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Red Blood Cell Anomalies Associated with Ischemic Stroke - An Observational Study

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ABSTRACT

Background: Cerebrovascular diseases, including stroke, are a major global health issue, ranking as the second most common cause of death globally. Alterations in red blood cells, such as variations in concentration such as polycythemia or anemia, as well as structural modifications in hemoglobin, can play a role in contributing to these conditions. **Aim:** To investigate whether abnormalities in red blood cell parameters relate to the progression of ischemic stroke disease. **Methodology: Study design** - Retrospective study **Study site** - Sudha Institute of Medical Science, Erode, Tamilnadu. **Study duration** - Six months from January 2023-June 2023 **Study population** - 150 patients with ischemic stroke and 150 patients with other comorbidities except ischemic stroke admitted to the hospital. **Study criteria -** Inclusion criteria include patients with known cases of stroke and age more than 18 years old and Exclusion criteria include patients with diseased condition that can elevate blood parameters, pregnant women. **Statistical analysis** – Chi-square test **Results:** Men were frequently impacted by ischemic stroke, with a higher prevalence observed in individuals aged 61 to 90 years and those with abnormal weight. Common risk factors among stroke patients include obesity, smoking, alcohol consumption, hypertension, and diabetes. Ischemic stroke patients also exhibit lower levels of Hb, HCT, MCV, MCH, MCHC, and RBC, along with higher RDW levels compared to those without ischemic stroke, showing a statistically significant difference between the two groups. **Conclusion:** This study concluded that standard red blood cell parameters such as RBC, Hb, HCT, MCV, MCH, MCHC, and RDW hold significant value and can serve as prognostic indicators for ischemic stroke.

INTRODUCTION:

Stroke is a significant global health concern, ranking as the second leading cause of death worldwide in 1990 according to the Global Burden of Diseases (GBD) study [1]. A systematic review of population-based stroke studies revealed that the incidence rate of stroke in Low and Middle-Income Countries (LMICs) has increased over the years, reaching 117 cases per 100,000 person-years between 2000 and 2008 [2]. Stroke is the second leading cause of death, physical disability, hospitalization, dementia, and depression in developed as well as developing countries [3]. This trend is expected to continue, with projections indicating a rise to 1.5 million cases by 2025 due to aging populations and persistent risk factors [4].

Clots that form in the brain can disrupt blood flow by blocking arteries and causing blood vessels to rupture, resulting in bleeding. This rupture of brain arteries during a stroke leads to the sudden death of brain cells due to oxygen deprivation [4]. The prevalence and incidence of strokes are strongly correlated with age, with the average age of stroke patients typically ranging from 70 to 75 years, and the majority of stroke cases occurring in individuals over 65 years old [5]. Primary abnormalities in red blood cells, such as changes in concentration like polycythemia or anemia, or structural changes in hemoglobin, can contribute to cerebrovascular diseases [6]. Factors including anemia can influence the development of stroke and lead to varying prognoses for ischemic strokes in the same arterial region [7]. Anemia refers to a decrease in red blood cells or hemoglobin levels in the blood [8], commonly caused by blood loss, insufficient production of red blood cells, or increased breakdown of these cells. Both high and low levels of hemoglobin increase the risk of developing ischemic stroke in both men and women [9]. Abnormalities in red blood cell indices have been identified as risk factors for thromboembolism in adults, including conditions like cardiovascular disease, ischemic stroke, and venous thromboembolism [10].

Numerous factors play a role in predicting stroke prognosis, including stroke subtype, patient age, stroke severity, and the location of the infarct [11]. Laboratory findings have also been suggested as prognostic markers, with red cell distribution width (RDW) being used to anticipate functional outcomes and the seriousness of cerebrovascular events, although not universally supported by all research [12-13]. Mean platelet volume (MPV) has also been proposed as a potential indicator of ischemic stroke prognosis [14]. Inflammation plays a significant role in the development of strokes, with previous research indicating a strong connection between red cell distribution width (RDW) and inflammatory reactions [15--16].

Controversial prognostic factors within laboratory findings have been identified in stroke research. The study seeks to establish whether deviations observed in red blood cell parameters are linked to the progression of ischemic stroke. It aims to investigate the potential association between these anomalies and the advancement of the disease, particularly focusing on how variations in red blood cell characteristics may influence the course and severity of ischemic stroke over time.

AIM:

To assess whether abnormalities in red blood cell parameters correlate with the progression of ischemic stroke disease.

OBJECTIVES:

- To assess changes in hematological parameters throughout the progression of ischemic stroke.
- To determine the specific red blood cell (RBC) parameters, including RBC count, hemoglobin (Hb) levels, hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and red cell distribution width (RDW), that are closely linked to the prognosis of ischemic stroke.
- To ascertain if changes in RBC parameters can serve as predictive indicators for the progression of ischemic stroke.

MATERIALS AND METHODS:

Study design - Retrospective study

Study site - The study is carried out in the inpatient department of neurology in Sudha Institute of Medical Science, Erode, Tamilnadu.

Study duration - The study was performed for six months from January 2023-June 2023.

Study population - The study includes 150 patients with ischemic stroke and 150 patients with other comorbidities except ischemic stroke admitted in the hospital.

Design of proforma - A separate data collection form is used to record patient details (Patient demographics, social history, past medical and medication history, laboratory values of RBC parameters, diagnosis, other co-morbidities.

Study criteria

Inclusion criteria

- Inpatients admitted with symptoms suggestive of acute Ischemic stroke.
- Inpatients aged greater than ≥ 18 years who presented with Acute Ischemic Stroke and Transient Ischemic Attack within 7 days of symptoms.

Exclusion criteria:

- Pregnant women
- Individuals with abnormal hemoglobin levels or sickle cell disease
- Patients with hematological conditions such as leukemia or myeloproliferative disorders
- Patients experiencing heavy bleeding or abnormal menstruation symptoms (in females) were excluded from the study.

Study procedure - The current study collected data including complete blood reports, past medical and medication history, diagnosis, and other co-morbidities of patient case group who were visited and admitted in neurology department of tertiary health care hospital, Erode. The information for the control group was obtained from another department within the same hospital.

Ethical consideration -The study is approved by the Institutional Ethical Committee (IEC) for ethical approval. [Registration No: ECR/948/Inst/TN/2018/RR-22 Approval No: SH/IEC/Approval-032/April 2023]

Data collection - The study data were collected from patient records and laboratory assessments using customized forms. These forms encompassed patient details such as demographics, social background, medical history including medications, laboratory results for red blood cell parameters, diagnoses, coexisting conditions, and drug treatments administered during hospitalization and discharge.

Statistical analysis - The gathered data were inputted into MS Excel and subsequently analyzed utilizing IBM-SPSS. Comparisons were evaluated employing the Chi-square test, with statistical significance set at a P-value of ≤ 0.05.

RESULTS:

This study comprises 150 individuals diagnosed with ischemic stroke as the case group and an equal number of individuals with a different disease as the control group. The gender distribution, age demographics, body weight status, past hypertension history, and hematological parameters were evaluated across both groups.

Figure 1 outlines the gender distribution, indicating a higher incidence of ischemic stroke among males compared to females. **Table 1** highlights that the majority of stroke patients fall within the 61-90 age category. **Table 2** reveals that most ischemic stroke patients exhibit abnormal body weight.

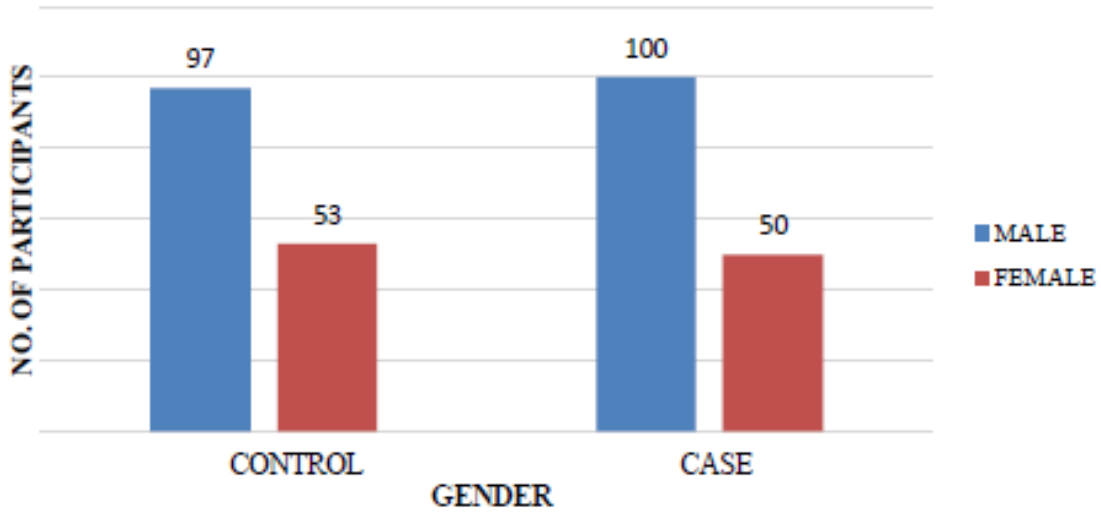

Figure 1: Gender-wise distribution

Table 1: Age-wise distribution

SI.NO	AGE (in yrs)	CONTROL (N=150)		CASE (N=150)	
		No. of patients	% of patients	No. of patients	% of patients
1	21 – 40	14	9.33	17	11.34
2	41 – 60	69	46	62	41.33
3	61 - 90	67	44.67	71	47.33
TOTAL		150	100	150	100

Table 2: BMI Based distribution of study participants

SI.NO	BMI Category	Control (N = 150)		Case (N=150)	
		No. of patients	% of patients	No. of patients	% of patients
1	Under-weight	0	0	0	0
2	Normal weight	100	66.67	17	11.33
3	Overweight	44	29.33	71	47.33
4	Obese Class-1	6	4	50	33.34
5	Obese Class-2	0	0	12	4
Total		150	100	150	100

Table 3 indicates a significant portion of participants with a history of hypertension.

Table 3: Risk factors based distribution among study participants

SI.NO	Risk factors	Number of patients	Percentage of patients
1	Obesity	88	58.66
2	Smoking	64	42.66
3	Diabetes	55	36.6
4	Hypertension	96	64
5	Alcohol intake	54	36

Figures 2 and 3 depict abnormal hematological parameters predominantly in male patients across both case and control groups. **Table 4** illustrates a substantial percentage (approximately 94%) of patients with low hemoglobin levels in the case group.

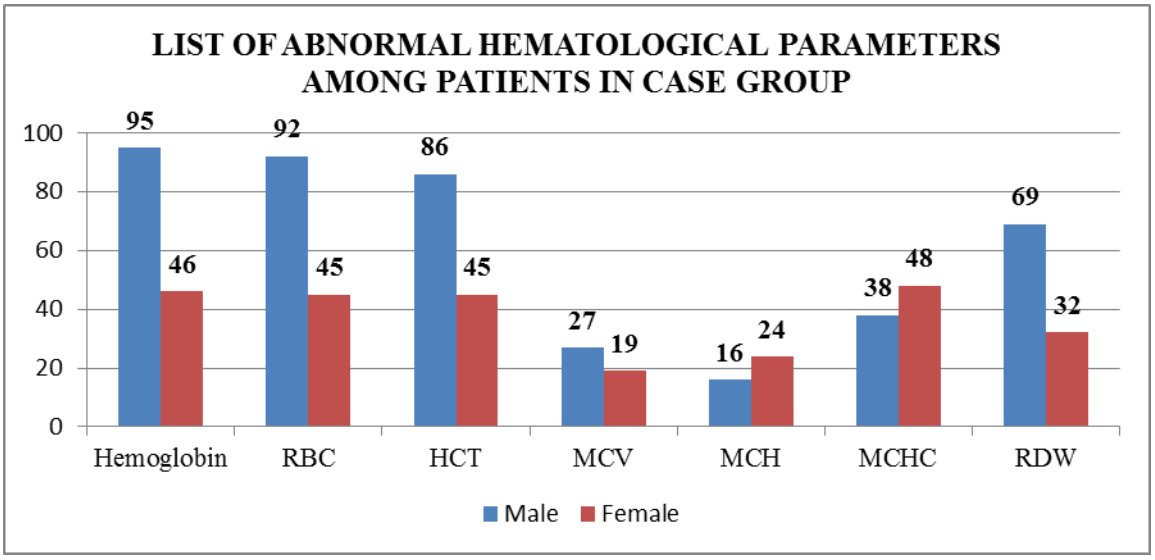

Figure 2: LIST OF ABNORMAL HEMATOLOGICAL PARAMETERS AMONG PATIENTS IN CONTROL GROUPS

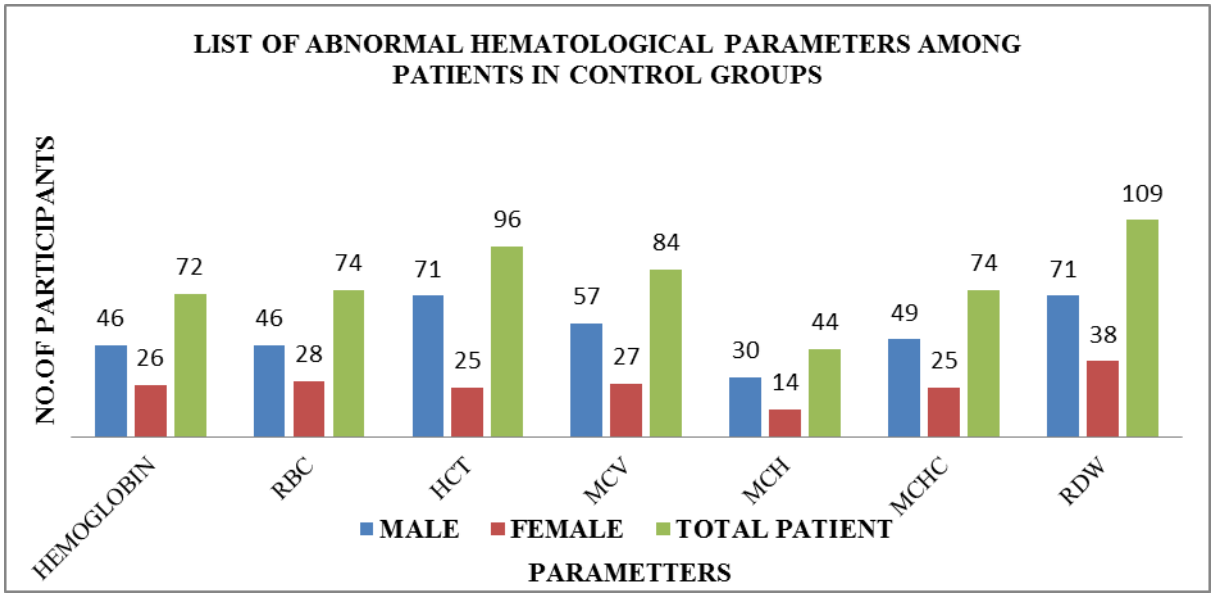

Figure 3: LIST OF ABNORMAL HEMATOLOGICAL PARAMETERS AMONG PATIENTS IN CASE GROUPS

Table 4: Comparison of Hb level in case and control groups

Hematological parameter (Hb - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total numbers	Percentage	Total numbers	Percentage		
Low	62	41.33%	141	94%	x^2 =95.21	<0.00001
Normal	78	52%	8	5.33%		
High	10	6.66%	1	0.60%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Table 5 shows a majority (78%) with low RBC levels in the case group. **Table 6** displays a high percentage (89.33%) with low hematocrit levels in the case group.

Table 5: Comparison of RBC level in case and control groups

Hematological parameter (RBC - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total numbers	Percentage	Total numbers	Percentage		
Low	60	40%	117	78%	x^2 =436.88	<0.00001
Normal	75	50%	30	20%		
High	15	10%	3	2%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Table 6: Comparison of Hematocrit level in case and control groups

Hematological parameter (HCT - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total numbers	Percentage	Total numbers	Percentage		
Low	64	42.66%	134	89.33%		
Normal	54	36%	16	10.66%	x^2 =339.634	<0.00001
High	32	21.33%	0	0%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Regarding MCV levels (**Table 7**), around 69.33% were normal, while approximately 30% had low MCV levels in the case group. Similarly, **Table 8** shows that 73.33% had normal MCH levels, with 20.66% exhibiting low MCH levels.

Table 7: Comparison of MCV level in case and control groups

Hematological parameter (MCV - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total Numbers	Percentage	Total numbers	Percentage		
Low	60	40%	45	30%		
Normal	66	44%	104	69.33%	x^2 =1245.76	<0.00001
High	24	16%	1	0.66%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Table 8: Comparison of MCH level in case and control groups

Hematological parameter (MCH - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total Numbers	Percentage	Total numbers	Percentage		
Low	29	19.33%	31	20.66%		
Normal	106	70.66%	110	73.33%	x^2 =158.54	<0.00001
High	15	10%	9	6%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Table 9 indicates that 53.33% had low MCHC levels, while 42.66% had normal MCHC levels in the case group. **Table 10** reveals that 62.66% had high RDW levels, with 32.66% showing normal RDW levels in the case group. The study found significant differences in hematological parameters between the case and control groups, indicating potential correlations with ischemic stroke.

Table 9: Comparison of MCHC level in case and control groups

Hematological parameter (MCHC - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total numbers	Percentage	Total numbers	Percentage		
Low	61	40.66%	80	53.33%		
Normal	76	50.60%	64	42.66%	x^2 =179.82	<0.00001
High	13	8.66%	6	4%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

Table 10: Comparison of RDW level in case and control groups:

Hematological parameter (RDW - status)	Control (n=150)		Case (n=150)		Chi-Square value	*p-value*
	Total numbers	Percentage	Total numbers	Percentage		
Low	20	13.33%	7	4.66%		
Normal	41	27.33%	49	32.66%	$x^2 = 201.39$	<0.00001
High	89	59.33%	94	62.66%		
Total	150	100%	150	100%		

(**p value* <0.05 is considered as significant)

The analysis highlights significant differences between the case group (ischemic stroke patients) and the control group across all measured hematological parameters. These findings provide valuable insights into the characteristics and health status of patients with ischemic stroke, contributing to a deeper understanding of the condition and its potential associations with other health factors.

DISCUSSION:

The results of this study revealed a higher incidence of stroke in males compared to females. However, another study conducted by Raghavendra L Girijala et al. in 2016 contradicts our findings, showing that females have a higher incidence of stroke than males [17]. Both Yousuffudin et al. in 2019 [20] and Rui-Cen MM et al. in 2019 [19] concluded that individuals above 60 years old are at a higher risk of developing ischemic strokes. Cerebral amyloid angiopathy and anticoagulant-related hemorrhagic stroke are significant causes of hemorrhagic stroke in the elderly, particularly those above 60 years old [21].

Abnormal weight individuals were found to have a higher risk of stroke in our study, consistent with the findings of Hongfei Gu et al. in 2019, who identified overweight as an independent predictor of stroke symptoms, possibly due to lifestyle modifications and associated risk factors in this population group [22]. The major risk factors among stroke patients identified in our study were diabetes, alcohol intake, smoking, hypertension, and obesity, which align with the conclusions of a study by Hankey GJ et al. in 2017 [18], highlighting the common association of these factors with stroke.

The findings of this study revealed that a majority of ischemic stroke patients exhibit low levels of Hb, RBC, Hct, MCV, MCH, MCHC, and high RDW levels. Dr. Shaheen B. Shaikh et al.'s 2020 study highlighted that decreased Hb levels can exacerbate brain ischemia [23]. Similarly, Hamidreza Hatamin et al.'s 2022 [24] study indicated that low RBC levels independently predict ischemic stroke. Dr. Shaheen B. Shaikh et al.'s 2020 research also linked low hematocrit levels to stroke progression [23]. Moreover, lower MCV levels were identified as an independent predictor of ischemic stroke in Hamidreza Hatamin et al.'s 2022 study [24]. Hafa Nasim [25] et al.'s 2021 study associated low MCH levels with ischemic group patients, while Janki Punekar et al.'s 2022 study found that lower MCHC levels were linked to mortality in ischemic stroke patients [26]. Additionally, Gang-Hua Feng et al.'s 2017 study reported higher RDW levels, aligning with similar results regarding RDW parameters in ischemic stroke patients [27]. The Framingham study in 1972 revealed a potential link between elevated hemoglobin levels and cerebral infarction, suggesting that high hematocrit (Hct) could be a risk factor for cerebral ischemia [28]. Subsequent clinical and clinic-pathological observations have also hinted at a connection between high Hct levels and the development of cerebral ischemia [29]. To thoroughly assess whether changes in hematological parameters contribute to a heightened risk of cerebral ischemic stroke, additional investigations and long-term studies are necessary.

Conclusion:

This study suggests that routine Red blood cell (RBC) parameters, including Red blood cell (RBC) count, Hemoglobin (Hb) level, Hematocrit (HCT), Mean corpuscular volume (MCV), Mean corpuscular Hemoglobin (MCH), Mean corpuscular Hemoglobin concentration (MCHC), and Red cell distribution width (RDW), hold significant value as prognostic indicators for ischemic stroke. Their accessibility, cost-effectiveness, and consistent interpretation among observers make them favorable compared to other newly discovered prognostic indicators. A continuous change in hematological parameters in individuals following a recent cerebral ischemic event suggests that these alterations may reflect a straightforward inflammatory response occurring during the progression of ischemic injury.

Conflict of interest:

Nil

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Nil

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Nil

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