



“A STUDY OF RED CELL DISTRIBUTION WIDTH AS A MARKER OF SEVERITY AND OUTCOME IN ISCHEMIC STROKE PATIENTS”

General Medicine

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ABSTRACT

Background: Stroke is an important cause of disability as well as mortality across the world. RDW has been reported to be linked to the thrombotic events as per the recent studies, including cerebrovascular disease. Our study aims to study the relationship of RDW with severity and outcome of ischemic stroke patients. **Aims and Objectives:** To determine the Red Cell Distribution Width in ischemic stroke patients and to correlate the RDW and severity and outcome of ischemic stroke. **Methodology:** A cross-sectional observational hospital-based study was conducted on 186 CT proven ischemic stroke patients; severity was assessed using NIHSS scale and RDW was assessed in each of them. Outcome of stroke was assessed using Modified Rankin Scale. **Results:** A significant positive correlation was noted between RDW and severity as well as outcome of ischemic stroke patients. **Conclusion:** RDW, a simple cost-effective test, can be used as a marker of severity and poor prognosis in ischemic stroke patients.

KEYWORDS

RDW, Ischemic Stroke, Severity and Outcome

INTRODUCTION

Annually, cerebrovascular accidents affect around 20 million people all over the world, and is the second leading cause of mortality^(1,2). Also, it accounts for significant disability among the survivors, resulting in need for physiotherapy and dependence. Ischemic stroke accounted for about 70% of all the cerebrovascular accidents. The ICMR report (2004) claims that stroke accounts for 41% of deaths and 72% of disability adjusted life years (DALY) among non-communicable diseases.³ The extent of disability and the occurrence of mortality following a stroke are dependent on the severity of stroke.

At present, we rely up on neurological examinations and neuro-imaging studies to assess the severity and prognosis of stroke. Several scoring systems are used to quantify the degree of severity of stroke: the Glasgow Coma Scale, Canadian Neurological Scale, Scandinavian Stroke Scale and National Institutes of Health Stroke Scale (NIHSS), and the final outcome of stroke could be measured by Barthel Index, Modified Rankin scale or Glasgow outcome scale. However, there is no biological surrogate marker to assess the stroke severity.

Red cell distribution width obtained from a standard complete blood count is a marker of anisocytosis. Emerging evidence suggests that, besides RBC abnormalities, many other diseases may be frequently associated with a high degree of anisocytosis.⁴ In recent years, many clinical studies have proved that the alterations of RDW levels may be associated with the incidence and prognosis in many cardiovascular and cerebrovascular diseases (CVDs).

There is no clear mechanism which can explain the elevated RDW values in acute ischemic stroke. The existing hypothesis includes microvascular disorder, anemia, inflammation cytokines etc.

Inflammation is important in the development of atherosclerosis, ischemia and ischemic stroke. As a marker of inflammation, RDW is correlated with other inflammatory markers such as CRP. The inflammatory cytokines may cause elevated RDW levels by inhibiting red cell maturation and enabling the release of new and large reticulocytes to the circulation. Furthermore, inflammation may contribute to morphologic changes in red blood cells by changing membrane glycoproteins and ion channels. Also, high oxidative stress may prolong the survival of red blood cells, increase the premature release of large red blood cells into the peripheral circulation, and cause elevation in RDW.

RDW is easily available to physicians as a parameter of the CBC and does not incur additional costs. In our study, we aimed to correlate RDW as predictive marker for the severity and outcome of ischemic stroke.

AIMS AND OBJECTIVES:

1. To determine the Red Cell Distribution Width in ischemic stroke patients.
2. To correlate the RDW and severity of ischemic stroke using NIHSS stroke scale, and compare it to the final outcome with MRS score.

METHODOLOGY:

Study Design: Cross sectional observational study

Study Duration: 12 months

Study Setting: Department of General Medicine, BGS GIMS Hospital, Bengaluru

Study Population: Patients with acute ischemic stroke (CT proven) admitted in medical wards, Department of General Medicine, BGS GIMS Hospital, Bengaluru

Inclusion Criteria:

1. Patients with ischemic stroke confirmed by CT imaging within 48 hours of presentation
2. Age 18-80 years

Exclusion Criteria:

1. Patients with hemorrhagic stroke
2. Pregnancy
3. Patients with previous history of stroke
4. Patients with anemia (as defined by WHO)
5. Known chronic illnesses like Chronic liver disease, CKD, heart failure, COPD

Sample Size:

Sample size was calculated using the formula

$$N = \frac{(Z1 - \alpha/2)^2 * \text{specificity} * (1 - \text{specificity})}{(1 - \text{prevalence}) d^2}$$

Where $Z1 - \alpha/2 = 1.96$ @ α error 5%, Specificity = 67.5, Prevalence = 0.4%

$N = 173$

Study Procedure

After obtaining clearance from institutional ethics committee, 186 patients were enrolled in our study as per the inclusion and exclusion criteria. An informed consent was obtained from the patients/ local guardian enrolled in the study. Detailed history from patients/bystanders was taken and clinical examination was done on patients admitted with acute ischemic stroke. CT brain was done at the time of admission and routine blood investigations including CBC were done to determine the RDW value. Other necessary investigations were done to exclude chronic illnesses. Patients were

categorized into mild, moderate and severe degree of ischemic stroke using NIHSS. The values of RDW were determined in each patients using TRANSASIA SYSMEX KX21-3 PART ANALYSER. The relationship between stroke severity and RDW was assessed using appropriate statistical tests and was compared to the outcome as per Modified Rankin Scale, calculated on day 5 or at the time of discharge.

Statistical Analysis

Data was entered in Microsoft Excel and analysis was done using the SPSS software. Association between quantitative variables was analyzed using paired t test. Qualitative assessment was analyzed using chi square test. Other parameters were utilized whenever necessary. Significance level was fixed at p value of $p < 0.05$.

RESULTS:

A total of 186 patients were included in the study.

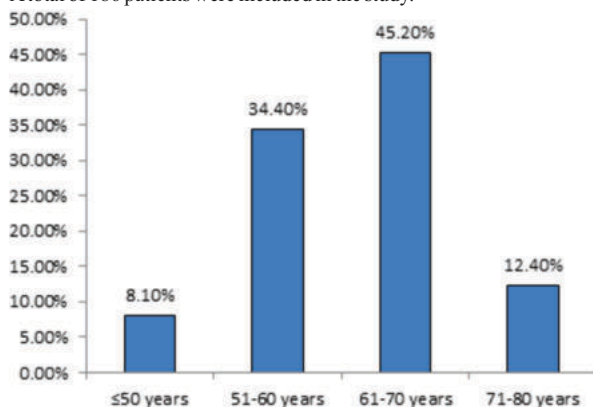


Fig 1- Age distribution of study population.

- The maximum numbers of patients were in the category of 61-70 years (45.2%).
- Mean age was 61.93 years. Out of 186 patients, 90(48.4%) were males and 96 (51.6%) were females.

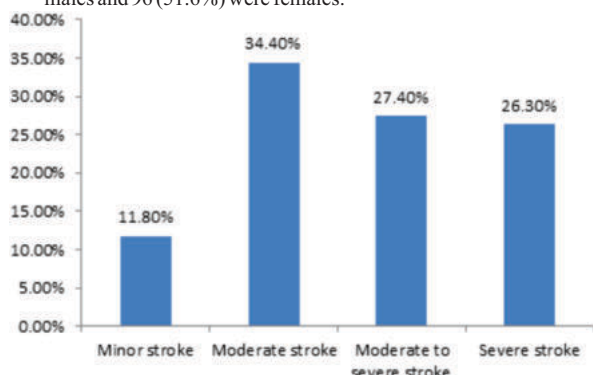


Fig 2- NIHSS Stroke severity Distribution

Out of 186 patients, 22(11.8%) had minor stroke, 64(34.4%) had moderate stroke, 51(27.4%) had moderate to severe stroke and 49(26.3%) had severe stroke. Mean score of NIHSS was 16.73.

Table 1- Value of RDW (mean and median) of the study population

RDW score	Value
Mean	15.59±3.7
Median	14.6 (12.4-18)

The mean value of RDW was 15.59 and the median was 14.6

Table 2- Disability categorization based on MRS scoring system

Modified Rankin Scale	Number (Percentage)
No significant disability	24 (12.9 %)
Slight disability	32 (17.2 %)
Moderate disability	57 (30.6 %)
Moderately severe disability	53 (28.5 %)
Severe disability	9 (4.8 %)
Death	11 (5.9 %)

According to MRS scale, the maximum number of patients belonged to the category of moderate disability with 30.6%.

Table 3- Association of RDW with stroke severity by NIHSS

VARIABLE	Stroke severity				P value
	Minor (N=22)	Moderate (N= 64)	Moderate to Severe (N= 51)	Severe (N=59)	
Mean RDW (%)	11.7±0.81	13.76±1.89	15.63±2.45	19.66±3.63	<0.001*

The mean value of RDW in category of minor stroke was 11.7, that of moderate stroke was 13.76, that of moderate to severe stroke was 15.63 and that of severe stroke was 19.66. There was significant correlation between severity of ischemic stroke and higher values of RDW ($p < 0.001$)

Table 4- Association of RDW with MRS

MRS CATEGORY	No disability (N=24)	Slight disability (N=32)	Moderate disability (N=57)	Moderately severe disability (N=53)	Severe disability (N=9)	Death (N=11)
Mean RDW in %	11.83±0.88	13.75±2.2	14.7±2.18	16.98±2.89	20.66±3.2	22.83±4.2

$p < 0.01$

The mean RDW value for MRS category with no disability was 11.83, that of slight disability was 13.75, moderate disability was 14.7, that if moderate to severe disability was 16.98 and that of severe disability was 20.66. The mean RDW value for patients who expired was 22.83. Higher the stroke disability, higher was the RDW values which was statistically significant at p value < 0.001

DISCUSSION

This study was conducted to determine the RDW values in patients admitted with acute ischemic stroke and to assess its correlation with severity of ischemic stroke using NIHSS and compare it to the final outcome with MRS score. Study population included patients with acute ischemic stroke admitted in medical wards, BGS GIMS Hospital, Bengaluru, who satisfied the inclusion and exclusion criteria. A total of 186 patients were included in this study.

Mean age of study population was 61.93 ± 7.6 years, consistent with a study by paramita *et al*, which showed that stroke occurred in older patients. Out of 186 patients, 90(48.4%) were males and 96 (51.6%) were females. Overall, more strokes occur in women than men, due to the longer lifespan of women compared to men. The higher stroke risk among women at younger ages likely reflects risks related to pregnancy and the post-partum state, as well as other hormonal factors, such as use of hormonal contraceptives.

Further on, the patients were categorized into different severities based on NIHSS scale. 11.8 % (22) of the study population belonged to minor stroke category, 34.4% (64) of the patients belonged to the moderate category, 27.4% (51) belonged to the moderate to severe category and 26.3% (49) of patients belonged to the severe category. Mean NIHSS was 16.73.

As per the study protocol, RDW values were compared with severity of the ischemic stroke. The mean RDW in the minor stroke category was 11.7 ± 0.81 , 13.76 ± 1.89 in the moderate stroke category, 15.63 ± 2.45 in the moderate to severe category and 19.66 ± 3.63 in the severe category of stroke. The p value for the relationship between RDW and severity of ischemic stroke was < 0.001 which is highly significant, indicating that higher RDW in ischemic stroke patients can be a predictor of higher severity. Similar observations were noted in a study by Song *et al*, where a total of 20 studies with 3,535,653 patients provided OR/RR and 95% CI regarding the risk of Ischemic stroke. Increased RDW was related to higher risk of combined stroke⁷. Kara *et al*. compared the RDW values in acute ischemic stroke patients in clusters with different severity scores and found RDW to be a predictive measure of stroke severity. The authors also reported a significant correlation between RDW and other parameters, such as NIHSS and Glasgow coma score (GCS), and found RDW with a cutoff point of 14⁸.

A comparison was also done between RDW and outcome of stroke as defined by MRS in ischemic stroke patients. The mean RDW value for MRS category with no disability was 11.83, that of slight disability was 13.75, moderate disability was 14.7, that if moderate to severe disability was 16.98 and that of severe disability was 20.66. The mean RDW value for patients who expired was 22.83. Higher the stroke disability, higher was the RDW values which was statistically

significant at p value < 0.001 , suggesting that RDW can be used as a predictor of outcome in ischemic stroke patients. A significant association has also been reported between NIHSS score and RDW value by Gianni Turcato et al. who reported that both the values of RDW (14.0% versus 13.6%; $p < 0.001$) and the NIHSS score (12 versus 4; $p < 0.001$) at admission, were found to be significantly increased in patients of acute ischemic stroke with unfavorable outcome compared to those with favorable outcomes. Turcato *et al.* studied 316 ischemic stroke patients undergoing thrombolytic therapy, and observed an over 6-fold higher mortality and 1.8-fold lower stroke recovery in patients with RDW values above the local cut-off⁹.

In summary, the present study showed that, RDW, a widely used and inexpensive test, is elevated in stroke patients. RDW has statistically significant positive correlation with the severity of ischemic stroke as assessed by NIHSS. Also, a statistically significant positive correlation was noted between RDW and outcome of ischemic stroke patients which was assessed by MRS.

Limitations:

The fluctuations in RDW and variations in RDW with time could not be accounted for as the RDW was measured only once (during admission).

CONCLUSIONS:

Our study concluded that, patients with acute ischemic stroke had a higher value of RDW. Testing RDW is simple, cost-effective and easily available. Hence, RDW can be used as a surrogate marker of severity as well as poor outcome in ischemic stroke patients.

Conflict Of Interest: Nil

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