



The predictive significance of ratio between white blood cells count and serum albumin in assessing the functional outcome of acute ischemic stroke

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Abstract

Introduction: The acute ischemic infarction is associated with significant damage to brain parenchyma, where the high degree of acute inflammation is found. This work aimed to study the predictive value of ratio between blood WBCs and serum albumin levels in assessing the functional outcome in subjects with acute ischemic stroke.

Materials and methods: A prospective observational study was conducted on 223 subjects from February 2022 to August 2022 at K.R. Hospital, Mysore. The data collected from patients of acute ischemic stroke, with the onset of stroke within 24 hours. Severity of stroke was assessed by using National Institute of Health Stroke Scale (NIHSS) at the time of admission. Data was collected using a pretested proforma meeting the objectives of the study.

Results: The study has 124(55.6%) male and 99(44.4%) of female patients. Most of the patients (65%) were in the age group of more than 66 years. Most of the patients i.e., 66 (29.6%) had moderate to severe stroke at presentation as assessed by NIHSS stroke scale. At the end of third month of follow up, the acute ischemic stroke patients with MRS of >3 had WBCs count/serum albumin ratio of 4361.1 (p value - 0.001).

Conclusion: The significant acute inflammation is found in acute ischemic stroke and it may be one of the causes of poor outcome and disability in so many ischemic stroke patients. This study once again endorses the use of high intensive statins and adequate dose of antiplatelet agents as early as possible in acute ischemic stroke patients.

Keywords: acute ischemic stroke; WBCs; Modified Rankin Scale; NIHSS; serum albumin

Introduction

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause [1]. Focal ischemia or infarction, conversely, is usually caused by thrombosis of the cerebral vessels themselves or by emboli from a proximal arterial source or the heart [2]. The cerebrovascular accident was the second most leading cause of death and the third leading cause of disability [3]. The 70% of strokes related deaths and disability-adjusted life years occur in low and middle income countries due to lack of standard care [1, 4]. For preventing the disability associated with the stroke, need to be proper assessment of patients is required, to give aggressive first aid [5]. The white blood cells (WBCs) count was significantly raised in any ischemic or structural insult in to the body tissues [6]. The elevated WBCs count indicates that there is a significant inflammation in the

body irrespective of the cause [7]. The inflammation was a novel and independent risk factor of atheroembolic insult in to the brain, cardia and other organs [8]. Human albumin as a negative phase reactant, has long been considered to be a factor that directly influences

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the outcome in patients with spectrum of chronic illnesses [9, 10]. The neuroprotective effect of albumin was due to its various properties like anti-oxidant and anti-inflammatory effects with inhibition of thrombosis in microcirculation [11, 12]. The available prognostic indicators of stroke at present are based on neurological findings. As per my literacy search, there is needed to be study for cost effectiveness of WBCs to albumin ratio as a haematological and blood bio marker in assessing the functional outcome in acute ischemic stroke.

This work aimed to study the predictive value of ratio between blood WBCs and serum albumin levels in assessing the functional outcome in subjects with acute ischemic stroke.

Materials and method

This was a prospective observational study conducted at KR. Hospital, Mysuru from February 2022 to August 2022 on 223 subjects with acute ischemic stroke. This study was started after getting the EC approval from Mysore Medical college and research institute Ethical committee and after obtaining the valid informed consent from subjects. The computed tomography (CT)/ magnetic resonance imaging (MRI) of brain was done to confirm the diagnosis of acute ischemic stroke by looking for hypodensity and hypointense lesions in patients with classical symptoms and signs. The patients data and blood samples were collected within 24 hours of onset of acute ischemic stroke. Data was collected using a pretested proforma meeting the objectives of the study. Severity of stroke was assessed by using National Institute of Health Stroke Scale (NIHSS) at the time of admission. Detailed history, clinical examination and necessary blood investigations such as, blood WBCs count, serum albumin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lipid profile, urine routine, random blood sugar (RBS), renal function tests (RFT), liver function test (LFT), neck vessels doppler and 2D-ECHO were done in all the subjects at day one, day 7 and at the end of 3rd month. The cut of values of serum albumin and WBCs were 3.5gm/dl and 11000 cells/ μ l of blood respectively [6, 7, 12]. The ratio between WBCs and serum albumin of 3142.85 was taken as average cut of value. The WBCs to serum albumin ratio with hsCRP levels were correlated with the severity of stroke. The severity of stroke was assessed by NIHSS scale and disability with other outcomes were assessed by Modified Rankin Scale (MRS). The patients were followed up for 3 months from the day of admission. The outcomes were assessed on day 1, day 7 and at the end of 3rd month of onset of acute ischemic stroke.

Patients presenting with symptoms and signs of acute ischemic stroke within 24 hours of onset time, and the

patients with radiological evidence of ischemia on brain imaging (CT scan/ MRI of brain) were included in this study.

Excluded the patients from this study who refusal of consent, hemorrhagic stroke, recurrent stroke, cerebral venous sinus thrombosis, serious medical illness leading to prolonged immobilization, chronic gastrointestinal disease, chronic liver disease, chronic renal disease, malignancy, patients on steroids, patients with any inflammatory or autoimmune illness.

The neurological status was assessed for each patient at admission using the NIHSS [12] and the scores were assigned, the patients were classified into the categories, i.e., (i) Minor stroke - 1 to 4 points, (ii) Moderate stroke - 5 to 15 points, (iii) Moderate to severe stroke - 16 to 20 points, (iv) Severe stroke - 21 to 42 points. The scale is a clinical assessment scale, used to assess neurological impairment in a patient.

Patients were given routine care and were followed up for functional outcome, by using the MRS [13] at day one, day 7 and end of 3rd month of admission. The functional outcome was predicted as poor outcome: MRS \geq 3; and non poor-outcome: MRS < 3 (Table 1).

Table 1: Modified Rankin scale for stroke disability assessment [13].

Score	Clinical features
0	No symptoms at all.
1	No significant disability despite symptoms; able to carry out all usual duties and activities.
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance.
3	Moderate disability; requiring some help, but able to walk without assistance.
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance.
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention.
6	Dead

Statistical analysis

The statistical software SPSS version 25 from IBM Chicago was used for this study. The results obtained were subjected to standard statistical methods for analysis and relevant conclusions were drawn from them. Descriptive statistics were used to analyse the general characteristics of the patients. Measures of central tendency including mean and standard deviations were used to ascertain the data regarding the different

laboratory parameters. Analysis of variance (ANOVA) and Chi square tests were applied in correlating and looking for significance between multiple variables. The correlation between mean values of the variables and functional outcome was ascertained by Spearman's correlation coefficient. The P value of less than 0.05 was considered to be statistically significant throughout the study.

Results

A prospective observational study was conducted on 223 acute ischemic stroke subjects. In this study the majority of subjects were in the age group of more than 66 years and most of them were male patients. At the end of 3rd month of follow up period, the majority of patients with acute ischemic stroke had high WBCs count, low albumin and high hsCRP level (Table 2).

The more common comorbid conditions were hypertension in 35(15.7%), type 2 diabetes mellitus in 43 (19.3%), ischemic heart disease (IHD) in 12(5.2%) and dyslipidaemia in 22(9.9%) subjects. The major five

comorbid conditions (Hypertension, type 2 diabetes mellitus, smoking, IHD and dyslipidaemia) were found in 24 (10.8%) study subjects. Alcoholic patients were not enrolled in the study, since baseline serum albumin levels were expected to be deranged in those subjects (Table 3).

Table 2: Distribution of demographic and base line parameters.

Parameters		Numbers (%)
Mean age (Years)	<66	78 (34.97%)
	>66	145 (65.03%)
Sex	Male	124 (55.6%)
	Female	99 (45.73%)
Blood WBCs count (cell/cmmg) Mean±SD	13126.2±1516.2	223 (100%)
Serum albumin level (gm/dl) Mean±SD	3.8±0.2	223 (100%)
Hs-CRP (mg/l) Mean±SD	12.0±4.8	223 (100%)

Table 3: Association between age and comorbidity

Comorbid conditions-age	HTN no. (%)	Type 2 diabetes mellitus in no. (%)	IHD no. (%)	Dyslipidaemia no. (%)	HTN, type 2 DM, dyslipidaemia, smoking no. (%)	HTN, type 2 DM, IHD, dyslipidaemia & smoking no. (%)	Total no. (%)
<60	5 (2.2%)	6 (2.7%)	3 (1.3%)	5 (2.2%)	10 (4.5%)	2 (0.9%)	31 (13.9%)
60-70	13 (5.8%)	22 (9.9%)	6 (2.7%)	8(3.6%)	40 (17.9%)	10 (4.5%)	99 (44.4%)
>70	17 (7.6%)	15 (6.7%)	3 (1.3%)	9 (4.0%)	28(12.6%)	12 (5.2%)	84 (37.7%)
Total	35(15.7%)	43 (19.3%)	12 (5.2%)	22 (9.9%)	78 (35%)	24 (10.8%)	223

In this study the majority of acute ischemic stroke cases were in the moderate to severe group, constitutes of 66(29.6%) cases with the mean serum albumin level of 3.01 gm/dl, mean WBCs count of 14673/ μ l of blood,

mean WBCs count to serum albumin ratio of 4,874.75 and hsCRP of 12.31mg/l (P value - 0.04) at admission (Table 4).

Table 4: Association between stroke severity score (NIHSS) with baseline WBCs, serum albumin, WBCs / serum albumin ratio and hsCRP level at admission.

Stroke severity category (NIHSS score)	No. of patients (%)	Serum albumin gm/dl (mean and SD)	WBCs count in cm mg of blood (mean & SD)	Mean ratio of WBCs/ albumin	MeanhsCRP±SD (mg/l)	Anova
Minor (1-4)	38 (17.0%)	4.70 ± 0.1	12301 ± 1153	2617.2	11.0±0.5	0.15
Moderate (5-15)	62 (27.8%)	4.05 ± 0.3	12987± 1764	3206.6	11.5±2.1	0.12
Moderate to Severe (16-20)	66 (29.6%)	3.0 ± 0.4	14673± 1177	4874.75	12.3±3	0.04
Severe (21 - 42)	57 (25.5%)	2.8 ± 0.4	14231 ± 1960	5082.5	12.0±2.1	0.05
Total			223			

The poor outcome (MRS>3) was found in the cases with five major risk factors group (Hypertension, type

2 diabetes mellitus, dyslipidaemia, smoking and IHD) p value was 0.05 (Table 5).

Table 5: Association between risk factors and outcome with MRS

Variables	7 th day outcome			At 3 rd month outcome		
	Poor outcome. in no. (%) (MRS>3)	Stable outcome with recovery. in no. % (MRS<3)	P value	Poor outcome in no. (%) (MRS>3)	Stable outcome with recovery. in no. (%) (MRS<3)	P value
Age						
<60	16 (7.1%)	21 (9.4%)	0.06	19 (8.52%)	18 (8.07%)	0.05
61-70	58 (26%)	48 (21.5%)		60 (26.90%)	46 (20.62%)	
>70	44 (19.7%)	36 (16.1%)		44(19.73%)	36 (16.14%)	
Sex						
Male	65 (29.1%)	59 (26.4%)	0.06	68 (30.49%)	56 (25.11%)	0.04
Female	51 (22.9%)	48 (21.5%)		50 (22.42%)	49 (21.97%)	
Hypertension						
Absent	95 (42.6%)	83 (37.2%)	0.06	95 (42.60%)	83 (37.21%)	0.01
Present	26 (11.6%)	19 (8.5%)		29 (13.00%)	16 (7.17%)	
Type 2 diabetes mellitus						
Absent	80 (35.9%)	101 (45.3%)	0.05	82 (36.8%)	99 (44.4%)	0.01
Present	27 (12.1%)	15 (6.7%)		28 (12.5%)	14 (6.3%)	
IHD						
Absent	85 (38.1%)	126 (56.5%)	0.02	87 (39.0%)	124 (55.6%)	0.02
Present	9 (4.0%)	3 (1.3%)		9 (4.0%)	3 (1.3%)	
Dyslipidaemia						
Absent	99 (44.4%)	102 (45.7%)	0.04	98 (43.9%)	103 (46.18%)	0.04
Present	18 (8.0%)	4 (1.8%)		19 (8.5%)	3 (1.3%)	
HTN, type 2 DM, dyslipidaemia, smoking						
Absent	99 (44.4%)	46 (20.6%)	0.06	102 (45.7%)	43 (19.3%)	0.06
Present	44 (19.7%)	34 (15.2%)		48 (21.5%)	30 (13.4%)	
HTN, type 2 DM, dyslipidaemia, smoking & IHD						
Absent	130 (58.3%)	69 (30.9%)	0.05	136 (61%)	63 (28.2%)	0.05
Present	20 (9%)	4 (1.8%)		20 (9%)	4 (1.8%)	

Abbreviations: HTN-Hypertension, Type 2 DM- Type 2 Diabetes mellitus, IHD-Ischemic heart disease.

The WBCs count /serum albumin ratio and hsCRP at 7th day was 3845.8 and 14.0±6.0 mg/l,at the end of third month was 4361.1 and 13.6±4.6 mg/l respectively and were significantly high in the group with poor outcome(MRS>3) as compared to stable and recovered group (MRS<3) of acute ischemic stroke[p-value-0.001] (Table 6).

Discussion

This study has shown significant association between high WBCs and albumin ratio with that of outcomes in acute ischemic stroke. The majority of patients in this study were more than the mean age of 66 years, i.e. 145

(65.03%). In other study by Ralph et al [14], the mean age of patients was 74.3 years and the study by Sani et al., the mean age was 57.7 years [15]. This shows that the acute ischemic stroke is still a disease of elderly population [15]. Sex distribution in this study was male patients in majority of population i.e. 124(55.6%). This was in comparison with other study by Pawan T et al. where that study had included 53% of male patients [16]. This shows that, the male population was at high risk of getting acute ischemic stroke in their lifetime [16]. In this study the majority (82%) of patients with the age above 66 years had major comorbidities like type 2 diabetes mellitus, hypertension, IHD, dyslipidaemia

Table 6: Correlation between WBCs count, serum albumin, WBCs/serum albumin and hs-CRP with Outcome (MRS)

parameters	Patients with Poor Outcome (MRS>3) Numbers-88(39.4%)		Patients with stable condition and recovery (MRS<3) Numbers-135 (60.5%)		ANOVA	Correlation coefficient (p)
	Day 7	Day 90	Day 7	Day 90		
	Mean WBCs (number/cummg (mean ± SD)	15345±1840	12560 ± 1720	13450±1150		
Serum albumin (gm/dl) (mean+SD)	3.9+0.4	2.8± 0.4	4.3±0.1	4.1 ± 0.1	0.001	0.05
Mean WBCs/ serum albumin ratio	3845.8	4361.1	3149.9	2667.5	0.001	0.001
hsCRP level (mean ± SD) (mg/l)	14.0±6.0	13.6±4.6	11.5±5.4	9±3.2	0.001	0.001

and smoking. In comparison to other studies by Zilong et al [17] and Boehme Amelia et al [18], where the major comorbid illnesses in acute ischemic stroke were type 2 diabetes mellitus, hypertension, smoking, dyslipidaemia and coronary artery disease (CAD). In this study, the ratio between WBCs to serum albumin level was significantly high in patients of severe degree of acute ischemic stroke. When compared with the other studies by Zhi-bing et al [6] and Welsh et al [8], where high level of WBCs counts were found with predominant neutrophils in severe degree of acute ischemic stroke. A study by Sani et al., had shown a mean serum albumin of 3.03gm/dL in patients with favourable outcome and 2.08gm/dL in those with unfavourable outcome patients [15]. The patients with major risk factors like type 2 diabetes mellitus, hypertension, dyslipidaemia, IHD and smoking were having significant poor outcome both at 7th day and end of 3rd month of follow up period. It was correlated with the study by Sanjana et al. stated that, the patients with type 2 diabetes mellitus, hypertension, smoking, dyslipidaemia and with other major risk factors were having poor acute ischemic stroke outcome with MRS of >3 [19]. In this study, the significant association was observed between the high WBCs count /serum albumin ratio and the poor outcome with MRS of >3 in majority of patients throughout the study period. It was noted that, the patients with poor outcome (MRS score ≥3) had higher WBCs count and lower serum albumin at admission day, at 7th day and at the end of 3rd month as compared to patients with stable outcome, who had higher serum albumin. Other studies by Zhi-bing et al and Welsh et al., where it was observed that the high level of WBCs counts were found in patients with poor outcome of acute ischemic stroke [6, 8]. According to the study by Tomasz Tomasz et al the mean serum albumin level of 3.41gm/dl in patients with poor outcome and 3.68gm/dl was found in recovered and stable patients [20]. The poor neurological outcome in the form of disability and bedridden status was very high with the high WBCs to albumin ratio patients of acute ischemic stroke in the whole post stroke period. The serum hsCRP was also high in all the patients with

poor outcome as compared to recovered group and this was correlating with the high WBCs count to albumin ratio in acute ischemic stroke patients in throughout the study period. These results suggesting that, the high degree of acute inflammation and hypoalbuminemia at admission and also in subsequent follow up period, predisposes a patient to a poor prognosis with a high MRS score (>3) [21-24]. The reasons for high WBCs count and hypoalbuminemia could be, the high acute inflammatory state and poor nourishment with high dependency of care for life in post-acute ischemic stroke period [25-28]. The high WBCs counts and low serum albumin levels were ignored in most of the patients, while treating acute ischemic stroke in the present era due to the availability of high end radiological investigations and blood biomarkers [29, 30]. So due importance should be given to WBCs count and serum albumin ratio, while predicting the stroke outcomes and management, because they are commonly available investigations in all types of hospital setup and they are cheap and also cost effective [31, 32].

The study sample was limited, needs to be studied on large sample size to further confirm the relevancy and importance of the studied parameters.

Conclusions

The ratio of WBCs count to serum albumin in comparison with hsCRP is a highly cost effective, easily feasible and can be considered as a common man's bed side blood biomarker for assessing the prognosis of patients with acute ischemic stroke even at present era. Once again this study endorses the use of high intensive statins as anti-inflammatory agent and adequate dose of anti-platelet agents in managing acute ischemic stroke patients. These feasible blood bio markers should not be ignored, while in search of high end investigations in managing acute ischemic stroke patients.

Conflicts of interest

Authors declare no conflicts of interest.

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