

Significance of Hematological Parameters in Determining Prognosis of Acute Ischemic Stroke

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ABSTRACT

Abstract: Stroke is the second most common cause of death worldwide. Various studies have highlighted the prognostic importance of hematological parameters in acute ischemic stroke including Erythrocyte Sedimentation Rate (ESR), C Reactive protein (CRP), Mean Platelet Volume (MPV), Total Leukocyte Count (TLC), platelet count, and hemoglobin.

Objectives: To determine the prognosis of acute ischemic stroke and compare mean hematological parameters based on the prognosis of acute ischemic stroke.

Material and Methods: 130 patients fulfilling the selection criteria were selected. Blood sample from each patient was obtained. Analysis for CRP and ESR obtained. Patients with acute ischemic stroke presenting within 72 hrs of the onset of symptoms of stroke were included. Correlation for the association between Outcome with Hemoglobin, TLC, Platelet, MPV, ESR & CRP. Means comparison between Expired group & Discharged group with Hemoglobin, TLC, Platelet, MPV, ESR and CRP using Independent sample's t-test done. A p-value of < 0.05 was taken as statistically significant.

Results: Our findings showed that mean±SD for quantitative variables like Hemoglobin, total leukocyte count, platelet, mean platelet volume, ESR & CRP were 10.2±2.9, 14.5±11.0, 142.4±93.8, 16.5±10.4, 42.3±35.9 & 18.5±23.4 respectively. There were 52.3% of patients who were expired and 47.7% of patients who were discharged. There was an association between outcomes of the patients with the variables like Hemoglobin, TLC, Platelet, MPV, ESR & CRP as all p-values are significant i.e.; 0.011, 0.020, 0.024, 0.000, 0.026 & 0.013. Moreover, total leukocyte count, mean platelet volume, ESR & CRP are inversely proportional to the patients who expired or were discharged. Means comparison for the Expired group & Discharged group with Hemoglobin, TLC, Platelet, MPV, ESR & CRP are 9.56 & 11.02, 17.38 & 11.54, 126.22 & 160.27, 19.88 & 12.82, 49.91 & 34.10 & 25.47 & 10.86 respectively. The mean Discharged group is greater than the mean Expired group in Hemoglobin and Platelet. Mean Expired group is greater than the mean Discharged group in TLC, MPV, ESR & CRP.

Conclusion: We concluded that a significant change was found in hematological parameters in ischemic stroke patients. In light of our results that depicted the difference in the readings of the values for each parameter like hemoglobin, erythrocyte sedimentation rate, platelets count, mean platelet volume, c-reactive protein, and leukocyte count we suggest that these hematological parameters can be used as a tool to take the measures necessary for the prevention of future damage by stroke.

Key Words: Stroke, Hematological Parameters, and Prognosis.

Introduction

Stroke is the second most common cause of death and is a major cause of serious morbidity and mortality worldwide.¹

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It is now the need of the hour to have a reasonable assessment of the burden of diseases like

Stroke as evaluated by the highly influential Global Burden of Disease (GBD) publications.²

The most important feature of ischemia is impeded perfusion to the brain due to poor blood flow. The chance of having infarction increases if more than 95% of cerebral blood flow (CBF) in the affected tissue area falls to less than 25% of its normal value as revealed by the literature review. However, the chance of

infarction is just 5% if CBF in the affected tissue area is above 50% of its normal value.³

Given the high prevalence and mortality rate, prognosis and accurate prediction are vital in clinical settings while selecting proper management strategies.⁴ Apart from clinical and neuro-imaging parameters, many studies have highlighted the prognostic importance of various hematological parameters in acute ischemic stroke such as ESR, CRP, MPV, TLC, platelet count, and hemoglobin.⁵

A study conducted in India in 2015 revealed significant changes in hematological parameters in patients suffering from acute ischemic stroke. Among a total of 205 cases, 140 (68.29%) patients were discharged and 65 (31.70%) patients expired during the hospital stay. Mean value of ESR, TLC, CRP, and MPV was high in expired group, i.e., 30.33 (\pm 5.6), 15.6 (\pm 2.9), 4.5 (\pm 1) and 11.8 (\pm 0.9) as compared to discharged group, i.e., 23.8 (\pm 8.94), 9.2 (\pm 3.4), 2 (\pm 0.5), 10 (\pm 0.5). Platelet count in the expired group was low, i.e., 1.68 (\pm 0.72) as compared to discharged group 2.02 (\pm 0.6).⁶

Predicting outcomes in stroke remains an unanswered question. Most studies focus on conventional risk factors, clinical conditions, and radiological parameters. While the aim of the study was to take into consideration hematological parameters which may present themselves as a better alternative in predicting the outcome of acute ischemic stroke.

Materials and Methods

This Descriptive case series was conducted in the Department of Hematology, Holy Family Hospital, Rawalpindi-Pakistan. Duration of Study was Six months after approval of synopsis. Sample Size was calculated using WHO sample size calculator, keeping a level of significance of 5%, confidence interval at 95%, anticipated population proportion at 0.317, absolute precision at 0.08 sample size was 130. Sampling Technique used was Nonprobability consecutive sampling.

Patient with acute ischemic stroke presenting within 72 hrs of the onset of symptoms of stroke was included. Exclusion Criteria used was:

- Patients were admitted 72 hours after the onset of symptoms of a stroke.
- Patients with stroke due to trauma, tumor, infection, infarction, or bleeding.
- Patients with known thyroid disease.
- Patients with known hematological disorder

Approval from the Institutional Research Forum of Rawalpindi medical university and informed consent was obtained. Data regarding demographic information (name and age) and hospital registration numbers were obtained. Then blood sample from each patient was obtained under aseptic measures by using a 3 cc syringe (purple top) containing EDTA. After mixing the sample on the rotator the complete blood picture was obtained with the help of an automated blood counter, i.e., sysmex or mindray. ESR was measured with the help of the westergren method. A sample for CRP was taken in gel tube and is then analyzed by means of an agglutination technique. Reports were assessed by the researcher herself and all the information was recorded in the study proforma

The collected data was entered and analyzed through SPSS version 22.0. Mean & Standard deviation was calculated for quantitative variables i.e; Hemoglobin, total leukocyte count, platelet, mean platelet volume, ESR & CRP. Frequency, percentage & Pie graph for qualitative variable Outcome. Spearman's rho Correlation for association between Outcome with Hemoglobin, TLC, Platelet, MPV, ESR & CRP. Means comparison between Expired group & Discharged group with Hemoglobin, TLC, Platelet, MPV, ESR & CRP using Independent sample's t-test. A p-value of < - 0.05 was taken as statistically significant.

Results

In table-1, results showed that the Mean \pm SD for the quantitative variables Hemoglobin, total leukocyte count, platelet, mean platelet volume, ESR & CRP are 10.2 \pm 2.9, 14.5 \pm 11.0, 142.4 \pm 93.8, 16.5 \pm 10.4, 42.3 \pm 35.9 & 18.5 \pm 23.4 respectively.

Table 1: Mean & Standard Deviation of quantitative variables

Variables	Mean	Standard Deviation
Hemoglobin (g/dl)	10.2	2.9
Total Leukocyte Count (TLC) x 10 ⁹ /L	14.5	11.0
Platelet x 10 ⁹ /L	142.4	93.8
Mean Platelet Volume (fl)	16.5	10.4
ESR Mm/hr	42.3	35.9
CRP mg/l	18.5	23.4

Results showed that there was 52.3% patients who expired & 47.7% patients who discharged out of 130 total study sample. Results were also shown graphically in figure-1 below.

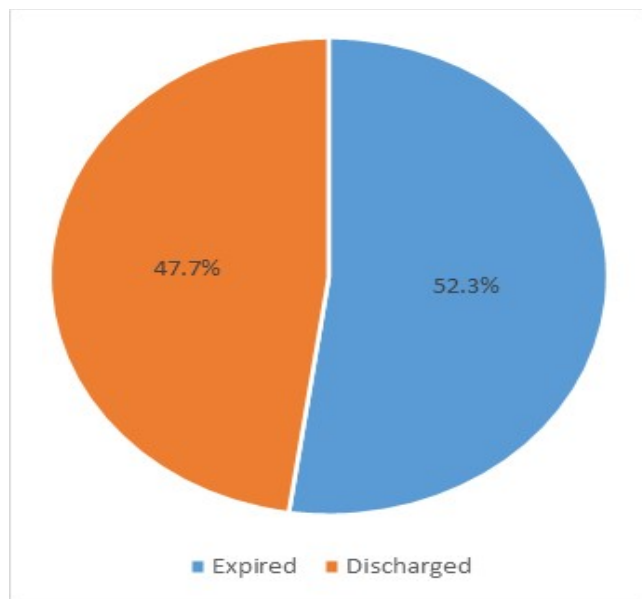


Figure1: Depicting Outcomes in Terms of Percentages

In table-2, results showed that there was an association between the Outcome (rather expired or discharged) of the patients with the variables like Hemoglobin, TCL, Platelet, MPV, ESR & CRP as all p-values were significant i.e; 0.011, 0.020, 0.024, 0.000, 0.026 & 0.013 (which are less than 0.05). Moreover, total leukocyte count, mean platelet volume, ESR & CRP are inversely proportional with the patients who expired or were discharged.

Table 2: Spearman’s Rho Correlation Association of Outcome with Hemoglobin, TCL, Platelet, MPV, ESR & CRP

Variables	P-value	Spearman’s Rho Coefficient
Hemoglobin (g/dl)	0.011	0.222
Total Leukocyte Count (TCL) x 109/L	0.020	-0.203
Platelet x 109/L	0.024	0.197
Mean Platelet Volume (fl)	0.000	-0.328
ESR Mm/hr	0.026	-0.195
CRP mg/l	0.013	-0.218

Means comparison for Expired group & Discharged group with Hemoglobin, TLC, Platelet, MPV, ESR & CRP are 9.56 & 11.02, 17.38 & 11.54, 126.22 & 160.27, 19.88 & 12.82, 49.91 & 34.10 & 25.47 & 10.86 respectively. Mean Discharged group is greater than mean Expired group in Hemoglobin & Platelet, mean Expired group is greater than mean Discharged group in TLC, MPV, ESR & CRP as shown in table-3 below.

Table 3: Means comparison with Discharged & Expired groups

Variables	Outcomes	Mean	Standard Deviation
Hemoglobin (g/dl)	Expired	9.56	3.25
	Discharged	11.02	2.26
Total Leukocyte Count (TCL) x 109/L	Expired	17.38	13.65
	Discharged	11.54	5.95
Platelet x 109/L	Expired	126.22	98.65
	Discharged	160.27	85.63
Mean Platelet Volume (fl)	Expired	19.88	12.39
	Discharged	12.82	5.90
ESR Mm/hr	Expired	49.91	39.14
	Discharged	34.10	30.30
CRP mg/l	Expired	25.47	27.41
	Discharged	10.86	15.11

In table 4, Levene’s Test for Equality of Variances had p-values for Hemoglobin, TLC, Platelet, MPV, ESR & CRP in Expired & Discharged group are 0.001, 0.000, 0.012, 0.000, 0.004 & 0.000 with F-values 11.937, 15.826, 6.439, 25.477, 8.833 & 40.462 showed all significant p-values as these were less than 0.05 & concludes that the variances of Expired group & Discharged group were significantly different.

Table 4: Independent Samples Test

Equal variances assumed / not assumed	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Upper	Lower
Hemoglobin (g/dl)									
Equal variances assumed	11.937	.001	-2.940	128	.004	-1.4598	.4965	-2.4422	-.4773
Equal variances not assumed			-2.988	120.015	.003	-1.4598	.4886	-2.4271	-.4924
Total Leukocyte Count X 109/L									
Equal variances assumed	15.826	.000	3.112	128	.002	5.8464	1.8788	2.1289	9.5640
Equal variances not assumed			3.212	93.383	.002	5.8464	1.8203	2.2320	9.4609
Platelet X 109 /L									
Equal variances assumed	6.439	.012	-2.093	128	.038	-34.054	16.274	-66.254	-1.853
Equal variances not assumed			-2.106	127.702	.037	-34.054	16.168	-66.045	-2.063
Mean Platelet Volume (fl)									
Equal variances assumed	25.477	.000	4.082	128	.000	7.060	1.729	3.638	10.482
Equal variances not assumed			4.204	97.830	.000	7.060	1.679	3.727	10.393
ESR Mm/hr									
Equal variances assumed	8.833	.004	2.558	128	.012	15.815	6.183	3.581	28.049
Equal variances not assumed			2.588	124.807	.011	15.815	6.112	3.719	27.911
CRP mg/l									
Equal variances assumed	40.462	.000	3.712	128	.000	14.608	3.935	6.821	22.394
Equal variances not assumed			3.805	106.183	.000	14.608	3.839	6.997	22.218

Discussion

The chance of stroke increases with the increase in age. Up to 3 percent of the population belonging to 45 to 64 years of age gets a stroke whereas, this percentage increases up to 6 percent for people in the age group of 65 to 74.18 It is 2-3 times more prevalent in men as compared to women.⁷ Due to its rapid occurrence, new and different treatment and diagnostic methods have been introduced.

For our study, the mean values of hemoglobin, total leukocyte count, platelet count, mean platelet volume, erythrocyte sedimentation rate, and C reactive protein were found to be different from the normal values for these parameters which indicated a change in them with an ischemic stroke.

Moreover, within the sample of 130, 68 patients met the poor outcome criteria and 52.3 percent of the population expired during the hospitalization period after the ischemic stroke. Hence predicting a bad prognosis. Whereas 62 patients met the good outcome criteria of the study that is 47.7 percent population was discharged from the hospital without any complications after the ischemic stroke. Hence predicting a good prognosis.

For our study, we compared the mean values of the hematological parameters for the two groups i.e good

prognosis (discharged without complications) and bad prognosis (expired or having complications). It was seen that the patients that expired within 72 hours of stroke had their mean hemoglobin levels at a much lower level as compared to the normal range of hemoglobin. Whereas the mean hemoglobin levels for the patients that were discharged had their hemoglobin levels close to the normal range. It was seen that for both groups, hemoglobin concentration was found to be lower than normal. The association between lower levels of hemoglobin and stroke is unknown. However, there is a possible explanation for its role in carrying and supplying oxygen. Hemoglobin is known to carry 98 percent of blood oxygen. Since the brain with a stroke is under the influence of trauma, this might hinder its ability to increase the extraction of available oxygen. However, the increased mortality rate can be explained through different mechanisms.⁸ First, with the decrease in hemoglobin levels, oxygen-carrying capacity is also lowered, hence intensifying ischemia. This can cause hypoxia within the penumbral lesions of patients with ischemic stroke.⁹ Secondly, lower levels of hemoglobin may lead to hyperdynamic circulation which is known to modulate the expression of adhesion molecules on vascular endothelial cells by upregulating their production. This can cause an inflammatory response

responsible for thrombus formulation.¹⁰ Our results were congruent with the results of Barlas et. al. (2016) they found that a change in hemoglobin level in ischemic stroke patients, whether high or low is linked with a higher risk of mortality.¹¹ They found that 25 percent of the population had anemia (low hemoglobin) which increased the mortality risk.

Similarly, our results showed twice an inclination in ESR than the upper limit of the normal range of ESR in the bad prognosis group which is 49.91 mm/h. whereas, an inclination also seen in the good prognosis group is 34.10 mm/h which is not as high as in the bad prognosis group but is still high than the normal range.

ESR is a commonly known inexpensive laboratory test that is used for the assessment of acute response. An increase in fibrinogen concentration is indicated, with an increase in the erythrocyte sedimentation rate at the time of acute stroke, which is responsible for the reduction in cerebral blood flow.¹² It has been reported in previous studies that an increase in leukocytes and ESR are associated with the worst outcomes in ischemic stroke patients.¹³

An increase in white blood cell or leukocyte counts right after the ischemic stroke indicates a strong prognosis for in-hospital mortality.¹⁴ In our study patients that died within the 72 hrs of hospitalization after ischemia had twice an increase in their leukocyte count. Therefore, for ischemic stroke patients, it is important to regularly monitor their ESR and WBC levels for the evaluation of the course of the disease. Nayak et. al. (2011) also found that high ESR and WBCs level at the time of admission was more in expired patients as compared to the discharged patients.¹⁵ So in ischemic patients having increased WBCs and ESR, a prognosis can be generated.

Our results are similar to the findings of Wang et. al. (2017). In which, low platelet count was found in ischemic stroke patients.¹⁶ Our results are similar to those found by previously done research. According to them, an elevation of mean platelet volumes is associated with poor outcomes in patients with ischemic stroke.¹⁷ This was further supported by the study of Mayda Domac et.al. (2010) who found an association between mean platelet volume and poor prognosis in ischemic patients.¹⁸ According to it, the higher platelet reactivity activity occurred before the stroke and contributed to worsening it (Mayda Domac et. al., 2010).

The mean value for C reactive protein for the bad prognosis and good prognosis is 25.47 mg/L and 10.86 mg/L. it is clearly seen that patients that died had

their C reactive protein levels way higher than the normal range. Whereas for the discharged patients, the value lay in the normal category. Our results were similar to the findings of other studies. Song et. al. (2010) found that there was a significantly positive relation between CRP levels and poor outcomes of ischemic stroke.¹⁹ Like this, Rajeshwar et. al (2012) did a comparative study and found that high CRP levels are associated with poor outcomes in ischemic stroke patients.²⁰

Limitations

Difference of gender with different hematological parameters and role of age differences could have been studied

We did not study the effect of other coexisting conditions like smoking, hypertension, cardiovascular disorders, etc.

Moreover, we did not study the stroke severity. We could have used the National Institutes of Health Stroke Scale to study the outcomes based on the severity of the stroke.

Additionally, the outcomes could have been studied using the modified Rankin Scale.

Another limitation of our study includes that we took all the participants that had an ischemic stroke. Whereas a comparative study design could have been used between the studies group (ischemic patients) and control group (healthy patients).

Strengths

Measurement of hematological parameters is very commonly known and practiced in hospitals. It is an inexpensive and efficient way of finding the prognosis of ischemic stroke which could help in taking reasonable measures to prevent future damage.

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