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A Study of Serum Albumin Level in Patients with Acute Ischaemic Stroke and Its Correlation with NIHSS Score and mRS Score

Yogananda M N [1], Nikhil Raj H M [2], Meghana B S [3] & Parvathi Mallesh [4]

[1]Assistant Professor, Department of General Medicine, Bangalore Medical College And Research Institute

[2]Post Graduate, Department of General Medicine, Bangalore Medical College And Research Institute

[3]Senior Resident, Department of General Medicine, Bangalore Medical College And Research Institute

[4]Assistant Professor, Department of General Medicine, Bangalore Medical College And Research Institute

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***Corresponding Author:**

Parvathi Mallesh

Assistant Professor, Department Of General Medicine Bangalore Medical College And Research Institute

ABSTRACT

Background: The word stroke was used as a synonym for apoplectic seizure as early as 1599, and is a fairly literal translation of the Greek term. In 1658, in his Apoplexia, Johann Jacob Wepfer (1620–1695) identified the cause of hemorrhagic stroke when he suggested that people who had died of apoplexy had bleeding in their brains. Rudolf Virchow first described the mechanism of thromboembolism as a major factor. Over the last four decades, the stroke incidence in low- and middle-income countries has more than doubled. Stroke caused an estimated 5.7 million deaths in 2005, and 87% of these deaths were in low-income and middle-income countries. Without intervention, the number of global deaths is projected to rise to 6.5 million in 2015 and to 7.8 million in 2030.**Methods:**100 patients with Acute Ischemic Stroke admitted as inpatients were included in this study. Serum Albumin levels were determined through blood investigation. Serum Albumin levels are correlated with NIHSS scoring scale and Modified Rankin Score. **Results:** Out of 100 subjects, 22 subjects were aged 66 to 75 yrs followed by 20 subjects each aged 46 to 55 years and 56 to 65 years. Overall, negative strong correlation was seen between albumin levels and NIHSS scores (r=-0.73; p=0.00). Moderate, negative non-significant correlation was seen between albumin levels and moderate to severe stroke (r=-0.45; p=0.1) and between albumin levels and severe stroke (r=-0.4; p=0.21). Overall, negative strong correlation was seen between albumin levels and mRS scores **Conclusion:** There was linear decrease of S. Albumin with severity of stroke (NIHSS scoring scale) and mRS Scale indicating that S. Albumin levels correlated with NIHSS scoring scale and mRS scale. This indicates that S.Albumin levels can also be used as an adjuvant tool for assessing the severity of stroke along with other tools and facilitate required treatment.

Introduction

Stroke is a rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin [1]. Types of stroke: ischemic 85% and Hemorrhagic 15%. Stroke is the leading cause of death in upper-middle-income countries, and also the leading cause of disability worldwide. Ischemic stroke is caused by multiple causes and has subsequent sequelae.Thrombus can form in arteries from both outside and inside the cranium, when the rou-ghened intima is colonized by plaque. In embolic stroke, clot blocks the cerebral vessels from a different source. Micro embolus has many sources such as from cardiac origin like patent foramen ovale, atrial fibrillation and infective endocarditis []. **Figure 1** explained that Stroke can result from two main causes: an ischemic stroke, where a clot obstructs blood flow to the brain, or a hemorrhagic stroke, which occurs when a blood vessel ruptures, disrupting blood flow to the brain. Additionally, a transient ischemic attack (TIA), often referred to as a "mini stroke," is caused by a temporary clot. In both ischemic and hemorrhagic strokes, the interruption of blood flow leads to a critical si-

-tuation where brain cells start to die or are at risk of significant damage. Immediate medical attention is essential to minimize the impact of a stroke and prevent further complications.

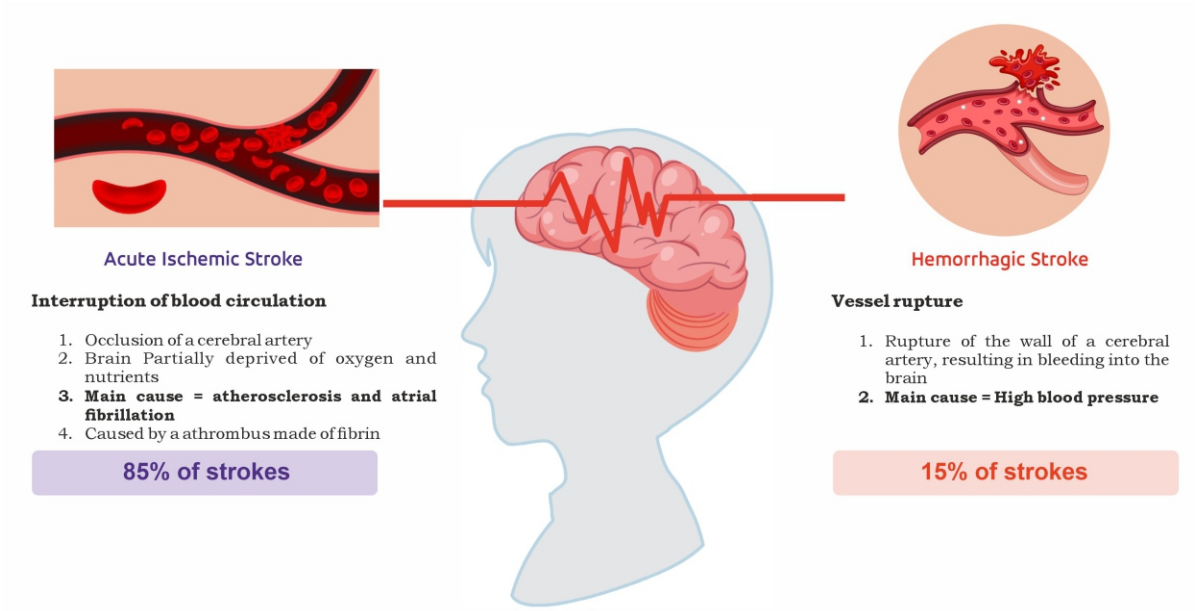

Figure 1: Types of Stroke (image with curtsy: Acticor Biotech 2021)

Cerebral infarction basically comprises two pathophysiolog--ic processes: one, a loss of the supply of oxygen and glucose secondary to vascular occlusion, and the other, an array of changes in cellular metabolism consequent to the collapse of energy-producing processes, ultimately with disintegration of cell structures and their membranes, a process subsumed under the term necrosis [5]. Of potential therapeutic importance are the observations that some of the cellular processes leading to neuronal death are not irrevocable and may be reversed by early intervention, either through restoration of blood flow, by prevention of the influx of calcium into cells, or by interdicting intermediary processes involved in cell death. Implicit in discussions of ischemic stroke and its treatment is the existence of a "penumbra" zone that is marginally perfused and contains at-risk but viable neurons. Presumably this zone exists at the margins of an infarction, which at its core has irrevocably damaged tissue that is destined to become necrotic[6-8].

The neurons in the penumbra are considered to be physiologically "stunned" by moderate ischemia and subject to salvage if blood flow is restored in a certain period of time. All patients with measurable neurological deficit after acute ischemic stroke who can be treated within 4.5 hours after symptom onset should be evaluated without delay to determine their eligibility for treatment with a thrombolytic agent. Patients with acute ischemic stroke should be considered for combination intravenous thrombolysis and intra-arterial clot extraction if they have internal carotid or proximal middle cerebral artery occlusion causing a disabling neurological deficit and patient can be referred to a tertiary healthcare facility, where the procedure can begin within 24 hours of last known well. Patients with indication for neurosurgery should be referred to a center with neurosurgical facility[9-11].

Albumin is a very important plasma protein. Major functions of albumin are regulation of colloid osmotic pressure of plasma, help in transportation of hormones, drugs, fatty acids and metabolites across plasma [12]. It also regulates the microvascular permeability and has anti-oxidant activity, anti-thrombotic and anti-inflammatory activity. Human albumin in high doses has been used in clinical trials for acute ischemic stroke based on its neuroprotective effects. The Albumin in Acute Stroke clinical trial showed that albumin in high doses decreases infarct volume and cerebral edema and improves behavioral function [13]. Neuroprotective effects of albumin are contributed through the improved venular perfusion and microcirculation, maintaining endothelial integrity, and anti-oxidant& anti lipid peroxidant activity. The serum albumin improves sub- occlusive microcirculation, vascular integrity, mitigates cerebral edema and prevents microvascular re-occlusion [14-16]. **Figure 2** explain that the presence of multiple health conditions can affect the required treatment for individuals recovering from a stroke. Consequently, it is crucial to comprehend how these conditions impact future therapeutic approaches for stroke patients. Among the numerous multimorbid conditions observed in stroke patients are diabetes, obesity, metabolic syndrome, alcohol consumption, smoking, physical inactivity, cancer, chronic pulmonary disease, hypertension, atrial fibrillation, and con-

congestive heart failure[17].

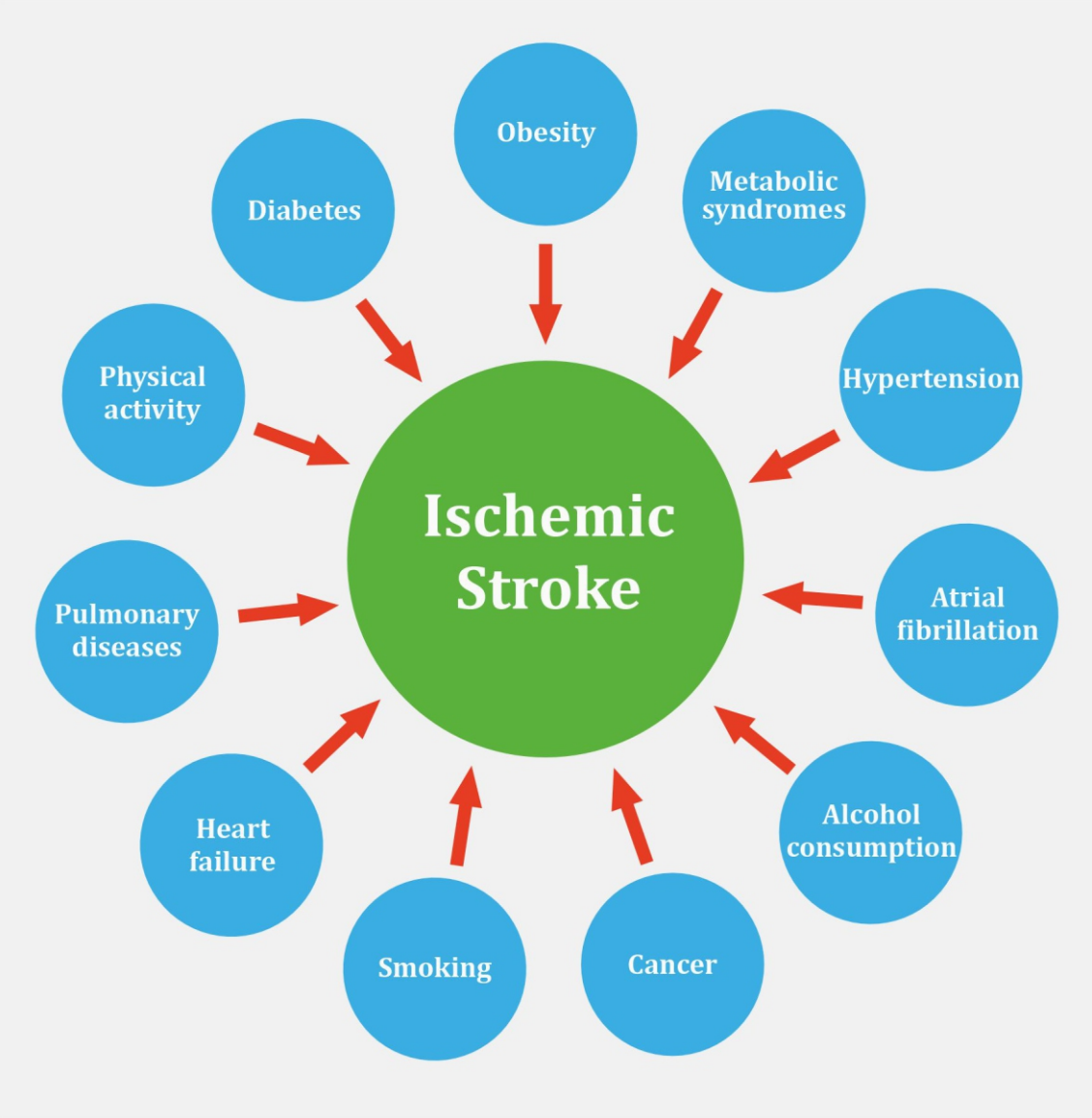

Figure 2: The influence of certain coexisting medical conditions on the results of ischemic stroke.

The National Institutes of Health Stroke Scale (NIHSS) is a systematic assessment tool that provides a quantitative measure of stroke-related neurologic deficit. The NIHSS was originally designed as a research tool to measure baseline data on patients in acute stroke clinical trials. Now, the scale is also widely used as a clinical assessment tool to evaluate acuity of stroke patients, determine appropriate treatment, and predict patient outcome. The NIHSS has been shown to be a predictor of both short- and long-term outcome of stroke patients. The NIHSS is a 15-item neurologic examination stroke scale used to evaluate the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss [18-20].

SCORE	STROKE SEVERITY
0	No stroke symptoms
1-4	Minor stroke
5-15	Moderate stroke
16-20	Moderate to severe stroke
21-42	Severe stroke

The modified Rankin Scale (mRS) is a commonly used scale for measuring the degree of disability or dependence in the d-

-aily activities of people who have suffered a stroke or other causes of neurological disability. The scale runs from 0-6, running from perfect health without symptoms to death [21].

- ➢0 - No symptoms
- ➢1 - No significant disability. Able to carry out all daily activities, despite some symptoms.

- ➢2 - Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
- ➢3 - Moderate disability. Requires some help, but able to walk unassisted.
- ➢4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
- ➢5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
- ➢6 - Dead.

MATERIALS AND METHODS

Objectives

- To estimate Serum Albumin levels in patients with Acute Ischemic Stroke.
- To Correlate Serum Albumin levels with NIHSS score and mRS score in patients with Acute Ischemic Stroke.

Study design: Cross sectional study.

Study period: March 2022-March 2023

Place of study: Hospital affiliated to Bangalore Medical College & Research Institute, Bangalore.

Inclusion Criteria

1. Acute Ischemic Stroke patients willing for examination after signing the informed consent.
2. Age more than 18 years.
3. All patients with new onset Ischemic Stroke, confirmed by CTpresented within 48 hours of onset of Stroke are taken into study.

Exclusion Criteria

1. Patient not willing to give informed consent.
2. Patients with features of Hemorrhagic Stroke will be excluded with the aid of CT scan.
3. Chronic liver disease.
4. Chronic kidney disease.

Statistical Analysis

1. Data was analyzed by descriptive statistics.
2. Chi square test used to see association between qualit--ative variables and correlation co efficient will be use--d to see relation between quantitative variables. A p v--alue < 0.05 will be considered statistically significant.

Sample Size Estimation

Sample size: 100 patients with Acute Ischemic Stroke at the time of admission. Based on previous study by Sandeep Fnu et al[6]

$$n = \frac{z_{\alpha}^2 \sigma^2}{d^2}$$

where $z_{\alpha} = 1.96$ $\sigma = 0.73$

$$n = \frac{(1.96)^2 x (0.73)^2}{(0.15)^2}$$

n= 100

Sample Size: 100 patients

RESULTS

Table 1: Age wise Distribution of the Patients

Age	Frequency	Percent
Less than 35 years	9	9.0
36 to 45 years	14	14.0
46 to 55 years	20	20.0
56 to 65 years	20	20.0
66 to 75 years	22	22.0
Above 75 years	15	15.0
Total	100	100.0

Out of 100 subjects, 22 subjects were aged 66 to 75 years followed by 20 subjects each aged 46 to 55 years and 56 to 65 years.

Table 2: Mean Age of males and females

	Min	Max	Mean	SD
Males	28	75	56.31	13.86
Females	19	89	62.6	19.25

Table 3: Gender wise stribution of the Patients

Gender	Frequency	Percent
Female	30	30.0
Male	70	70.0
Total	100	100.0

Out of 100 subjects, 70 were males and 30 were females

Table 4: Comparison of the S. Albumin levels among the groups based on NIHSS groups using anova

NIHSS-classified	N	Minimum	Maximum	Mean	Std. Deviation	p value
Minor stroke	25	3.50	5.00	4.02	0.33	0.00*
Moderate stroke	50	2.80	4.50	3.44	0.46	
Moderate to Severe Stroke	14	2.40	4.00	3.20	0.50	
Severe stroke	11	2.00	3.00	2.48	0.37	

*significant

Table shows comparison of albumin levels based on NIHSS score category. Subjects under minor stroke had higher albumin levels- (4.02 ± 0.33) followed by subjects with mod-erate stroke-(3.44± 0.46); moderate to severe stoke (3.20 ±0.50) and severe stroke (2.48 ±0.37). ANOVA was applied to compare the albumin levels among the groups. Statistically significant difference was seen with respect to albumin levels among the groups (p=0.00).

Out of 100 subjects, 22 subjects were aged 66 to 75 years followed by 20 subjects each aged 46 to 55 years and 56 to 65 years.

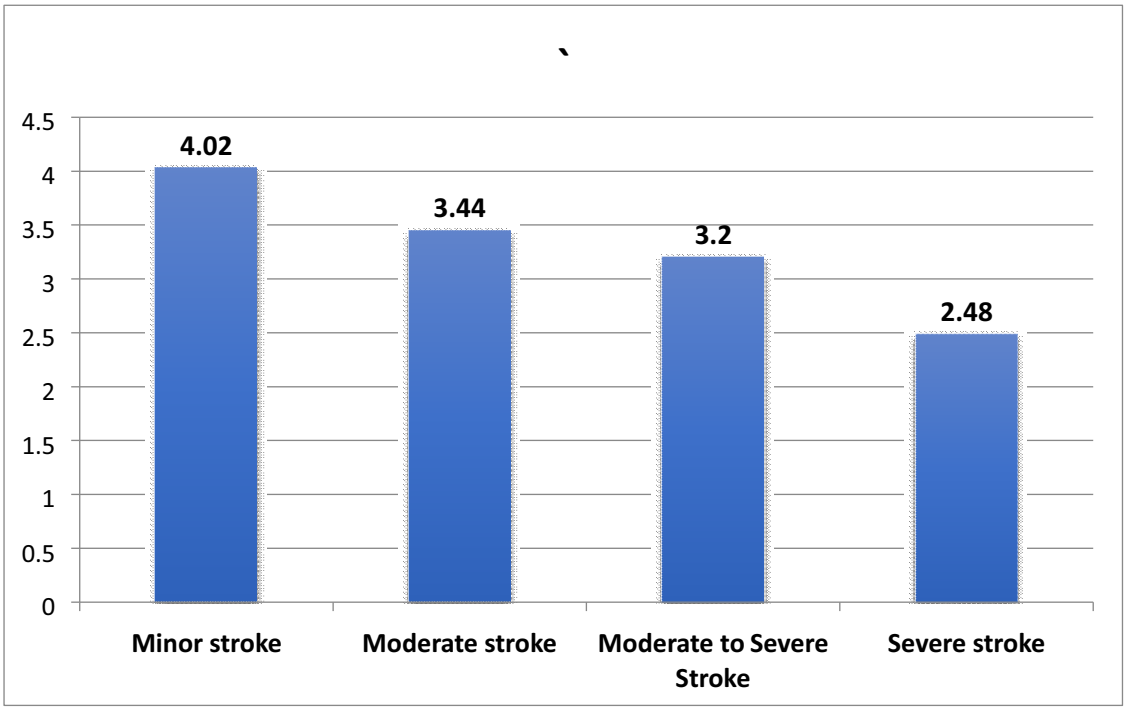

Figure 1: Graphical representation of comparison of the Serum Albumin levels with Stroke severity.

Table 5: Pearson's correlation between S.Albumin levels and NIHSS scores

	N	r value	p value
Minor stroke	25	-0.12	0.55
Moderate stroke	50	-0.35	0.012*
Moderate to Severe Stroke	14	-0.37	0.18
Severe stroke	11	-0.16	0.62
Total	100	-0.73	0.00*

*significant

Pearson's correlation was applied to correlate albumin levels with NIHSS scores. Negative, very weak, non-significant correlation was seen between albumin levels and minor stroke(r=-0.12; p=0.55) and severe stroke(r=-0.16;p=0.62). weak, negative nonsignificant correlation was seen between albumin levels and moderate to severe stroke(r=-0.37;p=0.18) whereas weak, negative significant correlation was seen between albumin levels and moderate stroke (r=-0.35;p=0.012). Overall, negative strong correlation was seen between albumin levels and NIHSS scores (r=-0.73; p=0.00)

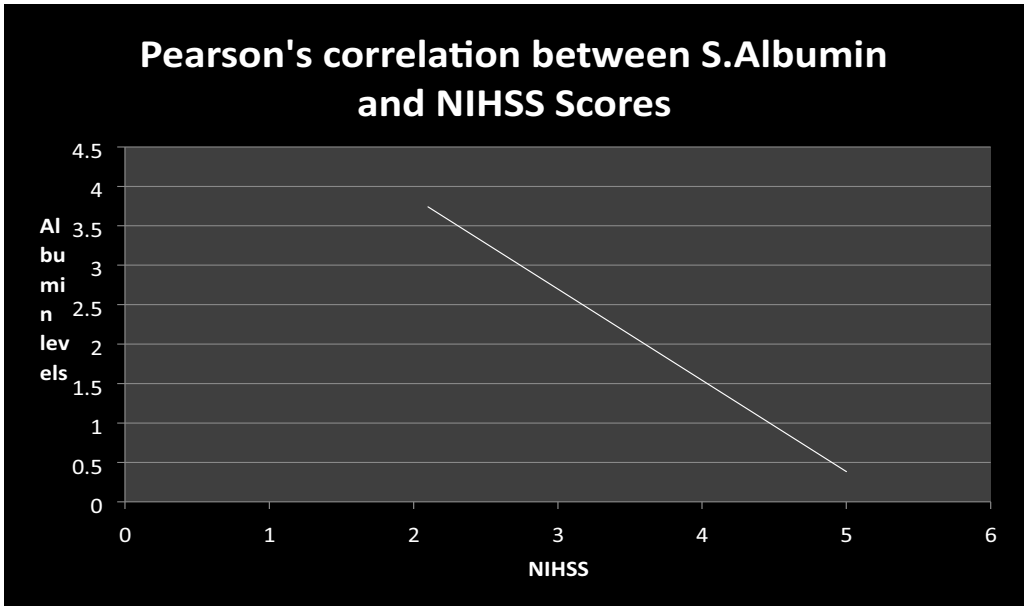

Figure 2: Graphical representation of correlation between Serum Albumin and NIHSS score

Table 6: Pearson's Correlation between S.Albumin Levels and mRS Scale

NIHSS-Classified	N	r value	p value
Minor stroke	25	0.48	0.014*
Moderate stroke	50	-0.23	0.1
Moderate to Severe Stroke	14	-0.45	0.1
Severe stroke	11	-0.41	0.21
OVERALL	100	-0.66	0.00*

*significant

Pearson's correlation was applied to correlate albumin levels with mRS. Positive, moderate -significant correlation was seen between albumin levels and minor stroke(r= 0.48; p=0.014) weak, negative non-significant correlation was seen between albumin levels and moderate stroke®=-0.23; p=0.1); Moderate, negative non-significant correlation was seen between albumin levels and moderate to severe stroke (r=-0.45;p=0.1) and between albumin levels and severe stroke (r=-0.41;p=0.21).Overall, negative strong correlation was seen between albumin levels and mRS scores (r=-0.66; p=0.00).

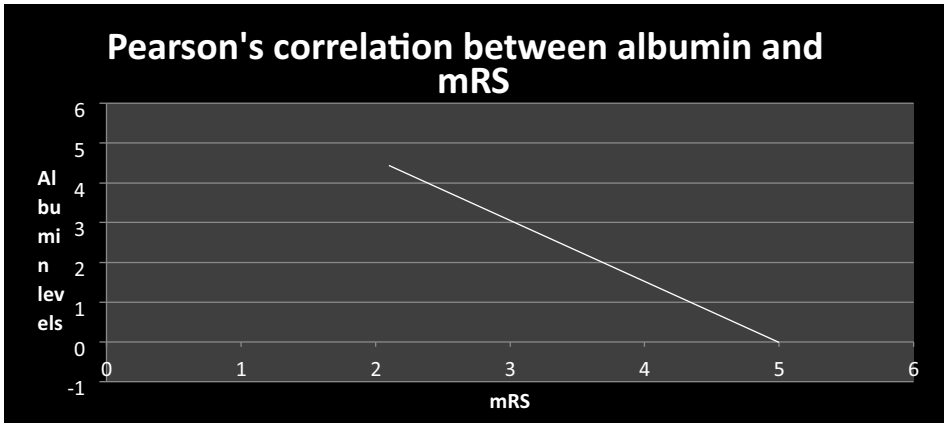

Figure3: Graphical representation of Correlation between Serum Albumin and mRS

Table 7: Comparison of the S.Albumin levels between Gender using unpaired t test

GROUPS	N	Minimum	Maximum	Mean	SD	Mean Diff	P value
Females	30	2.00	4.60	3.41	0.60	0.047	0.72
Males	70	2.00	5.00	3.46	0.62		

Table shows comparison of albumin levels between gender. Albumin levels were higher in males (3.46 ± 0.62) as compared to females (3.41 ± 0.60). Unpaired t test was applied to compare the albumin levels between the gender. Unpaired t test showed no statistically significant difference between albumin levels with respect to gender(p=0.72).

Cross-tabulation of Stroke with Habits and Co-morbidities

			NIHSS-classified				Total	Chi square value	p value
			Minor stroke	Moderate stroke	Moderate to Severe Stroke	Severe stroke			
Smoker	Absent	Count	24	48	12	10	94	2.42	0.48
		%	96.0 %	96.0%	85.7%	90.9%	94.0 %		
	Present	Count	1	2	2	1	6		
		%	4.0%	4.0%	14.3%	9.1%	6.0%		
Hypertension	Absent	Count	18	28	9	8	63	2.37	0.49
		%	72.0 %	56.0%	64.3%	72.7%	63.0 %		
	Present	Count	7	22	5	3	37		
		%	28.0 %	44.0%	35.7%	27.3%	37.0 %		
Diabetes	Absent	Count	17	36	9	9	71	1.06	0.78
		%	68.0 %	72.0%	64.3%	81.8%	71.0 %		
	Present	Count	8	14	5	2	29		
		%	32.0 %	28.0%	35.7%	18.2%	29.0 %		

Table shows the cross-tabulation of stroke with habits and co-morbidities. Chi square test was applied to associate the habits and co-morbidities with type of stroke. Chi-square test showed no significant association with respect to co-morbidities.

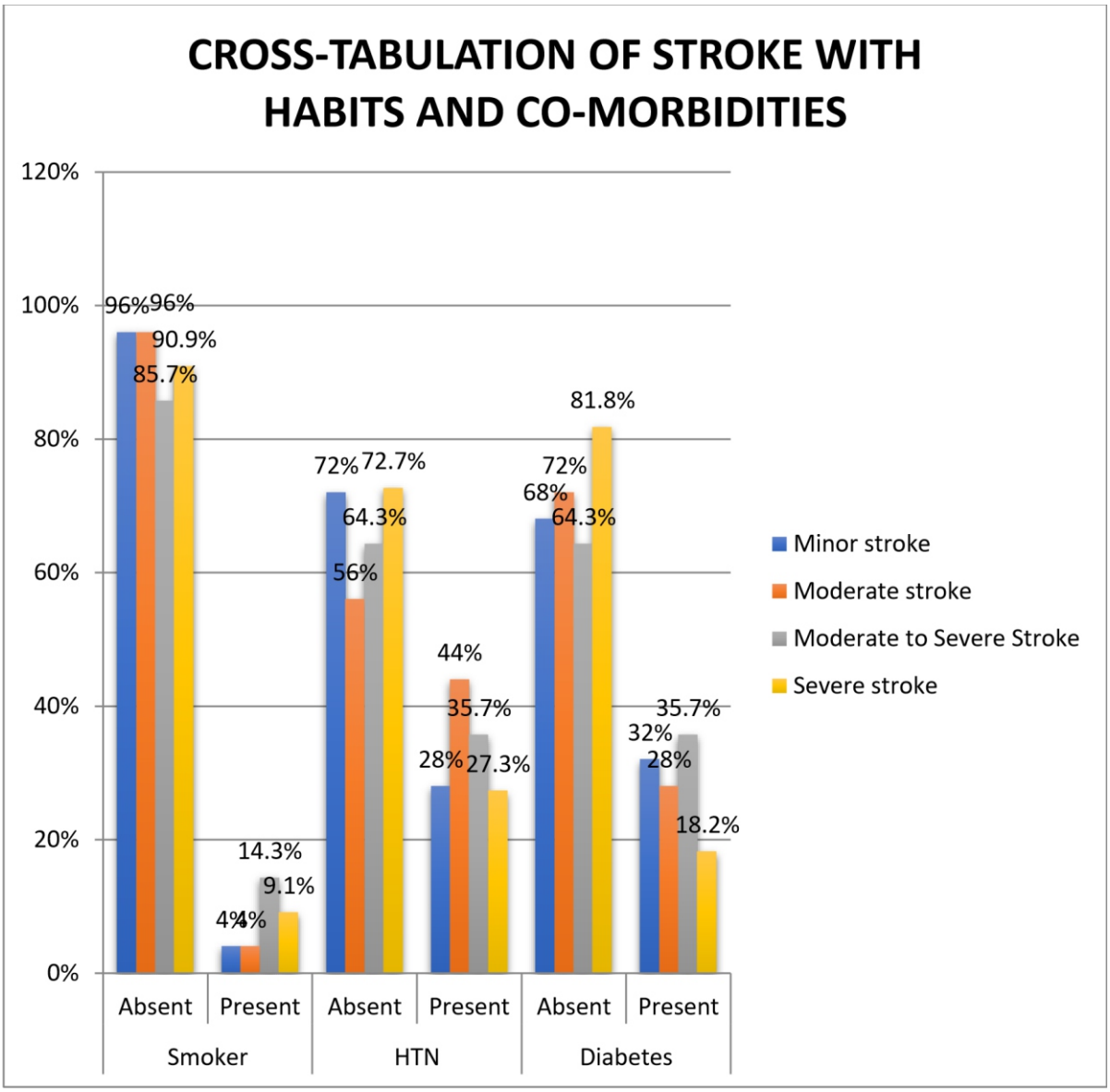

Figure 4: Graphical representation of Comparison of Co morbidities with Stroke Severity

DISCUSSION

The present cross-sectional study was conducted to analyze the correlation of serum albumin with stroke severity using NIHSS and mRS score. Our study was conducted on 100 patients. The mean age for male was 56.31 years and mean age for female was 62.6 years [22]. Study conducted by Fnu Sandeep *et al.,* showed mean age were 55.71±5.76 years for males and 59.31±787 years for female and study conducted Tomasz Dziedzic showed mean age was 68.3±12 years. Out of the 100 patients, 70 were males and 30 were females which is similar to study conducted by Fnu Sandeep *et al.,* were out of 135 patients, 105 patients were male and 30 were females, indicating male predominance in both the study. In our study, S. Albumin levels were higher in males (3.46 ± 0.62) as compared to females (3.41 ± 0.60). However, there was no statistically significant difference between S.albumin levels with respect to gender[23-25].

In our study, Serum albumin levels were compared with NIHSS score category. Subjects under minor stroke had higher albumin levels- (4.02 ± 0.33) followed by subjects with moderate stroke-(3.44 ± 0.46); moderate to severe stoke (3.20± 0.50) and severe stroke (2.48 ± 0.37). Statistically significant difference was seen with respect to albumin levels among the groups (p=0.00). This indicate that Hypoal bumi-

-nemia was more in groups of moderate to severe stroke [26, 27].

Negative, very weak, non-significant correlation was seen between albumin levels and minor stroke (r=-0.12; p=0.55) and severe stroke (r=-0.16; p=0.62). weak, negative non-significant correlation was seen between albumin levels and moderate to severe stroke (r=-0.37; p=0.18) whereas weak, negative significant correlation was seen between albumin levels and moderate stroke (r=-0.35; p=0.012). Overall, negative strong correlation was seen between albumin levels and NIHSS scores (r=-0.73; p=0.00). This indicates that severity of stroke increased with hypoalbuminemia. Study done by Fnu Sandeep *et al.,* showed a negative correlation of Serum albumin and NIH stroke scale which is similar to the findings in our study[28-30].

Study done by James R *et al.,* on 100 patients showed a significant association was observed between serum albumin and severity of stroke at presentation. A strong negative correlation was found between serum albumin at admission and mRS score, indicating a strong association between serum albumin and the functional outcome at 7 days. There was also significant association between the severity of stroke at admission and the functional outcome at 7 days. Study done by Reith *et al,* found negative correlation between serum albumin level and degree of neurological deficit[31-33].

Our study showed positive, moderate -significant correlation was seen between albumin levels and minor stroke(r= 0.48; p=0.014) weak, negative non-significant correlation was seen between albumin levels and moderate stroke(r=-0.23;p=0.1); Moderate, negative non-significant correlation was seen between albumin levels and moderate to severe stroke (r=-0.45;p=0.1) and between albumin levels and severe stroke (r=-0.41;p=0.21).Overall, negative strong correlation was seen between albumin levels and mRS scores (r=-0.66; p=0.00) which is similar to the findings in the study done by Fnu Sandeep *et al.,* indicating lower the serum albumin more was the disability[34] .

Study done by Dash PK *et al.,* on Patients with low serum albumin level at admission time were directly proportional to severity of stroke at presentation and poor clinical outcome. 1 week and 3 months follow up mean albumin level (g/dl) was 3.8±0.25 and 3.7±0.23 in patients with poor functional outcome respectively. Significant co-relation between mean serum albumin level and clinical outcome was observed [32, 35, 36].

Study done by Idicula T.T *et al.,* on 444 patients with Ischemic stroke showed the median NIHSS score (interquartile range) on admission was 4 (1–8) and the median mRS score (interquartile range) on day 7 was 2 (1–3). High serum albumin was independently associated with a better outcome (OR = 1.12, 95% CI = 1.05–1.20, p = 0.001). After adjusting for age, sex and NIHSS score on admission, high serum albumin was associated with lower mortality which indicates that high serum albumin is associated with better outcome and lower mortality in ischemic stroke patients. High serum albumin may be neuroprotective in ischemic stroke in humans[37-40].

Study done by Gillium *et al.,* showed reduced incidence of stroke and patients with Higher Serum albumin. A cross sectional study by Hostmark and tomten *et al.,*showed Low serum albumin was associated with increased prevalence and stroke and increased severity. Mechanisms of beneficent effects of serum albumin include the anti-thrombosis effects, decreases leukocyte adherence, and endothelial stasis of cells.Neuroprotective effects of albumin are also contributed through the improved venular perfusion and microcirculation, maintaining endothelial integrity, and anti-oxidant & anti lipid peroxidant activity. Low serum albumin adversely affects the prognosis of cardiac and kidney diseases. Studies have suggested the albumin exerts neuroprotective effects by reducing brain edema [41, 42].

CONCLUSION

This study explored the association between S. Albumin levels, NIHSS scoring scale and mRS score scale. There was linear decrease of S. Albumin with severity of stroke (NIHSS scoring scale) and mRS Scale indicating that S. Albumin levels correlated with NIHSS scoring scale and mRS scale. This indicates that S. Albumin levels can also be used as an adjuvant tool for assessing the severity of stroke along with other tools and facilitate required treatment. Several other studies have also found the same correlation between severity of stroke and S. Albumin levels .

SUMMARY

This study was a cross sectional study done on patients 'with acute ischemic stroke, to determine the association between Serum Albumin levels, NIHSS scoring scale and mRS scale, and to identify if a correlation exists between severity of stroke and Serum Albumin levels. It was done on 100 patients. It was also found Subjects under minor stroke had higher albumin levels followed by subjects with moderate stroke; moderate to severe stroke and severe stroke. Negative significant correlation was seen between albumin levels and moderate stroke. Overall, negative strong correlation was seen between albumin levels and NIHSS scores. Overall, negative strong correlation was seen between albumin levels and mRS scores. Hence, Serum Albumin levels could also be used as an adjuvant marker for assessing the severity of stroke, and facilitate treatment.

ETHICS APPROVAL

Not Applicable.

AVAILABILITY OF DATA AND MATERIAL

Not Applicable.

CONFLICT OF INTERESTS

Authors declared that there is no conflict of interest.

FUNDING

Research work was not funded.

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