Role of Red Cell Distribution Width in Severity Assessment of Ischemic Stroke

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Abstract:- Objective: To study the role of Red cell distribution width(RDW) in assessing the severity of ischemic stroke.

Materials and methodology: This cross-sectional observational study was conducted among 70 patients admitted in Bir Hospital with clinical symptomatology of stroke and/ or positive neuroimaging evidence of ischemic stroke during the study period (October 2019 to November 2020). Along with detailed history, clinical examination, routine CT scan, patient were subjected to routine blood investigations like Complete blood count (CBC) including RDW. RDW was categorised into high (RDW > 14.5) and low/normal (<14.5). National institute of health (NIH) stroke scorewas calculated to access the severity of stroke. The relationship between RDW and severity of ischemic stroke was checked statistically by Chi Square test.

Results: A total of 70 ischemic stroke patients were analysed for RCW among which 57% patient had RDW >14.5 and 43% had RDW<14.5. Among all, seven patients (10%) had mild, 51 (73%) had moderate, nine (13%) had moderate to severe and three (4%)) had severe stroke. The mean RDW in mild, moderate, moderate to severe and severe stroke were 12.886±1.11, 14.065±1.86, 16.922±2.06 and 18.200±1.04 respectively. High RDW was associated with greater severity of stroke. (p<0.01). An RDW value more than 14.5 was significantly associated with greater severity of stroke (p<0.01).

Conclusion: An RDW of 14.5 or more was associated with increased severity of stroke. Also greater RDW was significantly associated with higher grade of stroke.

Keywords:- Stroke; Ischemic stroke; Red cell distribution width.

I. INTRODUCTION

Traditionally,World Health Organization defined stroke as a "neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours".[1]In this definition emphasis was given to the reversibility of tissue damage and arbitrarily time frame of 24 hours was kept. The 24-hour time frame differentiates stroke from transient ischemic stroke, which usually resolves completely within 24 hours period.[2] Now as there are treatments available which when given in very early stage reduce stroke severity, newer terminologies, like acute ischemic cerebrovascular syndromeand brain attack are used to highlight the acute nature of disease and importance of prompt treatment.[3]

Broadly there are two types of stroke: ischemic and hemorrhagic. Ischemic stroke is the commonest form of stroke which occurs due to interruption in blood supply by thrombus or embolus. Clinical presentations of stroke may include weakness of one half of the body, speech abnormality in the form of aphasia, dysarthria or dysphonia, vertigo and visual disturbances.[2]

The Jaya Stroke Foundation, is an organization working in Nepal, which was established by Nepalese doctors and families of stroke patients. According to the foundations data, there are 50,000 new stroke cases every year and 15,000 mortality due to stroke.[4]While taking the data from Bir Hospital, one of the biggest tertiary hospital of Nepal, the incidence of ischemic and hemorrhagic stroke were 57.62% and 42.95% respectively.[5]

Red Cell Distribution Width (RDW) has nowadays been considered as a powerful predictor of morbidity and mortality in different cardiovascular diseases.[6] RDW is simple blood test indicating the variation of Red Blood Cell (RBC) size and volume. It can easily be determined by automated flow cytometry as a part of complete blood count (CBC). The normal value of RDW ranges from 11.5% to 14.5%.[7] Higher the value of RDW, poorer is the prognosis in certain disorders such as acute myocardial infarction, stroke and peripheral vascular disease.[8]RDW has emerged as a potential independent predictor of clinical outcomein patient with established cardiovascular disease. However, conclusion are yet to be made about the role of RDW in prognosis and severity of stroke.[9]

Inflammation has got a major role in development of red cell variability. It is responsible for changing membrane glycophorins and ion channels resulting in morphologic changes in the RBC. Chronic inflammation, oxidative stress and neurohumoral activation can all be contributory factors for the development of atherosclerosis. Hence we can conclude that higher value ofRDW may be a useful tool to follow the course of atherosclerosis and emergent stroke.[10] Several studies have been conducted to assess the relationship between RDW and ischemic stroke incidences along with its severity but such studies are lacking in our

population. This study aims to establish possible relation between RDW and ischemic stroke.

II. MATERIALS AND METHODOLOGY

This study is a hospital based cross sectional study conducted in department of internal medicine National Academy of Health Sciences (NAMS). Patients admitted in Bir Hospital with clinical symptomatology of stroke and/ or positive neuroimaging evidence of ischemic stroke during the study period were included as cases. Study was done from October 2019 to November 2020. A total of 70 cases were included in the study. Data analysis was done using statistical software IBM-SPSS (Statistical Package for Social Sciences) version 24.0. Analyzed data were presented as mean ± standard deviation for continuous variables and as numbers and percentages for categorical variables. Analyzed data were presented in the form of tables, graphs and charts. The p-value of less than 0.05 was considered significant.

III. RESULTS

Out of 70 cases, 61.3% were male and 38.57% were female, 52.86 % of the patient were smoker and 47.14% were nonsmoker, 44.29% were alcohol consumer and 55.71% were non-alcoholic, 24.29 % were non diabetic and 75.71 % were diabetic, 51.43% were hypertensive and 10% had previous history of CVD.(Table1)

Characters		Count	Percentage (%)
Sex	Male	43	61.43
	Female	27	38.57
Smoking	Yes	37	52.86
	No	33	47.14
Alcoholism	Yes	31	44.29
	No	39	55.71
Diabetes	Yes	17	24.29
	No	53	75.71
Hypertension	Yes	36	51.43
	No	32	45.71
Previous CVD	Yes	7	10.00
	No	63	90.00
Previous CAD	Yes	3	4.29
	No	67	95.71

Table 1: Risk factor profile of acute ischemic stroke

Characters		Count	%
<14.5	Male	24	34.29
	Female	16	22.86
>14.5	Male	19	27.14
	Female	11	15.71

Table 2: Red Cell Distribution Width

Table 2 shows that 24 males had RDW less than 14.5 and 19 had RDW more than 14.5, whereas 16 females had RDW less than 14.5 and 11 had RDW more than 14.5.
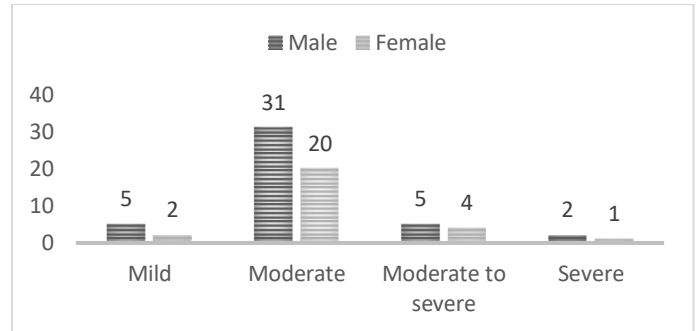

Fig. 1: Severity of stroke according to gender
Figure 1 shows that 51 patients had moderate stroke and only 3 patients had severe stroke

Severity	RDW			
	<14.5		>14.5	
	Count	%	Count	%
Mild	7	10.00	0	0.00
Moderate	32	45.71	19	27.14
Moderate / Severe	1	1.43	8	11.43
Severe	0	0.00	3	4.29
P-value	<0.001(Chi Square Test)			

Table 3: Association between RDW and Severity of Stroke

Table 3 shows significant difference in severity of stroke in relation to red cell distribution width.
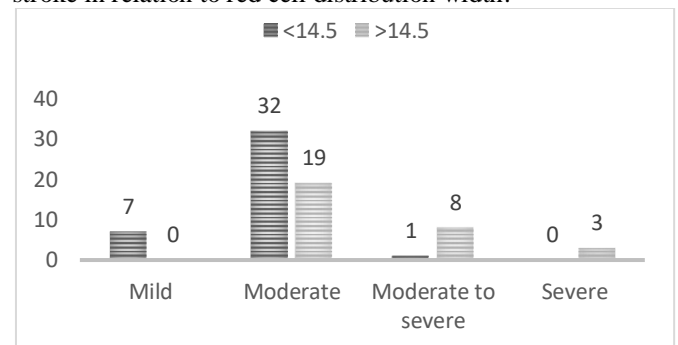
Fig. 2: Red Cell Distribution Width and Severity of Stroke

Severity	Count	Mean	Std. Deviation	P value
Mild	7	12.886	1.11	<0.01
Moderate	51	14.065	1.86	
Moderate to severe	9	16.922	2.06	
Severe	3	18.200	1.04	
Total	70	14.491	2.21	

Table 4: Mean RDW and severity of stroke

Table 4 shows that higher RDW is associated with greater severity of stroke significantly.

IV. DISCUSSION

Acute ischemic stroke is a sudden onset focal neurological deficit which can be described by a vascular territory. It can persist for more than 24 hours or can be fatal in less than 24 hours. Ischemic stroke can be diagnosed by history, neurological examination, and imaging methods like CT-Scan and MRI. There are few scoring systems useful in determination of severity and prognosis of ischemic strokes. Glasgow Coma Scale, Canadian Neurological Scale, Modified Rankin scale and National Institutes of Health Stroke Scale (NIHSS) are the common scoring systems used worldwide. These scoring systems are mainly based on the neurological examination of the patient. There is always a search for a biochemical parameter which can indicate the likelihood, severity and prognosis of ischemic stroke.

RDW is a simple blood parameter which indicates variability in size and volume of red cells.[12] The role of RDW traditionally was limited to studying the cases of anemia. However, recently there are various new studies concluding that, RDW elevation is not only seen in certain types of anemia but also in other diseases as well. Most of the studies are focused on RDW elevation in cardiovascular diseases [13], thrombosis [14], and stroke [15]. It has been suggested that inflammation has an important role in development of ischemic stroke. In other hand, RDW is also closely related to inflammatory responses. Thus there can be aclose relationship between RDW and stroke. Recent studies have shown that high RDW value can predict the incidence of ischemic stroke.[16] Also high RDW is associated with increased morbidity and mortality in such cases.[17]This study thus was done to evaluate the clinical value of RDW in ischemic stroke.

Seventy patients admitted in Bir Hospital with clinical symptomatology of stroke and/ or positive neuroimaging evidence of ischemic stroke from October 2019 to November 2020 were included in the study out of which 43 were male and 27 were female i.e. majority of stroke cases were male patient (61%) rather than female (39%). Similar result was observed in study done by Shrestha et al. in 2011, in which there were 59.05% males and 40.95% females.[5] Studies done by Pathak V et al.[4], and Maskey A et al.[18]in different medical colleges of Nepal showed similar results. This finding was consistent with the study done by Shah et al. in Nepalgunj Medical College in 2016.They observed that males (57.1%) were affected more than females (42.9%).[19]

In our study the most common risk factors were smoking- 53% and hypertension- 51% followed by alcohol consumption-44%, diabetes-24%, history of cerebrovascular disease-10%, history of coronary artery disease- 4%. In a study done by Shrestha et al. in 2011, the risk factors of ischemic stroke were smoking (60.48%), alcohol consumption(41.43%),hypertension (38.57%), diabetes mellitus (10%), dyslipidemia(9.05 %) and valvular heart disease (3.33%).[5]Whereas in a study done Shah et al. in Nepalgunj Medical College in 2016, conventional risk factors for ischemic stroke were as follows: alcohol use (63%),cigarette smoking (58.8%), hypertension (50.4%),diabetes (9.2%),previous vascular event (7.6%), heart disease (3.4%).[19] Similarly in a study at Manipal Medical college Teaching hospital by Maskey A et al. in cases of stroke, conventional modifiable risk factors were seen as follows: hypertension (61.2 %), cigarette smoking (59.4%), alcohol use (26.9%), left ventricular hypertrophy (27.5%), atrial fibrillation (23%), elevated triglyceride (23%), diabetes mellitus (9.3%) and elevated total cholesterol (7.5%). Multiple risk factors were seen in 76.5 % cases.[18] Also in studies done at Nepal medical college Teaching Hospital by Pathak V et al.,smoking (61%), hypertension (60%) and atrial fibrillation (8%) were the commonest modifiable risk factors in stroke patients.[4]

In our study population, majority of stroke cases were from age group 71-80 years (31.4%) followed by 61-70 years (25.7%), 51-60 years (21.4%), <30 years (10 %), 41-50 (8.6%), and 31-40 years (2.9%). This shows that increasing age is also an important factor to consider while evaluating the risk factors of stroke. Also, this suggest that the number of young stroke cases are also significant. In a study done by Shrestha et al. in 2011, 19 (9.05%) were below 45 years, 122 (58.10%) from 45 to 65 years age and 69(32.86%) more than 65 years.[5] Whereas in a study done Shah et al. in Nepalgunj Medical College in 2016, the mean age of stroke in study was 59.76±11.22 years.[19]Maskey A et al. in their study revealed the mean age of stroke patients was 65.98 years ± 10.69 with 126 (78.8%) of patients belonging to age group ≥ 60 years.[18]

Incidence of stroke is more in persons aged ≥65 years. As the aging population is increasing, the number of stroke cases is expected to rise.As the age advances,structural and functional alterations are expected to occur in both cerebral micro- and macro-circulations. In addition, with age there is increase in incidence of hypertension, diabetes and atrial fibrillation, which are important risk factors for development of ischemic stroke.[20]

Among the ischemic stroke cases we took for studies, majority of cases presented with focal motor weakness predominantly hemiplegia- 68 (97.14%), speech abnormality- 46 (65.71%) and other manifestations- 4 (5.71%). Our study was consistent with most of the studies done to evaluate the clinical profile of ischemic stroke patient. A study done by Punna et al. showed results similar to our study. In their study majority of the patients presented with hemiparesis (75.48%), whereas 5.8% with hemiplegia. Various other presentations observed were upper motor neuron (UMN) type of facial palsy (19.35%), followed by aphasia (5.8%), seizures (3.87%), and blurring vision (1.93%).[21] In a study done by Patne et al. most common clinical presentation was hemiplegia (55.28%) followed by speech involvement (13.82%), altered sensorium (9.75%), deep coma was seen in 7.31% patients and more than 2 associated clinical features were seen in 19.51%.[22]However,aphasia was the commonest presentation of ischemic stroke in a study done by Acharya et al. Headache and speech abnormalitywere significantly associated with different types of stroke.[23] Considering the clinical profile of the patientsin our study, advancing age

was the most common non-modifiable risk factor, smoking and hypertension being the most prevalent modifiable risk factor and focal motor weakness being the most common presenting manifestation. This finding is consistent with the finding of Acharya et al.[23], Pathak et al.[4]

In calculation of RDW in all patients with ischemic stroke, 40 patients (43%) had RDW more than 14.5 whereas 30 patients (57%) had RDW less than 14.5. And while the results of our study was consistent with the findings of the study done by Vijayashree et al., where mean values for RDW varied with severity of stroke.In mild form,the mean value of RDW was comparatively lower than that in moderate form of stroke. RDW values more than 13.0 were associated with increase in the risk of stroke.[24] Similar were the results in a prospective observational cohort study done between Jan 2014 to July 2014 in Turkey by Kara et al. including patients with acute ischemic stroke and control group of 40 patients, whose RDW, Glasgow Coma Scale (GCS) and national institute of health stroke scale (NIHSS) were calculated. Higher RDW values were associated with increased severity of stroke with each scoring system. According to them, there were few studies available about the association between RDW and stroke and there is no clear cut off value of RDW in prediction of ischemic stroke. This study showed an optimal RDW cut off of 14%.[10] Similar results were seen in a case control study done by Moreno et al. which was published on International journal of stroke on 2013 where RDW in cases of ischemic stroke ranged from 12.2% to 26.1%.and in control ranged from 11.30% to 21.70% . Patient with RDW more than 14.61% were significantly more likely to have a stroke compared with patients with RDW less than 13.27%.The study showed stepwise association between RDW levels and risk of stroke.[25] Another study that had similar results as ours was done by SoderHolm et al. in Lund University, Malmo, Sweden between 1991 and 1996 where high RDW was associated with increased incidence of total stroke. In addition, they also found that carotid plaque was more prevalent in patients with high RDW.[26]

In contrast to most of the studies, Lappegard et al. concluded that higher RDW levels was not associated with the risk of stroke-induced mortality after exclusion of anemia.[27] However, Turcato et al. indicated that RDW could independently predictseverity and prognosis in patients with acute ischemic stroke who underwent antithrombotic therapy. [28]

Most of the case control studies done to evaluate the relationship between the RDW had finding of higher RDW value in cases of stroke in comparison to control group. But in our study which is a cohort study, among the stroke patients most of the patient had RDW in the normal ranges. This may be because of the fact that most of the cases in our study were not severe. However while analysing grades of stroke in relation to RDW, it is clear in our study that with increasing severity of stroke, the value of RDW has also increased.

In most of the clinical settingsthere is a delay in diagnosis of ischemic stroke because of late presentation and delay in neuroimaging. Due to this delay most of the patients cross the golden time frame for thrombolysis therapy. It is important to minimize these delays in order to increase the number of effective thrombolysis. If a blood test is available the report of which can be beneficial in suspicion and early diagnosis of stroke, the number of effective thrombolysis can be increased. The blood test should be easy to perform, less expensive, less time consuming and available at most of the clinical settings. RDW can be one of such blood marker which when increased not only indicates high likelihood of stroke but also can give some idea about stroke severity and prognosis. In ageing population because of anemia and various other comorbidities RDW may not be appropriate screening tool to measure the risk and severity of stroke.[10]

V. CONCLUSION

RDW of 14.5 or more was associated with increased severity of stroke. Also, greater RDW was significantly associated with higher grade of stroke

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