



Study Of Correlation Between The Red Cell Distribution Width With Severity Of Acute Ischemic Stroke

Toppo Archana¹, Sori Manjusha², Dubey Prachi³, Lakra DP⁴

^{1,3}Associate Professor, ²Post Graduate Resident, ⁴Professor and Head,

Department of General Medicine, Pt. Jawaharlal Nehru Memorial Medical College and Hospital, Raipur

***Corresponding Author:**

Sori Manjusha

Post Graduate Resident, Department of General Medicine, Pt. Jawaharlal Nehru Memorial Medical College and Hospital, Raipur

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Abstract

Introduction-

Red blood cell distribution width (RDW) may be a potential biomarker of inflammation in patients with acute ischemic stroke (AIS). This study focuses to correlate RDW and severity of AIS.

Methods-

146 clinically and radiologically confirmed cases with AIS were assessed for a period of 1 year. Patients were categorised using national institute of health stroke scale (NIHSS). RDW was assessed and compared.

Results-

Maximum cases belonged to age group of more than 60 years (44.5%) with male preponderance (62.3%) having past history of diabetes (73.3%). A NIHSS grade 5 (30.1%), and high RDW (65.1%) was observed in majority in our study. No correlation between weight, height, BMI, pulse, systolic and diastolic blood pressure (BP), white blood cells, platelet count, mean corpuscular volume, total cholesterol, triglyceride, haemoglobin with RDW and NIHSS score was established (all p-values >0.05). Weak downhill correlation was observed between NIHSS score and RDW ($r = -0.118$, p-value = 0.205). Mild uphill correlation was observed for NIHSS grade-2 with respect to RDW ($r = 0.310$) and was statistically significant (p-value = 0.034). Grade-5 had weak downhill correlation with RDW ($r = -2.49$, p-value = 0.030). No correlation between RDW and NIHSS grade 3 ($r = 0.01$) and 4 ($r = 0.073$) was found.

Conclusion-

RDW should be integrated into clinical practice as a predictor of AIS occurrence and outcome.

Keywords: Acute ischemic stroke (AIS), Red blood cell distribution width (RDW), national institute of health stroke scale (NIHSS)

Introduction

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurological deficit that is attributable to a focal vascular cause thus, the definition of stroke is clinical and laboratory studies including brain imaging are used to support the diagnosis. Stroke has occurred if the neurologic sign and symptoms last for >24 hours or brain infarction is demonstrated [1]. Globally stroke is the commonest

cause of mortality post coronary artery disease and is also the commonest cause of chronic adult disability [2]. The prevalence of stroke ranges from 119-145/100,000. Among these, 80% are ischemic stroke and haemorrhagic stroke makes up the remaining 20% of the population. Ischemic strokes result from the interruption of the blood supply to the brain, while haemorrhagic strokes result from the rupture of a blood vessel or an abnormal vascular structure [3].

The acute ischemic stroke (AIS) is further classified into five subtypes: 1) large artery atherosclerosis 2) cardio-embolism 3) small vessel occlusion 4) stroke of other determined etiology 5) stroke of undetermined etiology. Arterial occlusion in ischemic stroke is most commonly embolic: either cardioembolic, from causes such as atrial fibrillation or valvular heart disease, or arteroembolic, from atherosclerotic disease in the extracranial cervical carotid or vertebral artery [3,4].

Given the enormous burden of stroke, new markers are the need of hour to better identify patients with poor outcomes in order to accurately predict prognosis and optimize the administration of management [5]. The red cell distribution width (RDW) is a haematological parameter representing the variability in size of circulating erythrocytes, which is one of the biomarkers potentially involved in inflammation process, oxidative stress and endothelial dysfunction in vascular diseases [6]. Other than anaemia, the prognostic importance of high RDW levels due to lack of knowledge. However, high RDW is associated with a poor prognosis in certain disorders such as acute myocardial infarction, stroke, and peripheral artery disease. RDW is also predictor of mortality in patients with cardiovascular disease, cancer, chronic lung disease, symptomatic chronic congestive cardiac insufficiency, acute stroke, or acute cardiac insufficiency [7].

Utility of RDW in predicting stroke severity is under evaluation and topic of ongoing research. Several potential mechanisms direct the relationship between RDW and its prognosis regarding AIS. An underlying inflammation and oxidative stress might relate to the increased RDW and poor clinical outcome. Previous evidence has suggested low oxygen saturation and reduced RBC deformability in patients with higher RDW. Therefore, the higher the RDW value, the lower the oxygen supply in tissues which implies that increased RDW levels may contribute to the development and exacerbation of stroke by reducing oxygen content in the brain [8].

Elevated RDW may be a useful parameter to follow the development of atherosclerosis and hence stroke. Recently RDW has emerged as a potential independent predictor of clinical outcome in patients with established cardiovascular disease [9]. However,

little is known about the role of RDW as a predictor of severity among persons with AIS. With the available data as mentioned above we found studies in strong support of RDW as an efficient marker and also studies with negative results in this regard. More research in this area is required to show strong and reliable correlation between RDW and AIS. Not many such studies are carried out in the Indian population also no such study has been done in the central Indian population. Thus we designed the present study to correlate RDW and severity of AIS. Hence, paving a way to evaluate the significance of RDW in AIS severity.

Material And Methods-

This single centre, hospital based cross-sectional observational study was conducted in department of Medicine, DR. B.R.A.M.H Raipur located in Central India. 146 patients of either gender, aged more than 18 years who were clinically and radiologically confirmed with AIS admitted in the Medicine In Patient Department (IPD) for a period of 1 year from November 2020 to October 2021 were included in this study. Patients with hemorrhagic stroke, iron deficiency anemia, sepsis, sickle cell anemia, thalassemia or megaloblastic anaemia were excluded from the study. After explaining the study procedure, written informed consent obtained from all the subjects selected for the study. Data was collected in a predesigned questionnaire after availing necessary ethical approval from the institution, cases were meticulously diagnosed with detailed demographic data in respect to age, sex, address, presenting complaints, past history, drug history, history of smoking, history for alcoholism, family history and clinical examination findings. Laboratory investigations like complete blood count (CBC) (by Auto Hematology Analyzer machine [Mindray BC - 6000]), fasting blood sugar, post prandial blood sugar (by Glucose oxidase-peroxidase method with Automatic Biochemistry Analyzer machine IL Model I Lab 650), liver and renal function tests, serum electrolytes, lipid profile, RDW were performed. Radiological investigations like computed tomography (CT) brain was done in all recruited cases. Stroke was categorised as minor, moderate, moderate to severe and severe stroke using national institute of health stroke scale (NIHSS). The collected data were tabulated and statistically analyzed using SPSS© for windows™ Vs 17, IBM™

Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA. Kolmogorove-Smirnove analysis was performed for checking linearity of the data. Analysis of variance (ANOVA) and Student's t test was used to obtain the significance of difference between parameters in parametric data. Chi square test or Fisher's exact test was used to analyse the significance of difference between frequency distribution of the data. Quantitative data was expressed as mean and standard deviation (SD) whereas categorical data was expressed as number and percentage. P-value <0.05 was considered as statistically significant.

Results-

Patients demographic data showed that the most common age group interval affected belonged to the of more than 60 years of age 65 cases (44.5%), followed by 37 (25.3%) in age group interval 51-60 years, and 34 (23.3%) in age group interval 41-50 years of age. While, 9 (6.2%) pertained in 31-40 years of age group interval and only 1 (0.1%) case persisted in age group interval of 21-30 years. Male preponderance was observed with maximum males (62.3%) followed by females (37.7%). While appraising distribution of past history in the study subjects, out of 146 subjects, 107 (73.3%) subjects had history of diabetes mellitus, 97 (66.44%) subjects were diagnosed with hypertension, 75 (51.4%) subjects consumed alcohol in the past and 41 (28.1%) subjects had history of smoking.

Moreover, 103(70.5%) cases belonged to obese I category according to body mass index (BMI) findings, followed by 21 (14.4%) in obese II category, 14 (9.6%) in overweight category, and 8 (5.5%) in normal category. Mean systolic blood pressure found was 141.17 ± 19.02 mmHg and mean diastolic blood pressure was 83.90 ± 8.66 mmHg. An NIHSS grade 5 was observed in 44 cases (30.1%), followed by grade 3 in 43 cases (29.5%), and grade 4 in 42 cases (28.8%) and grade 2 in 17 cases (11.6%). 116 cases (65.1%) were observed with high RDW and 30 (20.5%) cases had normal RDW in our study.

We also sought to find correlation of various parameters like weight, height, BMI, pulse, systolic and diastolic blood pressure (BP), white blood cells (WBC), platelet count (PLT), mean corpuscular volume (MCV), total cholesterol, triglyceride, haemoglobin (Hb) with RDW and NIHSS score in

our study. We could not establish any statistical significant correlation between these parameters with respect to NIHSS Score and RDW (all p-values >0.05). A correlation analysis was performed between NIHSS score and RDW in our study. Weak downhill correlation was observed between NIHSS score and RDW ($r=-0.118$), however this correlation failed to reach statistical significance (p-value=0.205). Also, weak uphill correlation ($r=0.116$) was observed regarding NIHSS score and normal RDW but failed to reach statistical significance (p-value= 0.540)

Correlation of NIHSS score with RDW in different NIHSS grade was also assessed. Mild uphill correlation was observed for NIHSS grade 2 with respect to RDW ($r=0.310$). This correlation was found to be statistically significant (p-value= 0.034). However, no correlation was observed between RDW and NIHSS grade 3 ($r= 0.01$) and 4 ($r= 0.073$). The p-value for these correlations was found to be statistically significant. In case of grade 5, a weak downhill correlation ($r=-2.49$) was observed and the p-value was 0.030, which was statistically significant.

Discussion-

1) Baseline characteristics-

In present study, maximum 65 (44.5%) belonged to the age group >60 years of age with mean age of 57.92 ± 10.77 . Ulker et al., found the mean age to be 69.54 ± 12.8 years in their study of relationship of RDW with AIS Severity and Prognosis in AIS supporting our study findings [10]. Similar results regarding gender appraisal were obtained by Yogitha et al., who investigated the association between RDW and AIS severity and outcome, found 62% were males, showing male preponderance [11]. Regarding past history, Sarhan et al., supported us as they noted past history of diabetes mellitus (44%), hypertension (66.7%), and smoking (17.3%) [12]. Obesity has been established as a risk factor for AIS and coronary disease, but several studies have suggested that obese and overweight stroke patients have significantly better long-term survival rates [2]. In our study, it was found that maximum (70.5%) subjects belonged to obese I category and Seo et al., conducted a study showing relationship between BMI and AIS after thrombolysis among 321 study subjects in which 14 belonged to under weight, 123 subjects belonged to normal weight, 90 belonged to overweight, 94

belonged to obese category [13]. The severity of AIS in present study was assessed using NIHSS score and the mean NIHSS score found was 17.17 ± 9.60 . NIHSS grading in present study among 146 subjects was assessed and NIHSS grade 5 was found in 44 (30.1%), followed by grade 3 in 43 (29.5%), and grade 4 was observed in 42 (28.8%), and grade 2 in 17 (11.6%). Shamsavari *et al* performed similar study and the mean NIHSS score at the time of admission was 13.6 ± 6.39 [14]. Among 146 study subjects, in our study 116 (65.1%) subjects had high RDW values and 30 (20.5%) subjects had normal RDW. The mean RDW in study subjects was 15.58 ± 1.05 . Similar observation was also made by Sarhan *et al*. The authors noted the mean RDW to be 15.4 ± 1.8 [12]. Ulker *et al* conducted a study to find the RDW with AIS Severity and Prognosis in AIS, observed the mean RDW was 15.39 ± 1.4 which is consistent with our study [10].

In present study, mean systolic BP and mean diastolic BP was 141.17 ± 19.02 mmHg and 83.90 ± 8.66 mmHg respectively. The BP is typically at maximal at admission but decreases spontaneously thereafter during the natural course of stroke. This temporal pattern also occurs in control patients without a diagnosis of stroke, the BPs are higher in stroke patients [2,3,4]. Morfisi *et al*., conducted a study blood pressure changes in acute cerebral infarction and haemorrhagic stroke. The authors found that the systolic BP on arrival significantly higher in those with ischemic lacunar and thromboembolic infarcts than in controls [15]. Bangalore *et al*., studied blood pressure and in-hospital outcomes in patients presenting with AIS, and observed that 73% and 34% of patients presented with post-stroke hypertension (systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg, respectively). Moreover, 19% and 8% of patients presented with a systolic BP ≥ 185 mmHg or diastolic BP ≥ 110 mmHg, respectively, a BP range that is considered to be a relative contraindication for thrombolytic therapy. Although the majority of patients with AIS present with elevated BP, data suggest that there is spontaneous reduction of BP within days following the acute event in the majority of patients [16].

2) Correlation analysis of NIHSS and RDW with various parameters-

Comparison of various parameters like weight, height, BMI, pulse, systolic and diastolic BP, WBC, PLT, MCV, total cholesterol, triglyceride, haemoglobin and RDW as well as NIHSS revealed no significant difference (all p-values > 0.05). Similar results were observed in a study conducted by Vaya *et al*. The authors observed no differences in the erythrocyte indices or in glucose, cholesterol, and triglycerides levels (p-value > 0.05) [17].

3) Correlation analysis of NIHSS score, NIHSS grading, and RDW with respect to each other-

The severity of AIS is generally assessed by NIHSS, which has been shown to be a reliable predictor of outcome. Recently, several studies have tried to find a simpler alternative to NIHSS. Some of these studies have focused on RDW, as it has already been established as a prognostic biomarker in a variety of medical conditions, cardiovascular disease, pulmonary disease and diabetes [10]. A correlation analysis was performed between NIHSS score and RDW. Weak downhill correlation was noted between two parameters ($r = -0.118$) which was not statistically significant (p-value = 0.205). A correlation analysis was performed between NIHSS grading and RDW. No correlation was observed between two parameters ($r = -0.082$) however this correlation failed to reach statistical significance (p-value = 0.384). Mild uphill correlation was observed for NIHSS grade 2 with respect to RDW ($r = 0.310$) and was statistically significant (p-value = 0.034). However, no correlation was observed between RDW and NIHSS grade 3 ($r = 0.01$) and 4 ($r = 0.073$). The p value for these correlations was found to be statistically significant. In case of grade 5, a weak downhill correlation ($r = -2.49$) was observed and the p value was found to be 0.030, which is statistically significant. Correlation of NIHSS score with RDW in different RDW group was assessed. Weak uphill correlation ($r = 0.116$) was observed regarding normal RDW and NIHSS score. This correlation failed to reach statistical significance (p = 0.540). Whereas, in High RDW group, RDW had weak downhill correlation ($r = -0.118$), and the correlation failed to reach statistical significance (p-value = 0.205). In a case control study by Ramirez-Moreno *et al* involving 224 stroke patients and an equal of matched controls it was found that RDW was a powerful predictor of stroke. In addition, the researchers observed that higher values of RDW was associated with increased risk of stroke [18]. Sarhan

et al. Conducted a case control study and concluded that RDW can predicts the occurrence ,severity and functional outcome of AIS [12].Kara et al., studied to evaluate the association between the RDW and NIHSS scores in patients who had AIS. It was found that stroke patients had significantly higher median RDW than control subjects. The authors concluded that in stroke patients who have symptoms <24 hours, the RDW may be useful in predicting the severity and functional outcomes of the stroke [19]. A study conducted by Ülker et al failed to show a correlation between RDW values and AIS severity and prognosis [10]. A study conducted by Ntaios et al.,found that red cell distribution width, assessed during the early phase of AIS, does not predict severity or functional outcome [20].Similar observations were also made by Shamsavarinia et al.They suggested that RDW does not predict the severity and outcome of AIS in patients who undergo antithrombotic therapy [14].Association between NIHSS grading and RDW was observed in present study. No significant association was observed between these two parameters. ($p=0.405$)

Conclusion-

We conclude, High RDW is associated with increased severity of AIS, thus increase in RDW is independently associated with severity of AIS. There is no significant correlation between RDW and NIHSS score, but significant correlation was observed between RDW and NIHSS grade 2 and grade 5. So we can say that RDW can be an important predictor and simple inexpensive biomarker for the prognosis of AIS patients. However, since the correlation failed to reach statistical significance we recommend further studies with greater scope and population to clarify the results of the present study.

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Tables And Figures-

“Table 1 : Baseline characteristics of patients included in the study (n=146)”

Categorical variables	Percentage
Sex	
Males	62.3
Females	37.7
Age (Years)	
21-30	0.7
31-40	6.2
41-50	23.3
51-60	25.3
>60	44.5
Past history	
Diabetes mellitus	73.3
Alcohol	51.4
Smoking	28.1

Hypertension	66.44
BMI	
Normal	5.5
Overweight	9.6
Obese I	70.5
Obese II	14.4
NIHSS Grade	
2	11.6
3	29.5
4	28.8
5	30.1
RDW (%)	
Normal	20.5
High	79.5
Continuous variables-	
Mean Systolic BP (mmHg)	141.17 \pm 19.020
Mean Diastolic BP (mmHg)	83.90 \pm 8.6601
Mean age (years)	57.92 \pm 10.77

BMI- body mass index, NIHSS- national institute of health stroke scale, RDW- red cell distribution width, BP- blood pressure, SD- Standard deviation

“Table 2 : Correlation of various parameters with RDW and NIHSS Score (n=146)”

Parameters	RDW (%)		NIHSS Score	
	Pearson Correlation	P-value*	Pearson Correlation	P-value*
Weight (Kg)	0.016	0.867	-0.034	0.717

Height (m)	0.068	0.467	0.004	0.968
BMI (Kg/m ²)	-0.061	0.516	-0.042	0.657
Pulse (/min)	0.160	0.087	0.176	0.058
Systolic BP (mmHg)	0.049	0.604	0.071	0.448
Diastolic BP (mmHg)	0.152	0.104	0.126	0.178
WBC (/cumm)	-0.085	0.366	-0.104	0.265
MCV (fl)	-0.012	0.899	-0.006	0.949
PLT (/cumm)	-0.024	0.800	0.033	0.724
Total Cholesterol (mg/dl)	-0.057	0.545	-0.083	0.379
Triglyceride (mg/dl)	-0.089	0.344	-0.143	0.125
HB (gm%)	-0.082	0.224	-0.077	-

BP- blood pressure, WBC- white blood cells, MCV- mean corpuscular volume, PLT- platelet count, HB- haemoglobin,NIHSS- national institute of health stroke scale, RDW- red cell distribution width

* P-value <0.05 is considered as statistically significant.

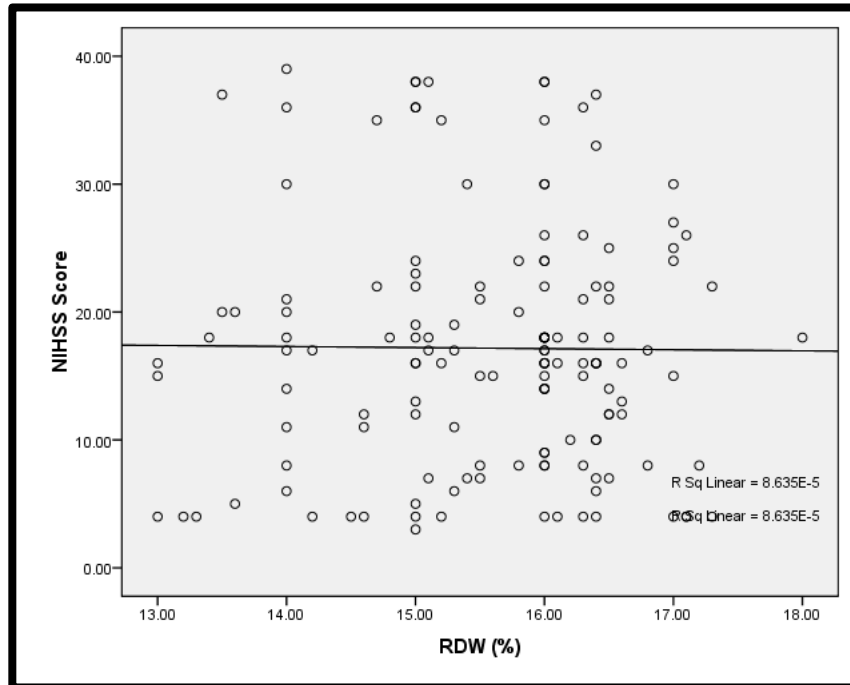
“Table 3: Correlation of NIHSS score with RDW in different NIHSS grade (n=146)”

NIHSS grade	Correlation coefficient	P-value*
2	0.310	0.034
3	0.190	0.01
4	0.053	0.073
5	-0.249	0.030

NIHSS- national institute of health stroke scale, RDW- red cell distribution width

* P-value <0.05 is considered as statistically significant.

“Figure 1: Correlation analysis between NIHSS Score and RDW(n=146)”



NIHSS- national institute of health stroke scale, RDW- red cell distribution width