

Increased Blood Glucose Level At Admission is A Predictor of Poor Functional Outcome in Cases of Stroke.

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Abstract

Background: The role of inflammation in the pathogenesis of ischemic and haemorrhagic stroke has been well established. We studied the prognostic value of blood glucose level in determining the functional outcome 28 days following stroke.

Method: 205 cases of acute stroke confirmed by CT were evaluated for blood glucose on admission. Functional outcome was determined after a 28 day period by the modified Rankin scale.

Results: A higher blood glucose found in patients of ischemic stroke ($p < 0.002$) and haemorrhagic stroke ($p < 0.001$) was associated with poor functional outcome after a 28 day period.

Conclusion: Blood glucose level can be used to assess the clinical severity following both ischemic and haemorrhagic-stroke.

Keywords: stroke, haemorrhagic, ischemic, glucose, inflammation

I. Introduction

Stroke has often being highlighted as the 3rd highest cause of mortality¹, but little is known about the burden of the disease on survivors in developing countries.

The need for better planning of care of stroke survivors is being realized now more than ever. Recently, neurologists have started to identify the need of markers to reliably predict prognosis promptly following stroke.

Keeping the need of easily available, inexpensive and expedient markers in mind, peripheral markers, such as blood glucose level are now being considered.

How inflammation is involved in the pathogenesis of ischemic stroke is now being extensively studied. An increasing body of evidence has suggested that early inflammation is an important factor contributing to unfavourable prognosis following stroke². This has been attributed to elevated levels of triglyceride rich lipoproteins and increased plaque volume in stroke patients with elevated acute phase reactants³. The Insulin Resistance Atherosclerosis Study⁴ found an association between acute inflammatory markers and insulin resistance, suggesting chronic subclinical inflammation as a part of insulin resistance syndrome.

On the other hand, the role of inflammation in intracerebral haemorrhage (ICH) is a poorly understood issue. Statistical evidence indicate that inflammatory processes play a role in the severity of ICH induced brain injury⁵. A small number of studies report the association of inflammatory markers and mortality following ICH, but there is limited data on the effect of this inflammation on functional outcome^{6,7}.

This study was performed to assess the role of blood glucose in stroke and its association with clinical severity.

II. Objectives

To study the association of blood glucose levels with clinical severity following stroke.

III. Methods

This prospective cross-sectional study was conducted in AVBRH, 1300 bedded rural hospital in central India. This patient population fairly represents the disease pattern in this region. Consent was taken from the hospital institutional ethical committee. Written informed consent was obtained from all patients or from a relative. From the period of January 2013 to December 2014, all patients admitted to the hospital with a diagnosis of acute stroke were included and data was collected in a prospective manner for routine inflammatory markers.

Case definition:

Acute stroke was defined as rapidly developing clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin.⁸

Neuro-radiological diagnosis: The diagnosis of stroke was confirmed by CT scan performed within 24 hours after admission and patients diagnosed with brain infarction (ischemic stroke) or brain haemorrhage (intracerebral haemorrhage) according to the Stroke Data Bank Subtype Classification were studied ⁹.

Exclusion criteria: Patients with ICH secondary to trauma, or any secondary haemorrhage including cerebral aneurysms and tumours. Patients diagnosed with subarachnoid haemorrhage following CT scan. Diabetic patients.

Blood Glucose: Venous blood samples collected before the administration of fluids and blood glucose level was estimated. Diabetic patients were excluded based on the following criteria: past history of diabetes, or random blood glucose level of >200mg/dl, or patients on hypoglycaemic agents. ¹⁰

Clinical Evaluation: Improvement in clinical severity was evaluated at 28 days following admission. Patients who were discharged before 28 days were called to the OPD for follow up. The severity of clinical features was graded by the modified Rankin Score. The scale graded from 0-6, from perfectly healthy asymptomatic patients to death. ¹¹ Patients were divided into two groups based on the degree of impairment. Patients without significant impairment (i.e. ≤ grade 2 on mRS) were classified as group A. Those with significant impairment (i.e. > grade 2 in mRS) were classified as group B.

Statistical Analysis: Normally distributed baseline characteristics were compared with Student's t-tests, from which p value was calculated.

IV. Results

In the 2 year period, there were a total of 243 confirmed cases of stroke. Consent could be obtained from 240 of these cases. 21 patients with history of diabetes mellitus were excluded from the study, as was 1 patient diagnosed with a subarachnoid haemorrhage following CT. Blood was drawn from 218 patients at the time of admission. 3 patients were diagnosed with diabetes mellitus after review of reports of the blood analyses. There was 1 death at the time of admission and 2 deaths due to complications arising from stroke (recurrent stroke and infection) within 28 days following admission.

The functional outcome at 28 days was assessed in 205 patients. The mean delay between the time of admission and drawing blood sample was 3 hours.

The mean age was found to be 60±8. Mean age for males was 57±5 and females was 63±3 years. Males constitutes 65% (n=133) of the cases, whereas the females were 35% (n=72).

The diagnosis of stroke was confirmed by CT and subtyping was done according to stroke data bank criteria in 205 patients. The diagnosis of ischemic stroke was made in 78% of the patients (n=160). Haemorrhagic stroke accounted for 22% of the cases (n=45). Table 1 summarizes the distribution of patients based on subtypes.

	Ischemic stroke		ICH	
	N	%	N	%
Male	106	51.7	27	13.3
Females	54	26.3	18	8.7
Total	160	78%	45	22%

Table 1: Frequency and percentage of stroke subtypes

Blood glucose level was measured at admission. After a 28 days post admission follow up, degree of clinical impairment was determined using the mRS scale. Out of the 205 patients that were assessed clinically, 112 (55%) had good functional outcome (mRS score ≤2) and 93 (45%) had poor functional outcome (mRS score >2). The relationship between blood glucose and the degree of clinical impairment was studied.

As illustrated in Table 2, for both ischemic stroke and ICH patients, the mean blood glucose at admission was higher in group B patients (with significant clinical impairment at day 28) compared to group A patients. This difference was statistically significant for both stroke subtypes.

mRS at day 28 Stroke subtype	score	Group A (mRS score \leq 2)	Group B (mRS score $>$ 2)	P value
Ischemic Blood glucose (mg/dl)	stroke	121 (22.1)	177.2 (23.2)	0.002
ICH Blood glucose (mg/dl)		128 (22.5)	174 (11.9)	0.001

Table 2: Glucose level at admission and degree of clinical impairment in different stroke subtypes

Ischemic stroke patients with significant clinical impairment at day 28 (group B patients) had a mean blood glucose (mg/dl) was 177.2 ± 23.2 (p 0.002). Whereas, ICH patients with significant clinical impairment were found to have an admission mean blood glucose value (mg/dl) of 174 ± 11.9 ($p=0.001$).

V. Discussion

In a 24 months period, there were a total of 205 cases of diagnosed acute stroke evaluated for this study. Out of these, the most common subtype was found to be ischemic stroke (78%) followed by ICH (22%) (table 2). This distribution is similar to those found in stroke registries of other parts of country as cited in Trivandrum Stroke Registry¹² and that of western countries^{13,14}, but lower as compared to other parts of Asia¹⁵. This can be attributed to ethnic differences owing to a predominantly Chinese population in the other studies.

The average age of the patients was found to be 57 ± 8 years. This is similar to results obtained from other studies in Middle East and East Asia¹⁶, but lower than that of reported in the western world¹⁷. This could be explained by the lower life expectancy in the developing countries compared to the western world¹⁸.

The male: female ratio was 3:1. Male predominance is particularly seen in the age group of 60-70 years, but a female predominance exists in age group above 70 years, probably due to the lower life expectancy and earlier death in men, and the protective effect of oestrogen in females. These findings are consistent with other reports^{19,20}.

Several studies support the conclusion that increase in inflammatory markers in the acute phase following stroke are associated with poor outcome²¹⁻²⁵. The link between high admission blood glucose and hematoma expansion as well as high inflammatory markers and poor functional outcome in ICH patients has also been established^{26,27}. We have discussed the role of the blood glucose level in the clinical outcome following both ischemic and haemorrhagic stroke.

We found a significant increase in RBS measured on admission in patients with worse neurological outcome at 28 days for patients with ischemic stroke (table 2). These findings are consistent with several studies that suggest a worse prognosis in non-diabetic hyperglycaemic patients, compared to normoglycemic patients²⁸. Murros et al found that FBS in non-diabetics strongly correlated with the severity of hemiparesis and predicted poorer outcome²⁹. Likewise, Candelise et al found a correlation between RBS and both functional score and size of lesion on CT³⁰. A large prospective study in Hong Kong showed a positive correlation between admission glucose level and neurological outcome. However, no such correlation could be established in ICH patients³¹. Cox and Lorain reported acute hyperglycaemia to be more important than diabetes mellitus in determining prognosis in stroke patients³².

In contrast, there is also evidence denying any prognostic significance of acute hyperglycaemia after stroke^{33,34}. Furthermore, Toni et al suggested a variable influence of acute hyperglycaemia on ischemic stroke depending on pattern of residual flow after arterial occlusion³⁵.

Studies conducted to relate poor functional outcome with higher RBS at admission in ICH patients have shown mixed results. On one hand, the value admission hyperglycaemia in predicting increased risk of mortality following ICH has been documented^{26,36,37}. Conversely, conclusions drawn by Tuhin et al, and Tetri et al contradict this finding^{38,39}. We found that higher glucose on admission in non-diabetic patients is significantly associated with poor functional outcome at 28 days in ICH patients. These findings can be justified by experiments that have proven that the acute stress hyperglycaemia following stroke increases tissue lactic acidosis which impairs post infarction recovery⁴⁰.

VI. Conclusion

Blood glucose level at admission can be used to predict the functional outcome in stroke patients. A higher level blood glucose was associated with poor functional outcome in patients of ischemic stroke and haemorrhagic stroke. Current management guidelines of ICH patients are based on decreasing BP and hematoma size, and have shown no decrease in mortality or morbidity. Easily measurable variables can be used to predict morbidity following stroke and provide more accurate information to patients. Further studies need to be done to study neuroinflammation as a potential target of treatment in the management of stroke.

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