Original Research Article

Clinical outcome of stroke with admission day glycemic status

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Abstract

Introduction: Cerebrovascular accident includes ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysm, AV malformation, and cortical venous thrombosis. Stroke, after heart disease and cancer, is the third most common cause of death Diabetics and stress Hyperglycemia have severe strokes resulting in a poor outcome. Stroke is twice more common in diabetics than in non-diabetics. Several risk factors determine the outcome of stroke. Hyperglycemia, fever, neuroprotective agents are those which are widely studied.

Aim of the study: To measure the blood glucose level within twenty-four hours of the onset of stroke in both diabetics and non-diabetics and to evaluate the severity and prognosis in both diabetics and non-diabetics about hyperglycemia.

Materials and methods: A total of a hundred and nine patients with acute stroke admitted to the department of medicine, Government Kallakurichi Medical College, Kallakurichi, in May 2021 were studied. The severity of stroke for each patient is calculated based on the NIH stroke scale, NIHSS which takes the following clinical findings into account, and each criterion awarded specific points.

Results: Among the hundred patients in our study group, 56 patients had elevated admission day blood glucose levels and 44 patients had normal blood glucose values. Diabetes was noticed in 28 patients and stress hyperglycemia in another 28 patients. In the ischemic stroke group, stress hyperglycemia amounted to one-third of the patients and one-fifth in the hemorrhagic group. Euglycemic patients had a better recovery after acute stroke. Sixty-five percent of euglycemic patients had a good functional recovery. On the contrary, only three percent of admission day hyperglycemia patients had good functional recovery at the end of thirty days follow up.

Conclusion: There is a linear correlation between admission day hyperglycemia and stroke in its severity, size, and outcome. Combined diabetes and stress hyperglycemia is found to have a larger-sized severe stroke and poor functional outcome in the form of increased mortality. There is a good correlation between admission day glucose level and the outcome in ischemic stroke. Admission day

elevated glucose level was a significant predictor of mortality and poor functional outcome after acute stroke. Hence, restoration of normoglycemia as soon as possible should be encouraged through conclusive evidence are lacking. In the interim, we should fare well with adhering to good general stroke management, normalization of body temperature, fluid balance, and hemodynamics or we may otherwise risk the favorable outcome even in the patients with normoglycemia.

Key words

Hyperglycemia, CVD, Hemorrhagic Shock, Venous Thrombosis.

Introduction

Among all the neurological diseases of adult life, Cerebrovascular accidents rank first in the frequency of importance. At least 50% percent of neurological diseases in general hospitals are due to stroke [1]. Cerebrovascular accident includes ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysm, AV malformation, and cortical venous thrombosis [2]. Stroke, after heart disease and cancer, is the third most common cause of death. With the introduction of effective treatment for hypertension, there has been a marked reduction in the frequency of stroke [3]. Diabetes mellitus by its association with microvascular and macrovascular disease is an important risk factor in the genesis of stroke. Most of the diabetic patients with stroke have raised glycosylated hemoglobin indicating that most of them have uncontrolled diabetes [4]. Diabetics and stress Hyperglycemia have severe strokes resulting in poor outcomes. Stroke is twice more common in diabetics than in non-diabetics [5]. Hypertension is common in diabetes and accelerates atherosclerosis which promotes intracranial small vessel disease and heart disease leading to lacunar and embolic infarction respectively [6]. Ischemic stroke, which includes TIA, is the most common type of stroke is a blockage that cuts off blood supply to affected parts of the brain. Ischemic strokes are often referred to as cerebrovascular accidents (CVA) and could be a thrombotic or embolic event [7]. The effects of the blockage are related to the location of the blockage in the brain rather than the source; however, the source becomes vitally important in identifying the cause for individual management and secondary stroke prevention [8]. Intracerebral hemorrhagic stroke differs from an ischemic stroke in that it is caused by a ruptured blood vessel as opposed to a blood clot. The ruptured vessel interrupts blood flow and delivery of essential nutrients and oxygen to the affected area of the brain. A ruptured blood vessel may release blood very rapidly which may lead to a sudden build-up in cerebral pressure resulting in unconsciousness or death [9]. Approximately 10-15% of all strokes are hemorrhagic and have an estimated 40%-50% mortality rate several risk factors determine the outcome of stroke. Hyperglycemia, fever, neuroprotective agents are those which are widely studied [10].

Materials and methods

A total of a hundred and nine patients with acute stroke admitted to the Department of Medicine, Government Kallakurichi Medical College, Kallakurichi, in May 2021 were studied.

Inclusion criteria: Patients should be above the age of forty. Patients should have been admitted within twenty-four hours of the onset of symptoms. This should be the first cerebrovascular accident for the patient. Blood sugar was recorded within twenty-four hours of the onset of stroke.

Exclusion criteria: Patients admitted after twenty-four hours of the stroke, those patients who received intravenous glucose before or during the study period. Patients with reliable information about diabetes could not be obtained. Patients who died before it could be established whether or not they had diabetes, Illness presenting with stroke-like symptoms.

Out of the hundred and nine patients, nine were dropped as follow-up could not be done. Complete history was taken, clinical examination was done and clinical diagnosis for each patient arrived. Blood pressure measurement, blood sugar, urea, creatinine, electrolytes, hemoglobin, total count, differential count; urine sugar, albumin, deposits; electrocardiogram and chest X-ray were done for all patients. The severity of stroke for each patient was calculated based on the NIH stroke scale, NIHSS which takes the following clinical findings into account, and each criterion awarded specific points. Once a clinical diagnosis of acute stroke was made venous blood sample was taken, within twenty-four hours of the onset of symptoms, and sent to a laboratory for glucose estimation. In patients with blood sugar more than 6.1 mmol/l (110 mg/dl) and without a history of diabetes, Hemoglobin A 1c was performed. (Hemoglobin A1c is structurally similar to hemoglobin A except for the addition of glucose Group to the terminal amino acid of the beta chain of the hemoglobin Molecule (glycosylation). Therefore hemoglobin A 1c is a function of the exposure of the red blood cells to glucose. Since the glucose linkage to hemoglobin is relatively stable, Hemoglobin A1c accumulates throughout the life span of the erythrocyte and its concentration reflects the integrated blood glucose concentration over a period approximating to the half-life of erythrocytes i.e. six to eight weeks. Therefore measurement of hemoglobin A1c helps to monitor the overall degree of diabetic control achieved). The normal range of Hemoglobin A 1c is 3.8% to 6.4%. Hence the patients can be classified into four groups. Blood sugar less than 6.1 mmol/l: Nondiabetic (euglycemic). History of diabetes: Known diabetics. Blood sugar more than 6.1mmol/l, no history of diabetes, and hemoglobin A1c.more than 6.4%: Newly detected diabetics. Blood sugar more than 6.1 mmol/l, no history of diabetes, and hemoglobin A1c less than 6.4%: Stress hyperglycemia. The patients were followed up for thirty days and the outcome in the form of death; poor, moderate, and good improvement were recorded. Patients who were unable to return to any form of work, persistent disability need for residential placement, dependent in activities of daily living, and stable deficit with no recovery were classified as those with poor outcomes. Patients whose symptoms improved, who were independent in attending the day-to-day activities, improvement in motor function and aphasia, and no persistent disability were grouped as patients with a good outcome. Patients who fared in between these two groups were grouped as those with the moderate outcome.

Statistical analysis

Records of the patients' age, sex, fasting blood sugar, body mass index, and duration of diabetes were documented. An evaluation of the skin disease was made clinically after detailed examination. Data was analyzed using statistical package for social sciences version 21. Data cleaning was carried out and errors corrected. Quantitative variables were summarized using means and standard.

Results

Amongthehundredpatients,66had hypertension, 28 had diabetes, 14had hypercholesterolemia, 6 had a previous history of myocardial infarction, and one lady had atrial fibrillation. More than half of the male patients were smokers and one-third had a history of alcohol intake. Sixty patients had rightsided weakness and forty patients had a left-sided weakness.

Among the hundred patients in our study group, 56 patients had elevated admission day blood glucose levels and 44 patients had normal blood glucose values. Diabetes was noticed in 28 patients and stress hyperglycemia in another 28 patients. In the ischemic stroke group, stress hyperglycemia amounted to one-third of the patients and one-fifth in the hemorrhagic group (**Table – 1, 2, 3, 4**). Severity of stroke was assessed with the NIH Stroke scaling system. Admission day hyperglycemic patients had a higher score when compared to Euglycemic patients (17.27 vs. 9.5 respectively), which was

statistically significant with p = 0.001. Among the admission day, hyperglycemic patients with newly detected diabetes had the highest mean NIHSS. Hence an elevated blood sugar at the time of stroke resulted in severe stroke (**Table – 5**).

Table – 1: Age-wise distribution.

Age (Years)	Male	Female	Total	%
41-50	16	4	20	20
51-60	28	10	38	38
61-70	9	11	20	20
71-80	10	9	19	19
>80	3	0	3	3
	66	34	100	100

Table - 2: Risk factors.

Risk factors	Male	%	Female	%	Total
Hypertension	42	63.64	24	36.36	66
Diabetes	17	60.71	11	39.29	28
Hypercholesterolemia	10	71.43	4	28.56	14
Atrial fibrillation	0	0	1	100	1
Coronary artery disease	4	66.66	2	33.33	6
Smoking	40	100	0	0	40
Alcohol	25	96.15	1	3.85	26

Table – 3: Clinical presentation.

Clinical presentation	Male	%	Female	%	Total
Right hemiplegia	38	69.1	17	30.9	55
Left hemiplegia	25	64.1	14	35.9	39
Faciobrachial monoplegia	2	40	3	60	5
Cerebellarsymptoms	1	100	0	0	1
Loss of consciousness	31	60.8	20	39.2	51
Hemianopia	2	66.6	1	33.3	3
Aphasia	22	57.9	16	42.1	38
Bladder and Bowel involvement	16	59.3	11	40.7	27

Table – 4: Glycemic status.

Glycemic status	Total
Euglycemia	44
Stress Hyperglycemia	28
Known Diabetes	16
Newly diagnosed Diabetes	12

The size of the lesion was analyzed with the help of a CT scan brain. Most of the euglycemic patients had small-sized infarcts and hemorrhages whereas the majority of the admission day hyperglycemic patients had large-sized lesions with edema and midline shift. These data were statistically significant with p = 0.001. Hyperglycemia by increased anaerobic metabolism, increased brain lactate, impaired mitochondrial function, vascular disease,

increased free radical production, increased expression of c-fos and cox-2 causes severe brain injury and large-sized infarcts. Hyperglycemia can disrupt the blood-brain barrier resulting in large hemorrhage and hemorrhagic transformation of infarcts (**Table – 6, 7**).

Table –5: Stroke S everity.

Glycemic status	**NIHSS**
Euglycemia	9.5
Stress hyperglycemia	16.33
Known diabetes	17.3
Newly diagnosed diabetes	19.4

Table – 6: Glycemic status among ischemic and hemorrhagic stroke.

Glycemic status	**Ischemic stroke**		**Hemorrhagic stroke**		**Total**
	NO	**%**	**NO**	**%**	
Euglycemia	34	77.27	10	22.73	44
Stress hyperglycemia	23	82.14	5	17.86	28
Known diabetes	10	62.5	6	37.5	16
Newly diagnosed diabetes	6	50	6	50	12

Table – 7: Size of the lesion.

Glycemic status	**Total**	**Small**	**Medium**	**Large**
Euglycemia	44	29	8	7
Stress Hyperglycemia	28	1	14	13
Known Diabetes	16	2	6	8
Newly diagnosed diabetes	12	0	6	6

Table – 8: Clinical outcomes.

Glycemic Status	**Total**	**Death**		**Poor**		**Moderate**		**Good**	
		NO	**%**	**NO**	**%**	**NO**	**%**	**NO**	**%**
Euglycemia	44	7	15.91	2	4.54	6	13.64	29	65.91
Stress Hyperglycemia	28	10	35.71	8	28.57	9	32.14	1	3.54
Known Diabetes	16	7	43.75	3	18.75	5	31.25	1	6.25
Newly diagnosed diabetes	12	6	50	4	33.33	2	16.67	0	0

In this study of hundred acute stroke patients, euglycemic patients had a better outcome when compared to admission day hyperglycemic patients. Euglycemic patients had a better recovery after acute stroke. Sixty-five percent of euglycemic patients had a good functional recovery. On the contrary, only three percent of admission day hyperglycemic patients had good functional recovery at the end of thirty days follow up. Early inpatient mortality was high in admission day hyperglycemic patients. Forty percent of the admission day hyperglycemic patients died within the first thirty days. In the euglycemic patients, the early case fatality rate was only fifteen percent. Hence there was a two and a half-fold increased risk of early mortality in admission day hyperglycemic patients when compared to euglycemic. Poor outcome was noticed in twenty-seven percent of admission day hyperglycemic patients and four percent of euglycemic patients (**Table – 8, 9, 10**).

Statistical analyses were performed with SPSS 24.0. Descriptive statistics including mean, median, and standard deviation were computed for baseline characteristics. Chi-Square test was

used to compare categorical variables and Student t-test and Mann Whitney test was applied to calculate the *p*-value for continuous variables for univariate statistics. Wilcoxon signed-rank test was used to compare mRS at discharge and 90 days. Predictors of poor outcome and death at three months were analyzed using logistic regression analysis. Variables with a *p*-value less than 0.05 at a univariate level were considered significant.

Table – 9: Outcome in stroke subtypes.

GLYCEMIC STATUS			**Outcome**				**Total**
			Good	**Moderate**	**Poor**	**Death**	
HEMORRHAGE	**Group**	**Euglycemia**	3	3	0	4	10
		Stress hyperglycemia	0	1	1	3	5
		Known diabetes	0	3	2	1	6
		Newly diagnosed diabetes	0	2	3	1	6
	Total		3	9	6	9	27
INFARCT	**Group**	**Euglycemia**	26	3	2	3	34
		Stress hyperglycemia	1	8	7	7	23
		Known diabetes	1	2	1	6	10
		Newly diagnosed diabetes	0	0	1	5	6
	Total		28	13	11	21	73

Hemorrhage: □ 2=12.75,P=0.17**(Not significant)**

Infarct: □ 2=50.6,P=0.001**(Significant)**

Table – 10: Outcome of stroke in non-diabetes patients.

		Ischemic stroke		**Hemorrhagic stroke**	
		Euglycemia	**Stress Hyperglycemia**	**Euglycemia**	**Stress Hyperglycemia**
Total		34	23	10	5
NIHSS		7.62	15.56	14.4	19.8
Death	No	3	7	4	3
	%	8.82	30.43	40	60
Poor	No	2	7	0	1
	%	5.58	30.43	0	20
Moderate	No	3	8	3	1
	%	8.82	34.78	30	20
Good	No	26	1	3	0
	%	76.47	4.35	30	0
The average blood glucose level		91.68	144.43	102.12	240.6

Discussion

The National Institute of Neurological Diseases and Stroke (NINDS) is a division of the National Institute of Health (NIH) in the United States (NINDS, 2013). Since 1977 NINDS has sponsored 28 Phase 3 trials to evaluate treatments of stroke for 44, 862 stroke participants. The trials were designed to test drugs, devices, surgery, and behavioral intervention in stroke prevention, acute treatment, and rehabilitation. In the ischemic stroke group, the early mortality rate was 8.82 % in euglycemic patients and 46.15% in hyperglycemic patients. Poor outcome was noticed in 5.88% in euglycemic and 23.3% in hyperglycemia [11]. The early mortality rate was 30.43% in stress hyperglycemia and 8.82% in

euglycemic. Hence this study shows a three-and-a-half-fold increased risk of mortality in non-diabetes stress hyperglycemic patients when compared to non-diabetic euglycemic patients which were also statistically significant with p=0.001. However similar significance was not noticed in the hemorrhagic group. Our study clearly shows a positive correlation (r=0.71, p=0.01) between admission day sugar value and the outcome of stroke. Higher admission day elevated blood glucose level has increased mortality and high risk of poor functional recovery [12]. Lindsberg PJ, et al., hyperglycemia was noted in two- third (66%) of all ischemic stroke patients. In our study hyperglycemia was noticed in 56% of patients in general and in55% of patients with ischemic stroke. In their study is known diabetes and newly diagnosed diabetes contributed one-third of cases (33%) [13]. In our study, the same group contributed to 28%. In the journal of clinical endocrinology and metabolism, Lindsborg PJ, et al. in a study confirmed that patients with newly detected hyperglycemia had a significantly higher early mortality and a lower functional outcome than patients with a history of diabetes or normoglycemia. Our study in hundred acute stroke patients had the same results [14]. Malmberg K, et al. [15] analyzed thirty two similar studies and concluded that hyperglycemic patients had three fold increased early mortality than euglycemic patients. After ischemic stroke admission hyperglycemia was associated with three-fold increased 30-day mortality than euglycemic. After a hemorrhagic stroke, admission hyperglycemia was not associated with higher mortality in either diabetic non-diabetic patients. In our study, ischemic patients, who had elevated admission day glucose levels experienced three and a half fold increased early mortality than euglycemic [15]. Hemorrhagic patients with admission hyperglycemia did not show a statistically significant early mortality when compared to their euglycemic counterparts. Similar results were noticed in non-diabetic patients. Non-diabetic stress hyperglycemic patients with ischemic stroke had three and a half fold increased early mortality when compared to euglycemic [16]. In the diabetic group since the sugar value before the onset of stroke was not known, the effect of stress in the diabetic group could not be studied. The study clearly shows an increased early mortality rate and poor functional recovery in patients with diabetes and stress hyperglycemia when compared to euglycemic [17]. Hence, there is an urgent need to confirm the improvement in these patients by normalizing blood sugar. Several trials are now under way to improve the outcome of Stroke by normalizing the blood glucose with human recombinant insulin. Scott JF, et al., showed that administration of insulin to patients with hyperglycemia improves functional recovery and vital activity of mild to moderate ischemic stroke patients. However, other clinical benefits of insulin therapy remain to be determined [18, 19, 20].

Conclusion

There is a linear correlation between admission day hyperglycemia and stroke in its severity, size, and outcome. Combined diabetes and stress hyperglycemia is found to have a larger-sized severe stroke and poor functional outcome in the form of increased mortality. There is a good correlation between admission day glucose level and the outcome in ischemic stroke. Admission day elevated glucose level was a significant predictor of mortality and poor functional outcome after acute stroke.

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