DOI: https://doi.org/10.4038/jccp.v55i2.7989

Assessment of the relationship between blood glucose indices and short-term outcome of patients with acute stroke in a tertiary care hospital in Sri Lanka

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Journal of the Ceylon College of Physicians, 2024, **55**, 107-113

Abstract

Background: Studies reveal an inconsistent relationship between the prognostic effects of hyperglycaemia in acute stroke. The purpose of this study was to evaluate the relationship between blood sugar indices and short-term neurological deficit and short-term mortality in acute stroke patients.

Methodology: This prospective study included acute stroke patients admitted to the National Hospital Kandy in Sri Lanka, using systematic random sampling. The random blood sugar (RBS) measurements on admission were recorded. The NIHSS score was used to assess the stroke severity on admission, on discharge, and 30 days post-stroke. The modified Rankin Scale (mRS) was used to assess the 30-day functional outcome following the stroke. The data were analysed using Fisher's exact test and Pearson's correlation coefficient.

Results: For the 389 patients the mean age was 69 (±SD12) years with a female predominance (N=247,63.5%). There was a weak, positive, and significant correlation (r=0.164. N=307, P<0.05) between admission blood sugar value on the degree of disability (NIHSS) at the time of discharge.

Among patients who died within 30 days, despite higher RBS (M=181.22, SD=92.12) compared to live patients (M=181.22, SD=92.12), no significant association was seen. Furthermore, 91 respondents at 30 days follow-up for the mRS were significantly associated with stroke type.

Key words: random blood sugar, acute stroke, NIHS score, modified Rankin score

Introduction

A stroke is defined as a neurological injury triggered by an acute vascular event leading to focal damage in the central nervous system. It has been recognized as one of the foremost reasons for premature deaths worldwide. Stroke is a leading cause of debility and death in Sri Lanka too.[1] Research reports a stroke prevalence of 10.4 per 1000 adults aged above 18 years in the Colombo district with a 1:2 female: male ratio.[2]

There are multiple risk factors leading to stroke. Among the modifiable risk factors, hyperglycaemia is common among patients who had an acute ischaemic stroke with or without diabetes mellitus (DM).[3] A higher percentage of patients experiencing an acutely stressful event such as stroke may develop hyper-glycemia, even without pre-existing DM.

Some studies have evaluated the factors that contribute to the short-term poor outcomes following acute ischemic stroke. Among the acute ischemic stroke patients, high blood sugar, high blood pressure, age over 79 years, and history of atrial fibrillation were identified as contributors to in-hospital mortality and undesirable neurological consequences on discharge.[4]

Studies done on high blood sugar levels and stroke showed hyperglycaemia following stroke may

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Received 14 August 2023, accepted 14 November 2023.

result in poor outcomes at both 1 month and 3 months.[5,6,7] Few research studies have revealed that non-diabetes patients had a bad prognosis than those with DM if they get hyperglycaemia at the onset of stroke.[8,9] However, as per another research, DM patients with high blood sugar levels had no significant predictive value on stroke morbidity and mortality.[6] Stress hyperglycaemia was also identified as a crucial risk factor for short-term adverse outcomes among stroke patients.[10] Two recent studies have confirmed that high blood glucose levels are predictive of functional outcomes in diabetic and non-diabetic patients complicated by cerebral infarction.[11,12] As there were some inconsistencies, the relationship between elevated blood glucose levels and short-term outcomes after a stroke in both diabetic and non-diabetic patients has not been well recognised.

Therefore, the objective of this study was to evaluate the relationship between blood glucose levels, short-term mortality, and the degree of disability of patients with acute stroke admitted to the National Hospital, Kandy, Sri Lanka. The findings may provide clinicians with more evidence for research, to predict prognoses accurately, and eventually to develop glycaemic control targets and strategies to adopt for stroke management.

Methodology

This longitudinal study was designed and conducted in general medical wards of the National Hospital Kandy (NHK) between April 2019 to November 2019. Ethical clearance was obtained from the Research and Ethics Review Committee of NHK (Ref: THK/ERC/19/2019) and administrative clearance was taken from the director of NHK (Ref: AN/Ethical/1-PL). Informed consent for the data collection was obtained from each patient or the next of kin if the patient was unable to consent.

Systematic random sampling was used as the sampling method and the sample size was calculated statistically.[13]

$$n = \frac{Z^2\, P(1\text{-}P)}{d^2}$$

n: Sample size, Z: Critical value of specified confidence interval, P: Estimate of the proportion and d: Desired precision

The following assumptions were made for the calculation. The critical value (Z) of the specified confidence interval for this study was assumed as 95% confidence level and its critical value of 1.96 is considered. As the exact proportion for the population is unknown, 0.5 is taken as the estimate of the proportion (P) to maximize the sample size and the desired precision (d) of 5% is considered for the calculation.

Newly diagnosed stroke patients, over 18 years of age, diagnosed by physicians were included as per the clinical definition.[14] The diagnosis was confirmed by CT brain reports. Patients with recurrent strokes, transient ischemic attacks, subarachnoid haemorrhage, subdural hematoma, traumatic brain injury, or space-occupying lesion in the brain, and end-stage organ failures were excluded to minimise the bias.

The administrator-interviewed questionnaires (part I & II) were used for the data collection. The part I questionnaire consisted of the demographic and clinical data including inward vital parameters, risk factors, National Institute of Health Stroke Scale (NIHSS) (used to assess the severity of stroke), and other investigations (random blood sugar, HbA1C, CT report, lipid profile). The interviewer completed the part I questionnaire during the hospital stay.

The NIHSS assessment was carried out on admission, on discharge, and for 30 days to evaluate the neurological deficit.[15] A series of random blood sugar (RBS) were collected on admission, at the emergency treatment unit (ETU), at ward admission within 24 hours and on discharge from the hospital.

A telephone interview was conducted 30 days after the initial stroke to collect data for part II of the questionnaire. The functional status of the patients was assessed using the modified Rankin Scale (mRS) during the telephone conversation.[16,17,18] In the situations where the patient was incapable of taking part in interviews, the next of kin or caregiver was allowed to participate in the interview. To assess mortality, deaths that occurred due to stroke within 30 days at the hospital were used.

For the continuous variables, the data were described as sample size, mean, and standard deviation. The categorical variables were described as frequencies. Patient on-admission glucose level and the primary outcomes were compared using following statistical methods. The difference between means of continuous variables was analysed with the Student t-test. Categorical variables were analysed using Chi-Square and Fisher's exact tests.

The correlation between continuous variables was determined by Pearson's correlation coefficient and multiple variable analyses were used to assess the relationship between blood glucose level and other risk factors with stroke outcome. A P value less than 0.05 was considered statistically significant.

Results

A total of 389 patients with acute ischemic stroke, were included in the data analysis. Mean age of the study population was 69 years (SD 12.7) and body weight was 61.8 kg (SD 10.3). The majority were female 247 (63.5%) which belonged to the 70-79 years (34.4%) category. There were 208 (53.5%) patients with hypertension and 116 (29.8%) with diabetes.

Table 1. Demographic data and risk factors (N= 389)

Demographic characteristics	*N (%)*
Gender	
Male	142 (36.5)
Female	247 (63.5)
Age category	
<50	26 (6.7)
50-59	56 (14.4)
60-69	95 (24.4)
0-79	134 (34.4)
80-89	65 (16.7)
90<	13 (3.3)
Ethnicity	
Sinhalese	325 (83.5)
Tamil	33 (8.5)
Muslim	29 (7.5)
Burgher	2 (0.5)
Level of education	
No	14 (3.6)
Primary	44 (11.3)
Secondary	50 (12.9)
Tertiary	15 (3.9)
High blood cholesterol	58 (14.9)
Current smokers	23 (5.9)
Alcohol consumption	23 (5.9)
Ischemic heart disease	22 (5.7)
Atrial fibrillation	10 (2.6)
Diabetes mellitus	116 (29.8)
Hypertension	208 (53.5)
Carotid artery disease	8 (2.1)

Table 2. Variables observed and outcome measurements

	Sample (n)	*Mean*	*SD*
Random blood sugar			
ETU	389	169	75
Ward admission	382	164	71
Discharge	207	144	44
NIHSS Score			
On Admission	389	9	8
24 hrs after admission	389	7	8
On discharge	307	5	7
After 30 days	82	2	4
30 days mRS	91	2	1

ETU = Emergency treatment unit, NIHSS = National Institute of Health Stroke Scale, mRS = Modified rankling score.

Mean random blood glucose measurements at ETU (N=389, 169 ±75) and at ward admission (N=389, 164 ±71) were higher than at discharge (N=307, 144 ±44) (Table 2). Meanwhile, the mean NIHSS score on admission was improved from 9 (±8) to 5 (±7) on discharge.

On admission to the hospital the diabetes patients' group (N=116) had a higher mean RBS level (M=212.92, SD=±97.28) than the non-diabetes group (N=272, M=150.78, SD=±53.63). A Chi-square test for independence indicated no significant difference between diabetes and non-diabetes groups in stroke mortality outcome at 30dyas, χ^2 (1,n=297)=0.18, p=0.61, phi=-0.03.

Table 3. Independent sample T-test to analyse the association between RBS and total mortality outcome

	Alive		Dead				
RBS measurement	*M*	*SD*	*M*	*SD*	*df*	*t*	*p*
ETU	168.4	68.9	181.2	92.1	199	1.28	0.200
Ward admission	162.5	57.5	177.6	95.3	171	1.52	0.127
At discharge	143.4	41.3	156.3	56.8	66	1.36	0.176

ETU – Emergency treatment unit.

Independent sample T-test revealed that there was no significant difference between RBS values in dead and live groups, (t (199)=1.28, p=0.2), despite ETU measured RBS in dead subjects (M=181.22, SD=92.12) attaining higher value than alive (M=168.43, SD=68.97). The study found that dead patients (M=177.59, SD=95.32) had statistically non-significant higher RBS at ward admission (M=6.15, SD=0.52 mmol/L), t (171)=1.52, p=0.127 compared to alive patients (162.52 ± 57.47). Furthermore, the mean RBS level at the time of discharge of those who died within 30 days (M=156.33, SD=56.75) was not significantly different from that of alive, (M=143.40, SD=41.30) t (66)=1.36, p=0.176).

Table 4. Pearson correlation for RBS levels, NIHSS, and mRS.

	On admission NIHSS		*24 hrs NIHSS*		*On discharge NIHSS*		*30days NIHSS*		*30 days mRS*	
RBS measurement	n	r	n	r	n	r	n	r	n	r
ETU	389	0.099	389	0.125*	307	0.164**	82	0.178	91	-0.057
Ward admission	382	0.075	382	0.106*	302	0.163**	82	0.233*	91	-0.024
At discharge	207	0.134	207	0.152*	181	0.207**	54	0.059	56	0.137

**Correlation is significant at the 0.01 level (2-tailed), * Correlation is significant at the 0.05 level (2-tailed), n-sample size. r-correlation coefficient. NIHSS-National Institute of Health stroke scale, mRS-Modified Rankin score, RBS-Random blood sugar, ETU-Emergency treatment unit.

A Pearson's correlation was performed to determine the relationship between RBS measurement with NIHSS and mRS scores. There was a weak, positive, and significant correlation between ETU RBS, ward admission RBS, and ward discharge RBS with 24 hours NIHSS and on discharge NIHSS (p<0.005). Furthermore, the ward RBS weakly and positively but significantly correlated with 30-day NIHSS, r=0.233, N=82, p<0.05.

Logistic regression was performed to create a model of the relationship between the predictor variables and outcome in the two groups (live and dead). The full model containing all predictors was statistically significant, χ^2(16, N=389)=51.482, Nagelkerke R2=0.141, p<.001. As shown in Table 5, significant unique contributions were made by age, gender, body weight, and history of high blood cholesterol.

Table 5. Predictors, unique contribution to 30 days mortality outcome in the logistic regression (N=389)

	Chi-Square	*df*	*Sig.*
Intercept	12.731	2	0.002*
Age	8.665	2	0.013*
Gender	7.391	2	0.025*
Bodyweight	8.168	2	0.017*
History high blood pressure	3.393	2	0.183
History diabetes	4.271	2	0.118
History high blood cholesterol	7.420	2	0.024*
Stroke type	5.180	2	0.075
RBS category on admission	3.043	2	0.218

* Variance is significant at 0.05 level (2 tailed), RBS-Random blood sugar.

As shown in Table 6, the strongest predictor of living was body weight and death were stroke type, recording an odds ratio of 1.036 and 1.506 respectively.

Table 6. Logistic regression predicting mortality outcome

					95% Confidence Interval for Exp(B)	
Predictor	*Outcome*	*B*	*p*	*OR*	*Lower Bound*	*Upper Bound*
Age	Live Dead	-0.099 0.211	0.379 0.095	0.906 1.235	0.727 0.964	1.123 1.582
Gender	Live Dead	-0.667 -0.754	0.016* 0.015*	0.127 0.471	0.298 0.256	0.885 0.865
Bodyweight	Live Dead	0.036 0.035	0.009** 0.016*	1.036 1.036	1.009 1.007	1.064 1.067
History high blood pressure	Live Dead	-0.031 0.415	0.91 0.164	0.970 1.515	0.570 0.845	1.650 2.717
History diabetes	Live Dead	0.641 0.313	0.053 0.382	1.898 1.368	0.992 0.678	3.633 2.761
History high blood cholesterol	Live Dead	-0.936 -0.209	0.014* 0.582	0.392 0.812	0.186 0.385	0.827 1.711
Stroke type	Live Dead	0.168 0.445	0.394 0.032*	1.182 1.506	0.804 1.038	1.738 2.346
RBS category on admission	Live Dead	-0.128 0.409	0.342 0.292	0.880 1.505	0.428 0.703	1.808 3.220

**Variance is significant at the 0.01 level (2-tailed), * Variance is significant at the 0.05 level (2-tailed), RBS-Random blood sugar.

Discussion

This research study evaluated the relationship between blood sugar levels on admission and acute ischemic stroke outcomes. There was a significant correlation between on-admission RBS and stroke disability at the time of discharge. Our finding is compatible with the study outcome by Yao M. et al[19] which demonstrates a significant association between elevated FBG after stroke and poor functional outcome in studied patients. Moreover, the GLIAS study demonstrated that hyperglycaemia on admission is a common characteristic in acute stroke involving more than 50% of patients and it affects all stroke subtypes.[20] The mechanism of increased disability may be due to hyperglycaemia causing larger infarct size due to decreased tissue perfusion and increased infarct volume described by Yip PK. et.al and Quast MJ. et al.[21,22]

Most stroke victims in this study were females (N=247, 63.5%) with a mean age of 69 years. This contrasts with the findings in a larger study done in the Colombo district, which reported a mean age of 44.2 years and a 2:1 male to female ratio.[2] The disparity may be due to district variability as Colombo is more urban than Kandy or due to the different sample sizes. Furthermore, the World Bank reports that the females of Sri Lanka have a higher life expectancy (80 years) than males (73 years), considering the age of participants, which may be the reason for a higher number of females with stroke than males in this study.[23]

One hundred sixteen diabetic patients in our study had a mean blood glucose level of 212.92mg/dl (±97.28) compared to 150.78mg/dl (±53.63) in the non-diabetes group (N=272). However, there was no significant association between the diabetes group and stroke mortality outcome at 30 days. The study finding was compatible with a study by Xue W-Y, et al. which also showed high blood glucose levels on admission in diabetic patients had no significant predictive value for functional outcome and mortality.[6]

There are many strengths in our study. This research was conducted at NHK, Sri Lanka which is a large tertiary care centre in Sri Lanka. The study used validated questionnaires and standard tools such as NIHSS and mRS. The sampling method was systematically designed and a well-trained researcher with a research assistant participated in data collection to minimise error.

However, this study has a few limitations. The availability of HbA1C data was limited due to a lack of resources in the clinical setting. Therefore, the data for overall control of patients' blood sugar levels were not used in the analysis. Furthermore, measurement of NIHSS and mRS at 30 days were carried out solely by interviewing patients and assuming it gives an approximate value to direct observation or examination. During the data analysis, the statistical methods we used were challenged by the reduced sample size by increasing dropouts at 30 days. However, alternative statistical methods such as the "Fisher's test" were used to minimise errors.

The outcome of this study opens more research avenues to discuss further the role of blood sugar as an important risk factor for prevention and early identification of poor stroke outcomes. Furthermore, in the situation of the increasing burden of stroke worldwide, this research gives another approach to reducing healthcare costs and improving quality of life by identification of hyperglycaemia on early admission.[24]

Conclusion

This study shows that high RBS levels on admission with acute stroke are associated with unfavourable neurological and functional outcomes on discharge. The study also expands the knowledge regarding the association between independent stroke risk factors which may increase morbidity and mortality following stroke. The evidence provided in the study highlights the place of blood glucose control in the event of acute stroke care which could have an impact on the neurological outcome and quality of life for patients.

Author declaration

Conflict of interest

There are no conflicts of interest. The study was self-funded.

Ethics approval and consent to participate

Ethical clearance was obtained from the Research and Ethics Review Committee of National Hospital Kandy (Ref: THK/ERC/19/2019). Informed written consent was obtained before the collection of data.

Author contribution

TNS study design, project implementation, data collection, data analysis, and preparation of the manuscript. AS: study design, project implementation, data analysis, and preparation of the manuscript. SE: study design and data analysis. SA: study design, project implementation, and data analysis.

Acknowledgments

We thank the staff of the medical wards of Teaching Hospital Kandy for their support during the study period. The research assistants Disna Rathnayake, Ayesha Medagedara, and H.G. Naduni Erandika contributed to the data collection and consolidation.

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