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Original Article

Admission Hyperglycemia an Independent Predictor of Outcome in Acute Ischemic Stroke: A Longitudinal Study from a Tertiary Care Hospital in South India

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Abstract

Background: Stroke is one of the important causes of long-term disability-related deaths worldwide. Incidence and prevalence of stroke have been steadily increasing in India. Increasing interest has been focused on the role of admission hyperglycemia in the evolution of acute ischemic stroke. Very few studies were conducted in south India; hence, we intended to do this study. **Methods:** A total of 198 patients with acute ischemic stroke were included in a hospital-based longitudinal study to identify the independent factors (demographic, clinical, and biochemical parameters) associated with poor outcome (functional impairment—mRS ≥ 3 and mortality at 90 days of follow-up. **Results:** Nearly, 75% of the patients presented with moderate-to-severe stroke. Out of the 198 patients, 117 (59%) had severe disability at admission. At 90 days of follow-up, it was observed that only 10 (5.5%) had severe disability. Patients with hyperglycemia exhibited greater functional impairment, that is, 96 out of 111 study subjects had modified Rankin score (mRS) ≥3, than those with normoglycemia ($P < 0.0001$). Mortality was high in hyperglycemics when compared with normoglycemics, that is, out of the 20 deaths, 13 patients had hyperglycemia and seven had normoglycemia at presentation ($P < 0.015$). Logistic regression analysis predicted that higher capillary blood glucose at first presentation, moderate-to-severe stroke, poor drug compliance, stress hyperglycemia, and newly detected diabetes mellitus were associated with poor functional outcome at 90 days of follow-up. **Conclusion:** Stress hyperglycemia in stroke was associated with higher risk of poor functional outcome in acute ischemic stroke. Hyperglycemia at stroke onset without prior history of diabetes mellitus have particularly poor prognosis, than those with hyperglycemia in known diabetes.

Keywords: *Acute ischemic stroke, diabetes mellitus, stress hyperglycemia*

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Introduction

Stroke is the second leading cause of long-term disability and death worldwide.[1] In 2005, 16 million people had a first stroke and 5.7 million died because of the effects of stroke.[2] According, to the study carried out in Kolakata in 2007, incidence rate of stroke is approaching western figures of 145/1,00,000 population.[3] Relation between disturbed glucose metabolism and ischemic stroke is bidirectional. On one hand, people with diabetes have more than double the risk of ischemic stroke, compared with people without diabetes.[3] On the other hand, acute stroke can give rise to abnormalities in glucose metabolism, which in turn could affect the outcome.[4]

Hyperglycemia is found in 30-40% of people with acute ischemic stroke.[5] Most of these individuals

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do not have a known history of diabetes mellitus (DM).[6] In some patients, hyperglycemia reflects preexisting but unrecognized diabetes, but more often it is the result of an acute stress response, typically named stress hyperglycemia. The stress reaction that results in hyperglycemia is initiated by activation of the hypothalamic-pituitary-adrenal axis, which leads to raised amounts of glucocorticoids (cortisols) and activation of the sympathetic autonomic nervous system. Increased levels of stress hormones stimulate glucose production by glycogenolysis, gluconeogenesis, proteolysis, and lipolysis.

Admission hyperglycemia is associated with poor functional outcome, possibly through aggravation of ischemic damage by impaired recanalization, decreased reperfusion, reperfusion injury, and direct tissue injury.[6]

There is a dispute on whether a raised plasma glucose concentration is independently associated with poor prognosis. Several studies have suggested that hyperglycemia in nondiabetic patients after acute stroke is a stress response[7-14] reflecting more severe neurological damage. Others have suggested that hyperglycemia influences outcome independently of stroke severity.[15-17] Hence we sought to address this issue with the following objectives, first to estimate the permissible blood glucose levels at the time of hospitalization for acute ischemic stroke (AIS). Second, to determine stroke severity and functional impairment among study subjects in relation to glycemic category. Third, to evaluate the impact of admission hyperglycemia at presentation in those with and without prior DM.

Methods

Study design and selection of participants

A hospital-based longitudinal study involving 198 patients of AIS was carried out in a tertiary teaching hospital in Mysuru between October 2013 and August 2015. All consecutive patients presenting to the emergency room with clinical history suggestive of acute ischemic stroke were examined and those fulfilling the inclusion criteria (presenting with AIS within 24 hours of symptom onset and whose capillary blood glucose was measured at the time of first presentation) were included in the study. Patients with hemorrhagic stroke and recurrent stroke were excluded from the study. Acute ischemic stroke was confirmed by using 128 slice Philips Computed Tomography/3 Tesla Philips Ingenia Magnetic Resonance Imaging. Patients demographic, clinical, detailed history regarding temporal profile of stroke, and history of diabetes (any patient who was on antidiabetic medication), hypertension (patient who was on antihypertensive medication), dyslipidemia (patients on lipid-lowering drugs), smoking (patient with history of using bidi or cigarette), and alcohol consumption (patient who consumed any form of alcohol on most days of a week) information were collected on pretested proforma. Admission capillary blood glucose was measured using one touch vireo instrument manufactured by One Touch Life Scan Verio, Manufactured by Life Scan INC, A Johnson & Johnson Company. HbA1c was measured by HPLC method using D-10™ Hemoglobin Analyzer Manufactured by BIO-RAD LABORATORIES hemoglobin system, Biorad, and fasting lipid profile measured by cholesterol oxidase method using Toshiba automated analyzer. TBA-FX8 AUTOMATED CLINICAL CHEMISTRY ANALYSER Manufactured by TOSHIBA CORPORATION and ECHO were done to rule atrial fibrillation and thrombo-embolism whenever needed. Patients were stratified as normoglycemics (CBG: Capillary Blood Glucose < 140 mg/dL) and hyperglycemics (CBG >140 mg/dL) and patients with hyperglycemia were further subdivided into Stress hyper glycemia, newly detected DM and with known diabetes based on sugar and HbA1c levels. Stroke severity at the time presentation was assessed by using NIH stroke scale. Functional impairment was assessed by using modified Rankin scale (mRS) at the time of admission, discharge and at 90 days follow-up. Functional outcome was measured by the modified Rankin Scale (mRS) and a poor Rankin was defined as a score more than 3. Subjects were either asked to come to the hospital or a telephonic follow-up was carried out at 90 days. During follow-up, patients were assessed for drug compliance (i.e., whether taking regularly antiplatelet and lipid-lowering drugs), functional impairment, measurement of stroke severity using mRS. Factors influencing poor functional status at 90 days (mRS) were evaluated by logistic regression models. The strength of the associations was summarized by calculating odds ratios (OR) and corresponding 95% confidence intervals (CI).

Ethical considerations

Prior to the commencement of the study, ethical clearance was obtained from the institutional ethics committee of JSS Medical College and informed consent was obtained from either the patient's attendant or the patient themselves.

Statistical analysis

All the statistical analysis were done using SPSS STATISTICAL SOFTWARE VERSION 21.0 BY IBM COMPUTERS, IBM INC version 21.0. The graphs were prepared using Microsoft Excel spread sheet. Descriptive statistics such as mean, median, standard deviation, and proportions were calculated to summarize the data.

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Inferential statistics was performed using independent *t* test, chi-square test, and logistic regression. A *P* value of <0.05 was considered as statistically significant.

Results

Demographic details of the study cohort are summarized in [Table 1]. Around 51% of the stroke patients were aged between 51 and 70 years. About 62.1% were men and 37.9% were women. Nearly 27.8% were known diabetic patients, an44.9% were known hypertensive patients, 55.1% had dyslipidemia, 28.8% consumed alcohol, 42.6% were smokers in the past, and 5.6% continued smoking even after stroke.

Table 1: Clinicodemographic details of study subjects (*N* = 198)

Factor	No. (%)	
Age (in years)		
<40	16 (8.1)	
41–50	35 (17.7)	
51–60	47 (23.7)	
61–70	54 (27.3)	
71–80	30 (15.2)	
>81	16 (8.1)	
Gender		
Male	123 (62.1)	
Female	75 (37.9)	
NIH stroke severity at presentation (assessed using NIH stroke scale)		
Minor Stroke	49 (24.7)	
Moderate stroke	77 (38.9)	
Moderate–severe stroke	45 (22.7)	
Severe stroke	27 (13.4)	
Comorbid conditions		
History of diabetes mellitus	55 (27.8)	
History of hypertension	89 (44.9)	
Past history of alcoholism	57 (28.8)	
Past history of smoking	84 (42.4)	
Smoking even after stroke	10 (5.6)	
Past history of dyslipidemia	109 (55.1)	
	Mean (SD)	**Median**
Age (in years)	61.18 (14.13)	61
Systolic blood pressure (mmHg)	149.50 (25.68)	150
Diastolic blood pressure (mmHg)	87.57 (12.44)	90
Capillary blood glucose (mg/dL) at first presentation to the emergency room	170.66 (77.58)	154
Fasting blood glucose (mg/dL)	137.61 (63.84)	110
Postprandial blood glucose (mg/dL)	181.06 (75.56)	150
HbA1c	7.04 (1.09)	6.0
Total cholesterol (mg/dL)	188.44 (47.77)	190
Triglyceride (mg/dL)	55.45 (88.4)	135
VLDL: Very low Density Lipoprotein (mg/dL)	30.72 (17.5)	27
LDL: Low density Lipoprotein (mg/dL)	120.66 (43.0)	122
HDL: High density Lipoprotein (mg/dL)	42.40 (12.8)	40

Mean age of the study participants was 61.18 ± 14.13 years. Mean SBP: SYSTOLIC BLOOD PRESSURE and DBP: DIASTOLIC BLOOD PRESSURE was 149.50 ± 25.68 mmHg and 87.57 ± 12.44 mmHg, respectively. Mean capillary blood glucose at the time of first presentation to the emergency ward was 170.66 ± 77.58 mg/dL.

Out of the 198 patients included in the study, 56.1% study subjects had capillary blood glucose >140 mg/dL on presentation. Around 41% of the stroke patients were normoglycemics, 21.2% had stress hyperglycemia, 24.2% were known diabetics, and 13.65% were newly detected with DM.

Functional impairment of stroke patients was assessed at the time of admission, at time of discharge, and at 90 days follow-up, and it was observed that 59.15% had severe disability at the time of admission, 38.9% had severe disability at the time of discharge, and only 5.5% had severe disability at end of 90 days [Table 2].

Table 2: Comparison of functional impairment at the time of first stroke presentation, at discharge and at 90 days follow-up

	Functional impairment		
	At admission	**At time of discharge**	**At 90 days**
Modified Rankin score	**No. of cases (%)**	**No. of cases (%)**	**No. of cases (%)**
0 (No symptoms)	0 (0)	2 (1.0)	12 (6.6)
1 (No significant disability)	6 (3.0)	19 (9.6)	20 (10.9)
2 (Slight disability)	19 (9.6)	15 (7.6)	27 (14.8)
3 (Moderate disability)	26 (13.1)	21 (10.6)	36 (19.7)
4 (Moderately severe disability)	30 (15.2)	49 (24.7)	73 (39.9)
5 (Severe disability)	117 (59.1)	77 (38.9)	10 (5.5)
6 (Dead)	0 (0)	15 (7.6)	5 (2.7)
Total	198 (100.0)	198 (100.0)	183 (100)

Table 3: Mortality in relation to glycemic level at presentation

	Mortality				
	Alive		**Dead**		
Glycemic severity at presentation (mg/dL)	*n*	**%**	*n*	**%**	
	<140	80	44.9	7	35
	>140	98	55.1	13	65
	Total	178	100	20	100

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Table 4: Comparison of severity of stroke at 90 days follow-up with various factors

		Stroke severity after 90 days				
		Score <3 (95)		Score ≥3 (103)		*P*
		n	%	n	%	
Age (years)	<40	4	25.0	12	75.0	0.1
	41–50	22	62.9	13	37.1	
	51–60	25	53.2	22	46.8	
	61–70	21	38.9	33	61.1	
	71–80	15	50.0	15	50.0	
	>81	8	50.0	8	50.0	
Sex	Male	68	55.3	55	44.7	0.008
	Female	27	36.0	48	64.0	
History of diabetes mellitus	Absent	74	51.7	69	48.3	0.09
	Present	21	38.2	34	61.8	
History of hypertension	Absent	53	48.6	56	51.4	0.8
	Present	42	47.2	47	52.8	
History of smoking	No	53	46.5	61	53.5	0.6
	Yes	42	50.0	42	50.0	
History of alcohol consumption	No	73	51.8	68	48.2	0.09
	Yes	22	38.6	35	61.4	
Blood pressure severity	<140/90 mmHg	39	42.4	53	57.6	0.1
	>140/90 mm Hg	56	52.8	50	47.2	
Glycemic severity at presentation	<140 mg/dL	77	88.5	10	11.5	<0.0001
	>140 mg/dL	18	16.2	93	83.8	
NIH stroke severity at presentation (assessed using NIH stroke scale)	No stroke	0	.0	0	.0	<0.0001
	Minor stroke	38	77.6	11	22.4	
	Moderate stroke	41	53.2	36	46.8	
	Moderate–severe stroke	9	20.0	36	80.0	
	Severe stroke	7	25.9	20	74.1	
Functional impairment at admission	1.00	6	100.0	0	.0	<0.0001
	2.00	18	94.7	1	5.3	
	3.00	25	96.2	1	3.8	
	4.00	17	56.7	13	43.3	
	5.00	29	24.8	88	75.2	
Functional impairment at time of discharge	.00	2	100.0	0	.0	<0.0001
	1.00	19	100.0	0	.0	
	2.00	13	86.7	2	13.3	
	3.00	19	90.5	2	9.5	
	4.00	19	38.8	30	61.2	
	5.00	23	29.9	54	70.1	
	6.00	0	.0	15	100.0	
Glycemic category	Normoglycemia	74	91.4	7	8.6	<0.0001
	Stress glycemia	3	7.1	39	92.9	
	Newly detected DM	3	11.1	24	88.9	
	Known DM	15	31.3	33	68.8	
Dyslipidemia	No dyslipidemia	49	55.1	40	44.9	0..07
	Dyslipidemia	46	42.2	63	57.8	
Continues smoking	No	89	52.7	80	47.3	0.7
	Yes	6	60.0	4	40.0	
Drug compliance	Good	94	56.6	72	43.4	0.001
	Poor	1	7.7	12	92.3	

The hyperglycemic group was noted to have significantly greater stroke severity ($P < 0.0001$). Interestingly, the association of hyperglycemia with stroke severity was noted to be high in those subjects with stress hyperglycemia, that is, 92.9% of the patients had mRS ≥3 at 90 days, in subjects with newly detected DM,

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Table 5: Comparison of mean values of glucose, blood pressure and lipid profile parameters and stroke severity on 90 days follow-up of AIS

Values at first presentation to hospital	Stroke severity score < 3	Stroke severity score > 3	*F*	*P*
Capillary blood glucose (mg/dL) at first presentation to the emergency room	129.95 (55.18)	208.20 (76.49)	6.7	<0.0001
Fasting blood glucose (mg/dL)	118.60 (37.86)	155.15 (76.83)	23.91	<0.0001
Postprandial blood glucose (mg/dL)	161.03 (00.14)	199.53 (83.53)	15.26	<0.0001
HbA1c	6.38 (1.38)	7.64 (2.10)	45.58	<0.0001
Systolic blood pressure (mmHg)	151.26 (26.23)	147.88 (25.17)	1.97	0.162
Diastolic blood pressure (mmHg)	88.48 (13.39)	86.73 (11.50)	2.64	0.105
Total cholesterol (mg/dL)	181.23 (46.65)	195.10 (48.05)	0.074	0.786
Triglyceride (mg/dL)	154.95 (96.75)	155.92 (80.41)	0.751	0.387
VLDL (mg/dL)	31.42 (19.72)	30.07 (15.27)	1.91	0.168
LDL (mg/dL)	114.48 (41.97)	126.35 (43.37)	0.045	0.832
HDL (mg/dL)	42.29 (12.97)	42.5 (12.71)	0.008	0.950

Table 6 : Multiple logistic regression analysis for association of independent risk factors with severity of stroke at 90 days

			95% CI for odds ratio	
Categories	**P**	**Odds ratio**	**Lower**	**Upper**
Increasing age	0.81	1.00	0.95	1.06
Female gender	0.68	1.44	0.24	8.65
History of diabetes mellitus	0.78	1.76	0.03	102.76
History of hypertension	0.56	0.65	0.15	2.84
History of smoking	0.85	1.19	0.16	8.51
History of alcohol intake	0.78	1.32	0.17	9.86
Minor stroke		1		
Moderate stroke	0.002	18.44	3.01	112.86
Moderate to severe stroke	0.000	42.75	5.49	332.53
Severe stroke	0.010	29.27	2.23	384.21
Systolic blood pressure at first presentation	0.42	1.01	0.98	1.05
Diastolic blood pressure at first presentation	0.61	0.98	0.90	1.05
Capillary blood glucose at presentation	0.004	1.02	1.01	1.04
Total cholesterol	0.94	0.99	0.96	1.03
Triglycerides	0.29	0.99	0.98	1.00
VLDL	0.77	1.00	0.95	1.06
LDL	0.44	1.01	0.98	1.04
HDL	0.49	1.02	0.96	1.08
Normoglycemia		1		
Stress glycemia	0.000	569.97	50.39	6446.64
Newly detected diabetes	0.000	250.12	20.08	3115.24
Known diabetes	0.14	24.14	0.33	1764.85
Poor drug compliance	0.003	298.58	7.09	12575.26

88.9% of them had mRS ≥3 at 90 days, and in subjects with a prior diagnosis of DM, 68.8% of them had mRS ≥3 at 90 days [Figure 1].

Among the 198 study subjects, 20 deaths occurred in the first 90 days of illness. Out of which 13 of them had CBG >140 mg/dL [Table 3].

A chi-square analysis was performed to identify the factors associated with severity of stroke at 90 days of follow-up, and it was observed that females' glycemic severity at time of presentation, stroke severity at presentation, severe functional impairment at admission, at the time of discharge, and poor drug compliance were associated with severe stroke at 90 days of follow-up [Table 4].

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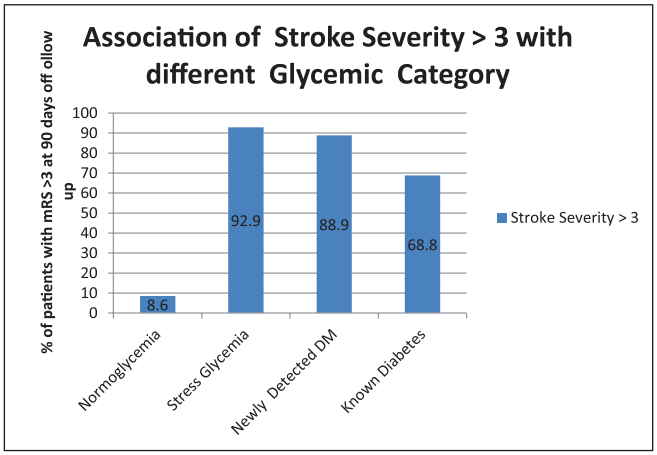

Figure 1: Association of worse outcome in relation to glycemic category.

[Table 5] shows that mean capillary blood glucose at first presentation, fasting blood glucose, postprandial blood glucose, and HbA1c levels were significantly higher among subjects who had stroke severity score above 3.

Multiple logistic regression analysis was performed to remove all confounding factors and to identify independent risk factor associated with outcome of ischemic stroke [Table 6]. Increasing severity of stroke (moderate-to-severe stroke), increasing capillary blood glucose at first presentation, newly detected diabetes, stress glycemia, and poor drug compliance were associated with poor functional outcome in acute ischemic stroke. Among these independent factors, stress hyperglycemia had the highest odds for poor outcome.

Discussion

Stroke is a common clinical problem in emergency department; current treatment for patients with established stroke is relatively ineffective. Approximately 50% of patients are left with permanent disability. Effective risk factor intervention offers a real hope in preventing stroke morbidity and mortality. Certain risk factors have been consistently identified as significant predictor of stroke outcome, while some are less consistent.

In the preset study, a total of 198 stroke patients were included and majority were male patients when compared with females. Mean age in stroke patients was 61.18 years, more than half of the patients were in the age group of 51–70 years.

In comparison with the studies carried out by Stead *et al.*,[18] Kissela *et al.*,[19] Baird *et al.*,[20] and Kostulas *et al.*,[21] the mean age of the patients with stroke is relatively low in our study. It is possibly because of lack of awareness regarding various risk factors of stroke at the population level. In India, stroke incidence is likely to increase in the coming years possibly due to increase in population, increase in life expectancy, rapid urbanization due to migration of villagers to the cities, changing lifestyles such as sedentary habits, smoking, excess alcohol use, and rising stress levels.[22]

In the current study, men (62.1%) were at greater risk for stroke than women (37.9%), which is similar to the studies done by Stead *et al.*,[18] and Kostulas *et al.*[21] The above studies concluded that worldwide stroke is more common among men than women. Male sex is one of the strong risk factor for stroke. Women have lower stroke incidence than men because of genetic factors, positive effects of estrogen on the cerebral circulation, and low blood pressure levels. Moreover, ischemic heart disease, peripheral artery disease and cigarette smoking are more prevalent among male stroke patients.[23]

The various risk factors associated with the stroke in study were hypertension 44.9%, diabetes 27.8%, smoking 42.4%, and alcohol abuse 28.1%. These observations correlate well with the studies done previously by Kostulas *et. al*,[21] Megherbi *et al.*[24] These observations correlate well with the studies done previously by Kostulas *et al.*[21] Megherbi *et al.*[24] Kissla *et al.*[19] and in the Copenhagen stroke study. The incidence of DM is high in our study as compared to other studies, it may be due to higher incidence of DM in south Indian population compared with western population.[25]

The observation in the present study that hyperglycemia at the time of presentation was seen in 56.1%, which is similar to Baird *et al.*,[20] but hyperglycemic patients were significantly high compared with those from Stead *et al.*[18] study. Lindsberg *et al.*[26] observed elevated blood glucose is common in the early phase of stroke. The prevalence of hyperglycemia has been observed in two-thirds of all ischemic stroke subtypes on admission. Although up to one-third of acute stroke patients have either diagnosed or newly diagnosed diabetes, probably a major proportion of patients have stress hyperglycemia mediated partly by the release of cortisol and norepinephrine. The observation in the present study that stress hyperglycemia was present in 21.2% of patients is similar to studies done by Melamed *et al.*[27] (35%) and Toni *et al* (36%).[14]

In the current study, overall 52% of the patients had poor functional outcome at 90 days, it appeared that those with normoglycemia had minimal functional impairment compared with patients with hyperglycemia ($P < 0.0001$). Among all these three subgroups of hyperglycemic individuals, the patients with stress hyperglycemia are associated with (92.9%) worse outcome, followed by the individuals with newly detected DM (88.9%), and those with previous history of DM are associated with 68.8% worse outcome at the end of 90 days.

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In the study of Stead *et al.*,[18] the outcome of functional impairment (mRS) was assessed; it appeared that those with normoglycemia did worse (poor mRS = 53.7% [normoglycemic] vs. 39.5% [hyperglycemic], $P = 0.004$). In particular, among the patients without a history of DM, patients with elevated glucose were more likely to have a poor mRS (OR 3.6; 95% CI 2.0–6.5, $P < 0.001$), whereas among the patients with a history of DM there was no clear impact of hyperglycemia on poor functional outcome (mRS) (OR = 0.7; 95% CI 0.3–1.5, $P = 0.32$).In the Capes *et al.*,[4] study the patients without diabetes, stress hyperglycemia was associated with a three-fold increased risk of mortality after stroke (pooled relative risk, 3.07; 95% CI, 2.50–3.79). In patients with diabetes, stress hyperglycemia was not associated with higher risk of short-term mortality after stroke (pooled relative risk, 1.30; 95% CI, 0.49–3.43).

In this study, we found that hyperglycemia at the time of presentation with AIS conferred a worse prognosis. This has been shown in numerous previous studies but debate continues as to whether it is a contributing factor to the more severe stroke or merely a stress response.

The majority of basic science research supports the theory that high blood glucose at the time of presentation has worsened the outcome, there are numerous mechanisms to explain how hyperglycemia may be toxic to the brain tissue and in particular to the vulnerable ischemic penumbra, possibly because of the accumulation of lactic acid due to anaerobic metabolism, enhanced glutamate release, and increased cerebral edema.[26]

In our study, we further subdivided our patients and found that the patients with hyperglycemia without history of DM have relatively more worse prognosis. Similar observation was found in a meta-analysis done by Capes *et al.*

Explanation for Capes *et al.* findings and our findings are that preconditioning by chronic elevated blood sugar levels may offset adverse metabolic effects, which may influence prognosis in nondiabetics. Certain medications that diabetics are frequently prescribed such as statins and antiplatelet agents confer a protective effect.

Currently, there is no sufficient evidence regarding treating hyperglycemia in the acute phase of stroke to improve the outcome. Clinical trials are currently underway evaluating the effect of achieving euglycemia in the acute phase of ischemic stroke.

Limitations of the present study are (i) diabetic patients have a higher baseline blood glucose level when compared with nondiabetics so we may need to use higher cutoff levels to detect stress hyperglycemia in this population when compared with nondiabetic population; and (ii) this study is done in a single centre located in Mysore with less ethnic diversity.

Conclusion

Stress hyperglycemia in stroke was associated with higher risk of poor functional outcome in acute ischemic stroke. Hyperglycemia at stroke onset, without prior history of DM have particularly poor prognosis, than those with hyperglycemia in known diabetes.

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Conflicts of interest

There are no conflicts of interest.

References

1. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors 2001. Systematic analysis of population health data Lancet 2006;367:1747-57.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6:182-7.
3. The Emerging Risk Factors Collaboration Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: A collaborative meta-analysis of 102 prospective studies. Lancet 2010;375:2215-22.
4. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in nondiabetic and diabetic patients: a systematic overview. Stroke 2001;32:2426-32.
5. Uyttenboogaart M, Koch MW, Stewart RE, Vroomen PC, Luijckx GJ, De Keyser J. Moderate hyperglycaemia is associated with favourable outcome in acute lacunar stroke. Brain 2007;130:1626-30.
6. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC Stress hyperglycemia and prognosis in nondiabetic and diabetic patients. Stroke 2001;332:2426-32.
7. O'Neill PA, Davies I, Fullerton KJ, Bennett D. Stress hormone and blood glucose response following acute stroke in the elderly. Stroke 1991;22:842-7.
8. Murros K, Fogelholm R, Kettunen S, Vuorela AL, Valve J. Blood glucose, glycosylated hemoglobin, and outcome of ischemic brain infarction. J Neurol Sci 1992;111:59-64.
9. Murros K, Fogelholm R, Kettunen S, Vuorela AL. Serum cortisol and outcome in ischemic brain infarction. J Neurol Sci 1993;116:12-7.
10. Woo J, Lam CWK, Kay R, Wong AHY, Teoh R, Nicholls MG. The influence of hyperglycemia and diabetes mellitus on immediate and 3month morbidity and mortality after acute stroke. Arch Neurol 1990;47:1174-7.
11. Woo E, Chan YW, Yu YL, Huan CY. Admission glucose level in relation to mortality and morbidity outcome in 252 stroke patients. Stroke 1988;19:185-91.
12. Candelise L, Landi G, Orazio EN, Boccardi E. Prognostic significance of hyperglycemia in acute stroke. Arch Neurol 1985;42:661-3.

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13. Melamed E. Reactive hyperglycemia in patients with acute stroke. J Neurol Sci 1976;29:267-75.
14. Toni D, Sacchetti ML, Argentino C, Gentile M, Cavalletti C, Frontoni M. Does hyperglycemia play a role on the outcome of acute ischemic stroke patients. J Neurol 1992;239:382-6.
15. Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS. Stroke in patients with diabetes: the Copenhagen stroke study. Stroke 1994;25:1977-84.
16. van Kooten F, Hoogerbrugge N, Naarding P, Koudstaal PJ. Hyperglycemia in the acute phase of stroke is not caused by stress. Stroke 1993;24:1129-32.
17. Kiers L, Davis SM, Larkins R, Hopper J, Tress B, Rossiter SC Stroke topography and outcome in relation to hyperglycaemia and diabetes. J Neurol Neurosurg Psychiatry 1992;55:263-70.
18. Stead GL, Glimore RM, Bellolio MF Hyperglycemia as an independent predictor of worse outcome in non-diabetic patients presenting with acute ischemic stroke. Neurocrit Care 2009;10:181-6.
19. Kissela BM, Khoury J, Kleindorfer D Epidemiology of ischemic stroke in patients with diabetes: the greater Cincinnati/Northern Kentucky Stroke Study. Diabetes Care 2005;28:355-9.
20. Baird A, Parsons W, Phan T. Persistent poststroke hyperglycemia is independently associated with infarct expansion and worse clinical outcome. Stroke 2003;34:2208-14.
21. Kostulas N, Markaki I, Cansu H. Hyperglycaemia in acute ischaemic stroke is associated with an increased 5-year mortality. Age and Ageing 2009;38:590-4.
22. Kamaleshwar P, Vibal D, Menaksji Cerebrovascular disease in South Asia. J R Soc Med Cardiovasc Dise 2012;1:20.
23. Peter A, Birgitten S, Andres T. Sex difference in stroke epidemiology. Stroke 2009;40:1082-90.
24. Megherbi SE, Milan C, Minier D., Association between diabetes and stroke subtype on survival and functional outcome 3 months after stroke: Data from the European BIOMED Stroke Project. Stroke 2003;34:688-94.
25. Sapna E, Unnikrishnan S, Incidence, type, risk factors and outcome of stroke in a developing country. Stroke 2009;40:1212-8.
26. Lindsberg JP, Roine RO., Hyperglycaemia in acute stroke. Stroke 2004;35:363-4.
27. Melamed E, Reactive hyperglycaemia in patients with acute stroke. J Neurol Sci 1986;29:267-75.