

# Assessment of Capillary Blood Glucose Levels as a Prognostic Indicator in Acute Ischemic Stroke

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## ABSTRACT

### BACKGROUND

Acute Stroke is an abrupt onset of a neurological deficit attributable to a focal vascular cause. The diagnosis of stroke is based on clinical examination, and brain imaging. Cerebral ischemia is caused by a reduction in blood flow lasting longer than several seconds with manifestation of neurologic symptoms due to infarction or death of brain tissue because neurons utilise only glucose and lack glycogen stores, so energy failure is rapid. Neurologic signs and symptoms lasting for >24 hours or brain infarction demonstrated on brain imaging is known as Acute Stroke.<sup>[1]</sup> Abnormal blood glucose at the time of acute stroke is associated with poor clinical outcomes, longer in-hospital stay and mortality. We wanted to evaluate the influence of abnormal capillary glucose levels on functional outcomes by grading the Acute Ischemic Stroke patient on modified Rankin scale.

### METHODS

This cross sectional study was conducted for a period of 6 months in the medicine and neurology wards, ICU in a tertiary care rural hospital in central India and included a total of 35 patients after obtaining institutional ethical committee clearance. The capillary blood glucose samples were taken using a standard glucometer. Capillary blood glucose was determined at the time of admission, each day within the first 72 hrs. Two values of blood glucose were considered; admission value and max. value within the 1<sup>st</sup> 72 hrs. Functional prognosis was assessed on Modified Rankin scale at the time of discharge or 1 month. The categorical variables were assessed using chi-square test and odd's ratio and p-value were calculated and assessed. The association of altered capillary glucose levels with functional outcomes on modified Rankin scale were analysed. The data were entered in excel spreadsheet and all the statistical analysis was conducted using STATA version 14.2 software.

### RESULTS

A significant correlation between the higher admission capillary blood glucose levels with the outcomes on modified Rankin scale after 1 month or after discharge was found (p=0.0032). Hyperglycaemia at the time of admission with poor prognosis on mRS (p-value 0.007) was also found.

### CONCLUSIONS

The results of the study reveal that the patients with admission hyperglycaemia have poor prognosis as compared to the normoglycemic patients. There is a significantly positive correlation between the altered capillary blood glucose levels at the onset of stroke and functional prognosis of the patients with stroke after treatment.

### KEY WORDS

Normoglycemia, Hyperglycaemia, Neurological, Modified Rankin Scale

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## BACKGROUND

Cerebral ischemia is caused by reduction in blood flow lasting for more than few seconds and rapid manifestation of neurologic symptoms because neurons utilise only glucose, and lack glycogen stores leads to rapid energy failure. According to the World Health Organisation, 15 million people suffer stroke worldwide each year. Of these, 5 million die from stroke making it the second most leading cause of death worldwide and another 5 million are permanently disabled. There was a rapid increase in the deaths due to stroke after year 2000 by 830,000/year. Although the incidence is declining among the affluent countries due to efforts to reduce Blood pressure and smoking. But it is rising among those with less access to medical care and overall incidence is also increasing due to ageing of the population. The Region having maximum prevalence and mortality is the south-eastern US. Stroke is becoming important cause of premature death and disability in low income countries like India driven by demographic changes and enhanced by increasing prevalence of key modifiable risk factors. India is facing transition in demographic, economic, epidemiology and health facilities resulting in increase in life expectancy and thus increase in ageing population.

The incidence of stroke ranged from 105 to 152/100,000 persons per year, and the crude prevalence of stroke ranged from 44.29 to 559/100,000 persons in different parts of the India in the past decade. Mechanisms contributing to exacerbated neurovascular injury and poor outcomes are not completely understood. Hyperglycaemia during Acute Stroke may impair Thrombolysis and Reperfusion. The reperfusion injury includes oxidative stress, leukocyte infiltration, mitochondrial mechanisms, platelet activation and aggregation, complement activation, and blood-brain-barrier (BBB) disruption, which ultimately lead to brain oedema or haemorrhagic transformation eventually causing significant neuron death and neurological dysfunction. The production of reactive oxygen species including peroxides, superoxide anions by NADPH oxidase. In mitochondria, reperfusion increases calcium influx leading to cell swelling, ATP deficiency thus causing cell necrosis. Abnormal glucose levels increases coagulation by increasing thrombin production and stimulating the tissue factor pathway. It reduces the fibrinolytic activity of tissue plasminogen activator (TPA) used in treatment of acute stroke by increasing the production of plasminogen activator inhibitor (PAI)-1.<sup>[2],[3]</sup> Abnormal capillary glucose levels during acute brain ischemia accelerate pathologic processes involved in ischemic brain injury and also increase the risk of cerebral haemorrhage in acute stroke patients treated with intravenous tPA.<sup>[4]</sup> Even though the exact association has not yet been established but it is recommended to control and maintain the glucose levels in acute Stroke patients.

The purpose of the study was to evaluate the prognostic utility of capillary blood glucose level at the time of presentation and persistent abnormal levels for up to 72 hrs. in patients with acute ischemic stroke. It is known that post stroke hyperglycaemia is common and prolonged. The understanding of this relationship would facilitate planning the policies and programmes for primary prevention of stroke and also address the stroke related disability in India. Due to disabling nature and epidemic of stroke in country

expects better rehabilitation by health care facilities. Despite the current guidelines based treatment; the potential contribution of hyperglycaemia to exacerbation of stroke is still unclear. This study will explore the outcome of ischemic stroke patients with admission and post 72 hours hyperglycaemia.

### Aim

To evaluate the influence of abnormal capillary glucose levels on functional outcomes of the acute ischemic stroke patients by grading the patient on modified Rankin scale and adjusting for other known prognostic factors.

### Objectives

1. To measure the capillary blood glucose level in acute stroke patients at the time of presentation to the tertiary care hospital and each day for the next 72 hrs.
2. To grade and compare the functional outcomes in hypoglycaemic, normoglycemic, hyperglycaemic subjects on the modified Rankin scale at the time of discharge OR 1 month whichever was earlier.

## METHODS

The cross sectional study was conducted after approval from institutional ethics committee on 35 patients diagnosed of acute ischaemic stroke clinically in which neurologic signs and symptoms lasted for >24 h or brain infarction demonstrated on computed tomography according to American stroke association guidelines,<sup>[5]</sup> followed up and treated in medicine and neurology OPD, wards and ICU in the tertiary care rural hospital for 6 months from April 2019 to September 2019. Data was collected in 5 months' duration. Finger prick capillary blood glucose was determined at admission and once each day for 1st 72 hours. Two values of blood glucose were considered; admission value and maximum value within the 1st 72 hrs. Outcome was graded and evaluated at the time of discharge or after 1 month whichever was earlier on Modified Rankin scale.<sup>[6]</sup> Scores on mRS were compared in hypoglycaemics, normoglycaemics and hyperglycaemics.

### Inclusion Criteria

1. Acute ischaemic stroke patients >24 hours irrespective of gender and age according to American Stroke Association criteria.
2. Patients willing to participate in the study.

### Exclusion Criteria

1. Patients with Transient ischaemic attack (TIA), Coma at admission, prior functional dependency with modified Rankin grade >2, concomitant disease with life expectancy less than 3 months were excluded from the study.
2. Patients with haemorrhagic stroke were excluded from the study.

- Subjects not willing to participate were also excluded from the study.

Informed consent was taken from all the study participants.

**Data Collection Procedure**

The subject's relatives were well explained about the nature and the purpose of study. After assuring the confidentiality and informed consent, the details of the subjects were entered in the data forms. Patient's pro-forma including demographic particulars, past medical and surgical history to rule out other compounding causes and factors affecting the functional outcome of stroke. History of other risk factors such as hypertension, diabetes mellitus, hypercholesterolaemia, heart diseases, symptomatic peripheral vascular disease, renal disease, obesity and cigarette smoking was collected by interviewing the patient by the physician. At the time of admission a finger prick capillary blood glucose levels (mg/dL) using standard glucometer, blood pressure (mmHg), temperature (°C) and Stroke severity (Canadian Neurologic Scale) was measured in the patients diagnosed with the acute ischemic stroke on admission and once each day during the first 72 hours. For the analysis, 2 values were considered regarding the capillary glucose levels (admission values and the maximum capillary glucose levels within the first 72 hours). The modified Rankin scale<sup>[7,8]</sup> was used to evaluate the outcome of the patients at the time of admission, at discharge OR after 1 month. Dichotomization (mRS<2= good outcome and mRS>2 is poor outcome) was considered for evaluation. For the study, capillary blood glucose levels <84 mg/dL were considered hypoglycaemic,<sup>[9-10]</sup> >140 mg/dL as hyperglycaemic according to American Diabetes Association.<sup>[11]</sup>

Determining the capillary blood glucose levels- Finger prick capillary blood was used for analysis using all the aseptic precautions. Capillary blood glucose was determined by Accu-Chek active glucometer using the same reagent strips. Patients were classified as hyperglycaemic, normoglycemic or hypoglycaemic according to American Diabetes Association scale. Patients were compared with regards to blood glucose levels and outcomes on mRS.

**Quality Control**

Quality control of the data management was maintained throughout the study. Following quality control measures were undertaken-

- Early involvement of local research support unit.
- We tried to adhere to the protocol.
- Data from the patients were concealed by statistician.

**Ethical Approval**

The study was started after approval from the institutional ethics committee (IEC) vide letter IEC/2019/8005.

**Statistical Analysis**

The categorical variables were assessed using chi-square test and odd's ratio were calculated and assessed. The association

of capillary glucose levels with Functional outcomes on modified Rankin scale were analysed. Analysis was conducted using intention to achieve better functional reversal rate in patients. The data were entered in excel spreadsheet and all the statistical analysis was conducted using STATA version 14.2 software.

**RESULTS**

The study was conducted in medicine and neurology OPD, wards and ICU in the tertiary care rural hospital for 6 months from April 2019 to September 2019.

Canadian Neurologic Scale	Hypoglycaemic			P-Value	Hypoglycaemic vs Normoglycaemic		P-Value	Hyperglycaemic vs Normoglycaemic		P-Value
	Hypoglycaemic	Normoglycaemic	Hyperglycaemic		Odds Ratio (95% CI)	Odds ratio (95% CI)				
<9	0	2	13	0.7655	0.6(0.02091 to 17.2198)	0.0065	81(3.4197 to 1918.6038)		0.0006	
9-12	2	6	3	0.8928	1.1667(0.1238 to 10.9909)	0.1928	8.0769(0.3482 to 187.335)			
>12	2	7	0		1		1			

*Table 1. Comparison of Canadian Neurologic Scale with the Capillary Blood Glucose Values at the Time of Admission*

At the time of admission, out of 35 patients, 16 were found to be hyperglycaemic, 15 were normoglycemic and 4 were hypoglycaemic. Out of 16 hyperglycaemic, 13 scored <9 on CNS implicating severe stroke. And out of 15 normoglycemic, 7 and 6 patients obtained good and intermediate scores respectively on CNS. Hyperglycaemics with score <9 on CNS obtained a p-value of 0.0065 and as a whole p-value of 0.0006 which are significant.

Canadian Neurologic Scale	Hypoglycaemic			P-Value	Hypoglycaemic vs Normoglycaemic		P-Value	Hyperglycaemic vs Normoglycaemic		P-Value
	Hypoglycaemic	Normoglycaemic	Hyperglycaemic		Odds ratio (95% CI)	Odds ratio (95% CI)				
<9	0	0	15	0.3012	13(0.1005 to 1680.9442)	0.0039	34.3333(4.8124 to 3749.7985)		0.0002	
9-12	0	4	9	0.8605	1.4444(0.02394 to 87.1699)	0.0352	13.5(1.1973 to 152.2181)			
>12	0	6	1		1		1			

*Table 2. Comparison of Canadian Neurologic Scale with the Maximum Capillary Blood Glucose Values within 72 Hours of Stroke*

Maximum capillary blood glucose levels within the 72 hours of admission were assessed on CNS. Out of 35 patients, 25 were found to be hyperglycaemic at some point within 72 hours out of which 15 scored <9 (severe) and 9 scored between 9-12 (intermediate severity) on CNS at the time of hyperglycaemia with a significant p-value of 0.0039 and 0.0352 respectively.

**DISCUSSION**

The study was undertaken to assess the association of the admission capillary blood glucose levels and 48-72 hours' capillary glucose levels with the severity of stroke (on Canadian neurologic scale)<sup>[12]</sup> and outcome after 1 month or discharge (on modified Rankin scale). Study comprised of 35 patients including 26 males (74.29%) and 9 females (25.71%).

All patients were between the age-group of 45-82 yrs. A significant positive co-relation between the severity of stroke (as on Canadian neurologic scale) with the altered admission capillary blood glucose levels (p-value 0.0006) and 72-48 hours capillary blood glucose levels (p-value 0.0002) was established. Significance of hyperglycaemia at the time of admission with poor score on CNS (p-0.0065) and hyperglycaemia within 48-72 hours with poor (p-value 0.0039) and intermediate scores (p-value 0.0352) was observed.

A significant co-relation between the altered admission capillary blood glucose levels with the outcomes on modified rank in scale after 1 month or after discharge (p-value 0.0032) and hyperglycaemia at the time of admission with the poor prognosis on mRS (p-value 0.007) was established. However, there was no significant co-relation between the 48-72 hours capillary blood glucose levels with the functional outcome on mRS (after 1 month or at the time of discharge). Similar findings were seen in other studies.<sup>[13-15]</sup>

There are several reasons or hypothetical theories that can justify the findings of our study. Hyperglycaemia during acute stroke impairs thrombolysis and reperfusion. Abnormal glucose levels increases coagulation by increasing thrombin production and stimulating the tissue factor pathway. It reduces the fibrinolytic activity of tissue plasminogen activator (TPA) used in treatment of acute stroke by increasing the production of plasminogen activator inhibitor (PAI)-1. Abnormal capillary glucose levels during acute brain ischemia are associated with poor prognosis.<sup>[16,17]</sup>

The prevalence of stroke is increasing in hypertensive patients and rapidly acquiring a status of rapid epidemic in India. The study can be of clinical relevance in future and can greatly enhance the knowledge in regards of understanding the altered capillary blood glucose levels in pathogenesis of microvascular complications leading to poor functional outcomes during recovery. It also helps us determine the association between capillary blood glucose levels and prognosis.

By maintaining the blood glucose levels we can prevent the onset of stroke in hypertensive and diabetic patients and also improve the prognosis in the stroke patients. This study can be of help to physicians to assess and monitor the blood glucose levels to prevent the development of microvascular complications and further improving the functional outcome in the patients. This study has some limitations. Although the patients were adjusted for the factors affecting the stroke outcome, but Patients were not characterised according to stroke complications.

Modified Rankin Scale	Hyperglycaemic	Normoglycaemic	Hyperglycaemic	P-Value	Hyperglycaemic vs Normoglycaemic	P-Value	Hyperglycaemic vs Normoglycaemic	P-Value
					Odds ratio (95% CI)		Odds ratio (95% CI)	
<2 OR Equal to 2	4	9	2		1	1		0.0032
>2	1	5	14	0.5228	0.45(0.03887 to 5.2091)	0.007	12.6(1.9985 to 79.4391)	

**Table 3. Comparison of Modified Rankin Scale (at 1 Month or Discharge) with the Admission Values of Capillary Blood Glucose**

Admission capillary blood glucose values were compared with functional outcome of patients on mRS. Out of 35 patients, 16 were hyperglycaemic with 14 of them being graded as poor outcome on mRS scale (p-value-0.007) and 5 were hypoglycaemic with 4 of them being graded as poor outcome on mRS. For both hyper and hypoglycaemics the p-value was found to be 0.0032 which is significant. Altered admission capillary blood glucose levels are associated with poor prognosis on mRS.

Modified Rankin Scale	Hyperglycaemic	Normoglycaemic	Hyperglycaemic	P-Value	Hyperglycaemic vs Normoglycaemic	P-Value	Hyperglycaemic vs normoglycaemic	P-Value
					Odds ratio (95% CI)		Odds ratio (95% CI)	
<2 OR Equal to 2	0	5	7		1	1		0.1791
>2	0	3	18	0.8307	1.5714(0.02495 to 98.9631)	0.0889	4.2857(0.8014 to 22.9178)	

**Table 4. Comparison of Modified Rankin Scale (at 1 Month or Discharge) with the Maximum Value of Capillary Blood Glucose in 72 Hours of Stroke Onset**

There was no significant relationship between the 72 hours capillary blood glucose levels with the functional outcome on mRS (after 1 month or at the time of discharge).

### CONCLUSIONS

Patients with admission hyperglycaemia have poor prognosis as compared to the normoglycemic patients. There is a significant positive correlation between the altered capillary blood glucose levels at the onset of stroke and functional outcome of the patients with stroke after treatment.

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