–	0.035

CI: Confidence interval; OR: Odds ratio; RDW: Reticulocyte distribution width; a: RDW >14%

Multivariate Logistic Model for Prediction of Mortality in Patients with Stroke

Based on our findings in supplementary 3, age decade (OR=1.304, 95% CI: 1.031–1.651), hemorrhagic stroke (OR=6.992, 95% CI: 3.863–12.656), high RDW, that is >14%, (OR=3.014, 95% CI: 1.701–5.340), and history of stroke (OR=3.329, 95% CI: 1.183–9.368) or HTN (OR=3.007, 95% CI: 1.665–5.430) predicted patient's death using multivariate hierarchical logistic modeling (Hosmer-Lameshow p-value=0.789, Nagelkerke Rsquare=0.342, p-value<0.001).

Multivariate Logistic Model for Prediction of Mortality in Patients with Ischemic Stroke

Supplementary 4 Table also represents multivariate logistic model for prediction of death in ischemic stroke (Hosmer-Lemeshow p-value=0.505, Nagelkerke R-square=0.245, p-value<0.001). According to the model adjusted for female gender and age decade, five percent increase in hematocrit (OR=1.356, 95% CI: 1.037–1.772), high RDW (OR=3.576, 95% CI: 1.633–7.830), and history of stroke (OR=6.365, 95% CI: 2.029–19.968) or HTN (OR=2.947, 95% CI: 1.291–6.728) were predictors of death in patients with ischemic stroke.

Multivariate Logistic Model for Prediction of Mortality in Patients with Hemorrhagic Stroke

We also sowed the multivariate logistic model for prediction of death in hemorrhagic stroke (Hosmer-Lameshow p-value=0.181, Nagelkerke R-square=0.389, p-value<0.001) (Table 4). After adjustment for the female gender, the multivariate logistic model showed that age decade (OR=1.734, 95% CI: 1.198–2.510), high RDW, that is >14%, (OR=2.982, 95% CI: 1.105–8.047), and history of DM (OR=0.072, 95% CI: 0.007–0.723) or HTN (OR=3.771, 95% CI: 1.459–9.746) were predictors of death in patients with hemorrhagic stroke.

DISCUSSION

Our data demonstrated that hemorrhagic stroke, along with diabetes mellitus, stroke IHD and hypertension history, as well as high RDW (14≤), had a weak prognosis with lower full remission and higher death rates. Notably, stroke history, RDW and IHD had no significant relationship with types of stroke. Our data also showed that there is a close and significant relationship between age, WBC and RDW with short term outcomes. According to hematologic parameters analysis, only the WBC amount had significant differences between two types of stroke. Overall, in this study, the mortality rate was 18.3%, which was more in the hemorrhagic stroke group. Hypertension was a major risk factor for mortality in both stroke groups. Unlike hypertension, diabetes had no significant effect on the mortality rate of the patients (20, 21). In this regard, our results proved that hypertension but not diabetes mellitus was a major risk factor in hemorrhagic stroke occurrence. Moreover, our study showed that RDW is a valuable predictor of death in both stroke subgroups. In line with our results, Kara et al. showed that RDW was a beneficial factor in predicting the stroke outcome in the first 24 hours of stroke (22). This study also showed that RDW was comparable and even more efficient in predicting the outcome compared with the Glasgow Coma Scale (GCS), Canadian Neurological Scale (CNS), and National Institutes of Health Stroke Scale (NIHSS) (22). In this line, other studies have shown that RDW is a promising predictor for some heart abnormalities, such as atrial fibrillation (23–25). In a study performed by Hong et al. demonstrated that RDW was able to predict clinical outcome in 567 patients who had atrial fibrillation (26). Another study performed by Vijayashree et al. also evaluated the efficacy of RDW in predicting stroke in 52 subjects. They found that RDW levels were able to as a predictor if stroke ever happened or not, but had no significant effect on predicting severity and clinical severity of stroke (27). In a case-control study, similar results were also found, which was shown that RDW could be able to predict stroke in 224 patients (28). In a systemic review performed by Li et al., RDW was assessed in patients with various cerebrovascular diseases. It was found that although RDW was a good item in predicting cerebrovascular diseases, it had the best use alongside other factors, such as Nitrogen Terminated-pro B-type natriuretic peptide (BNP), cardiac troponin, and C-Reactive Protein (CRP) (29). Similar beneficial results were also shown regarding RDW and the prognosis of diabetes and heart failure in a study conducted by Xanthopoulos, in which a higher RDW was associated with a higher event rate in both groups (30).

CONCLUSION

The results of this study show a potential tendency towards the use of RDW in clinical centers, but some important challenges, such as technical efficacy and affordability, still remain unclear. Moreover, our findings declared that although RDW had beneficial effects in the forecasting of stroke, further and stronger evidence need to be diagnostic criteria in stroke patients.

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Ethics Committee Approval: This study was approved by the ethics board of Tabriz University of Medical Sciences (IR.TBZMED.REC.1398.944).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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