## **Original research article**

# To investigate the clinical outcomes of hyperglycemic ischemic stroke patients

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#### Abstract

**Background and Objective:** Cerebrovascular accidents are the most prevalent and significant neurological illnesses affecting adults. The objective of this study was to assess the random blood glucose levels during the initial stage of ischemic stroke in individuals with diabetes and those without diabetes. Additionally, the severity and prognosis of both diabetic and non-diabetic patients were examined in connection to hyperglycemia.

**Material and Methods:** A study was conducted on a cohort of 40 patients diagnosed with acute ischemic stroke who were hospitalized to the Department of General Medicine, Great Eastern Medical School and Hospital, Andhra Pradesh, India. The study period spanned from June 2017 to June 2018.

**Results:** The majority of our 40 patients were male, consistent with the male preponderance reported in the vast majority of research. Fifteen of the patients were between the ages of 51 and 60, making up the largest age group. Twenty-two of the 40 patients had high blood pressure, twenty-four had diabetes, 29 had high cholesterol and a history of a heart attack, and one female patient had atrial fibrillation. About half of the male patients had a previous history of alcoholism, and over two-thirds had smoked cigarettes. The right side was weak in 36 cases, whereas the left side was weak in 24.

**Conclusion:** During the intervening period, it is advisable to prioritize the implementation of effective stroke treatment strategies, as well as the restoration of normal body temperature, maintenance of fluid balance, and optimization of hemodynamics. Failure to do so may potentially compromise the positive prognosis, even in patients with normal blood sugar levels.

Keywords: clinical outcomes, hyperglycemic, ischemic stroke

#### Introduction

Stroke is a prominent contributor to mortality rates and the occurrence of chronic impairment in the Indian population. Stroke is a significant contributor to premature mortality and disability in low- and middle-income nations such as India. This is primarily influenced by shifts in population demographics and exacerbated by the rising frequency of modifiable risk factors <sup>[1, 2]</sup>.

Cerebrovascular accidents (CVAs) are the most prevalent and significant neurological illnesses affecting adults. Approximately 50% of neurological illnesses observed in general hospitals can be attributed to stroke. Cerebrovascular accident encompasses various conditions, including ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysm, arteriovenous malformation, and cortical venous thrombosis. Stroke is the second leading cause of mortality among non-communicable disorders, following heart disease <sup>[3, 5]</sup>.

The implementation of efficacious hypertension medication has resulted in a notable decrease in the incidence of stroke. The presence of diabetes mellitus is a significant risk factor in the development of stroke due to its relationship with both microvascular and macrovascular diseases. The majority of individuals diagnosed with diabetes who also experience a stroke exhibit elevated levels of glycosylated hemoglobin, suggesting that a significant proportion of these patients have poorly managed diabetes. Individuals with diabetes and stress-induced hyperglycemia are prone to experiencing massive strokes, which often lead to unfavorable outcomes. The incidence of stroke is twice as high in individuals with diabetes compared to those without diabetes <sup>[6, 8]</sup>.

Hypertension frequently coexists with diabetes and contributes to the progression of atherosclerosis, hence facilitating the development of intracranial small vessel disease and heart disease, which in turn increase the likelihood of lacunar and embolic infarction, respectively. Multiple risk factors contribute to the prognosis of stroke. Hyperglycemia, fever, and neuroprotective drugs are extensively investigated topics within the academic community <sup>[9, 11]</sup>.

The objective of this study was to assess the random blood glucose levels during the initial stage of

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ischemic stroke in individuals with diabetes and those without diabetes. Additionally, the severity and prognosis of both diabetic and non-diabetic patients were examined in connection to hyperglycemia.

#### **Materials and Methods**

A study was conducted on a cohort of 40 patients diagnosed with acute ischemic stroke who were hospitalized to the Department of General Medicine, Great Eastern Medical School and Hospital, Andhra Pradesh, India. The study period spanned from June 2017 to June 2018.

### **Inclusion Criteria**

- Patients must be older than forty.
- This is the patient's first expected cerebrovascular accident.
- Blood sugar measured within 24 hours after the stroke started

#### **Exclusion Criteria**

- Patients admitted following a stroke lasting twenty-four hours
- Patients who had intravenous glucose administered either prior to or during the research period
- It was not possible to find patients with trustworthy diabetes information.

#### Results

In our study with a sample size of 40 patients, it was observed that a significant proportion of the participants were male, indicating a prevalent male preponderance as often observed in several investigations. The majority of the patients, specifically fifteen individuals, fell within the age range of 51 to 60. Out of the total sample size of 40 patients, it was found that 32 individuals exhibited symptoms of hypertension, 34 individuals were diagnosed with diabetes, 29 individuals experienced hypercholesterolemia, 3 individuals had a documented history of myocardial infarction, and a single female patient presented with atrial fibrillation. A majority of the male patients, namely over two-thirds, reported being smokers, while over half of them had a documented history of alcohol consumption. A total of 36 individuals had symptoms of right-sided weakness, while 24 patients presented with left-sided weakness.

Table 1: Gender wise distribution

Sr. No.	Gender	Frequency	%
1.	Male	30	75.0
2.	Female	10	25.0
3.	Total	40	100.0

Table 1 presents the distribution of patients employed in the study according to gender. Out of the total sample size, 30 individuals were identified as males, while 10 individuals were identified as females.

Т	able 2:	Age wise	distribution	
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Sr. No.	Age (Years)	Frequency	%
1.	40-50	08	20.0
2.	51-60	10	25.0
3.	61-70	10	25.0
4.	71-80	12	30.0
	Total	40	100.0

Table 2 presents the age-wise distribution of the patients included in the study. The majority of patients fell into the age groups of 71-80 and 51-70, showing that these age ranges were the most prevalent among the study participants.

Table 3: Hypertension

## **Risk factors**

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Sr. No.	Yes/No	Frequency	%
1.	No	18	45.0
2.	Yes	22	55.0
	Total	40	100.0

Table 3 presents the patient cohort utilized in the investigation, consisting of 18 individuals diagnosed with hypertension and 22 individuals without hypertension.

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Sr. No.	Yes/No	Frequency	%
1.	No	16	40.0
2.	Yes	24	60.0
	Total	40	100.0

Table 4 presents the data on patients included in the study, namely those diagnosed with diabetes mellitus. Out of the total number of patients, 24 individuals had diabetes mellitus, while 16 individuals did not have this condition.

Гable	5:	Dyslipidemia	a
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Sr. No.	Yes/No	Frequency	Percent
1.	No	11	27.5
2.	Yes	29	72.5
3.	Total	40	100.0

Table 5 provides the data pertaining to the employment status of patients included in the study, specifically focusing on individuals with Dyslipidemia. Out of the total sample size, 29 patients were identified as having Dyslipidemia, while 11 patients did not exhibit this condition.

Table 6: Smoker

Sr. No.	Yes/No	Frequency	%
1.	No	24	60.0
2.	Yes	16	40.0
3.	Total	40	100.0

Table 5 summarizes the data pertaining to the employment status of patients included in the study, specifically focusing on individuals with Dyslipidemia. Out of the total sample size, 29 patients were identified as having Dyslipidemia, while 11 patients did not exhibit this condition.

#### Discussion

In our investigation with a sample size of 40 patients, a significant proportion of the participants were identified as male, indicating a prevailing male predominance. This observation aligns with the findings often reported in similar studies. The majority of the patients, specifically fifteen individuals, fell within the age range of 51 to 60 years. Out of the total sample size of 40 patients, 22 individuals were diagnosed with hypertension, 24 individuals had diabetes, 29 individuals had hypercholesterolemia, one individual had a previous history of myocardial infarction, and there was one female patient who presented with atrial fibrillation. A majority of the male patients, namely over two-thirds, reported being smokers, while over half of them had a documented history of alcohol consumption. A total of 36 individuals had symptoms of right-sided weakness, while 24 patients presented with left-sided weakness<sup>[12, 14]</sup>.

Within our study cohort of 40 patients, it was observed that 50% of the individuals presented with increased blood glucose levels at admission, while the remaining 50% had normal blood glucose readings. A total of 32 patients were diagnosed with diabetes, while an additional 9 patients were found to have stress hyperglycemia <sup>[15, 16]</sup>. The prevalence of stress hyperglycemia was observed in about 33% of the patient population. The assessment of stroke severity was conducted using the NIH Stroke Scale. The results of the study indicate that hyperglycemic patients on admission exhibited a significantly higher score in comparison to euglycemic patients. Among the patients admitted with hyperglycemia on the day of admission. Patients with uncontrolled hyperglycemia exhibited the highest average National Institutes of Health Stroke Scale (NIHSS) score. Therefore, the presence of hyperglycemia during the occurrence of a stroke led to the manifestation of a more severe stroke <sup>[17, 18]</sup>.

The dimensions of the lesion were assessed using computed tomography (CT) imaging of the brain. The majority of patients with euglycemia exhibited small-sized infarcts, while the majority of patients with hyperglycemia on admission displayed large-sized lesions accompanied by edema and midline shift <sup>[19]</sup>. The data had statistical significance. Hyperglycemia leads to a range of detrimental effects on the brain, including heightened anaerobic metabolism, elevated brain lactate levels, reduced mitochondrial function, vascular disease, increased production of free radicals, and enhanced expression of c-fos and cox-2. These combined factors contribute to the development of severe brain injury and the formation of large-sized infarcts. Hyperglycemia has the potential to disturb the integrity of the blood-brain barrier, leading to the occurrence of significant hemorrhage and the transformation of infarcts into a hemorrhagic state. This study examined a cohort of one hundred individuals diagnosed with acute stroke, and found that patients with euglycemia had a more favorable prognosis in comparison to those who presented with hyperglycemia on the day of admission. Patients with euglycemia exhibited superior recovery outcomes following an episode of acute stroke <sup>[20, 21]</sup>.

A significant proportion of individuals classified as euglycemic demonstrated a favorable outcome in

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terms of functional recovery, with a prevalence of seventy-two percent. In contrast, it was shown that just three percent of patients with admission day hyperglycemia had satisfactory functional recovery after a thirty-day follow-up period <sup>[22]</sup>. The incidence of inpatient mortality was found to be significantly elevated among patients with hyperglycemia at admission. A mortality rate of 20 percent was seen among patients with admission day hyperglycemia within the initial thirty-day period. The early case fatality rate in euglycemic patients was found to be a mere fifteen percent. Therefore, patients with hyperglycemia on the day of admission had a threefold higher risk of early mortality in comparison to patients with normal blood glucose levels. A suboptimal outcome was observed in 38% of patients with admission day hyperglycemia, but just 3% of patients with normal blood glucose levels experienced a similar outcome <sup>[23, 24]</sup>.

The findings of this investigation, which examined a cohort of 20 individuals diagnosed with acute stroke, indicate a significant correlation between raised blood glucose levels at admission and both a heightened early mortality rate and an augmented likelihood of experiencing suboptimal functional recovery. The early death rate in the ischemic stroke group was found to be 2.07% in patients with normal blood glucose levels (euglycemic) and 14.8% in patients with elevated blood glucose levels (hyperglycemic) <sup>[25]</sup>. A suboptimal outcome was observed in 3.18% of individuals with normal blood glucose levels, but a much higher proportion of 38.3% experienced a poor outcome among those with elevated blood glucose levels. Therefore, the presence of hyperglycemia in the ischemic stroke group was found to be significantly linked with higher rates of early mortality and poorer functional outcomes. The findings of our study provide compelling evidence of a significant positive connection between the initial blood sugar level upon admission and the subsequent occurrence and severity of stroke. The occurrence of hyperglycemia upon admission to a healthcare facility has been found to be associated with heightened mortality rates and an increased likelihood of experiencing poor functional recovery <sup>[26, 27]</sup>.

In our research, we observed that patients with ischemia who presented with elevated glucose levels upon admission had a much higher early mortality rate compared to patients with normal glucose levels. Specifically, the former group faced a three and a half times greater risk of mortality during the early stages of their treatment. Comparable findings were observed in those without diabetes. Individuals with ischemic stroke who experience stress-induced hyperglycemia but do not have diabetes exhibit a 3.5-fold higher rate of early mortality compared to individuals with normal blood glucose levels. The study was unable to investigate the impact of stress on the diabetic group due to the lack of knowledge regarding the pre-stroke sugar levels <sup>[28-30]</sup>.

The research findings demonstrate a notable rise in premature mortality and suboptimal functional recuperation among individuals with diabetes and stress-induced hyperglycemia in comparison to those with normal blood glucose levels. Therefore, it is imperative to verify the enhancement in these individuals through the normalization of blood glucose levels. Numerous clinical trials are currently being conducted with the aim of enhancing the prognosis of Stroke through the normalization of blood glucose levels using human recombinant insulin. In a study conducted by Stephan M. Vinychuk and colleagues, it was demonstrated that the injection of insulin to individuals experiencing hyperglycemia resulted in enhanced functional recovery and improved vital activity among patients with mild to severe ischemic stroke. Nevertheless, further investigation is required to ascertain further therapeutic advantages associated with insulin therapy <sup>[31, 33]</sup>.

#### Conclusion

A positive linear link exists between the presence of hyperglycemia upon admission and the severity, magnitude, and outcome of ischemic stroke. The co-occurrence of diabetes and stress-induced hyperglycemia has been observed to be associated with a higher incidence of severe stroke and unfavorable functional outcomes, including increased mortality rates. A strong positive link exists between the initial glucose level upon admission and the subsequent outcome in cases of ischemic stroke. The presence of high glucose levels on admission day has been identified as a strong predictor of both mortality and poor functional outcome following an ischemic stroke. Therefore, it is imperative to promote the prompt restoration of normoglycemia. During the interim period, it is advisable to prioritize the implementation of effective general stroke care strategies, as well as the normalization of body temperature, maintenance of fluid balance, and optimization of hemodynamics. Neglecting these aspects may potentially jeopardize the positive prognosis, even in patients with normal blood sugar levels.

#### Funding

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Conflict of Interest None

References

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- 1. Khijn CJM, Hankey GJ. management of acute ischemic stroke, new guidelines from the American stroke association and European Stroke Initiative, Lancet Neurol. 2003;2:698-701.
- 2. Williams LS, Rotich J, Qi R, Fineberg N, Espay A, Bruno A, *et al.* Tierney WR. Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. Neurology. 2002 Jul 9;59(1):67-71.
- 3. Anderson RE, Jan WK, Martin HS, Mayer FB. Effects of glucose and paO2 Modulation on cortical intracellular acidosis, NADH redox state and infarction in the ischemic penumbra, Stroke. 1999;30:160-170.
- 4. Poppe AY, Majumdar SR, Jeerakathil T, Ghali W, Buchan AM, Hill MD, *et al.* Admission hyperglycemia predicts a worse outcome in stroke patients treated with intravenous thrombolysis. Diabetes care. 2009 Apr 1;32(4):617-22.
- 5. Ahire ED, Sonawane VN, Surana KR, Talele SG, Talele GS, Kshirsagar SJ, *et al.* Preventive Measures of Type 2 Diabetes via Nutrition. InThe Metabolic Syndrome; c2023. p. 71-99. Apple Academic Press.
- 6. Kruyt ND, Biessels GJ, DeVries JH, Roos YB. Hyperglycemia in acute ischemic stroke: pathophysiology and clinical management. Nature Reviews Neurology. 2010 Mar;6(3):145-55.
- 7. Pathan AS, Ahire MR, Diwane SA, Jain PG, Pandagale PM, Ahire ED, *et al.* Functional Foods in Prevention of Diabetes Mellitus. InApplications of Functional Foods in Disease Prevention; c2024 Jan 9. p. 139-164. Apple Academic Press.
- 8. Kerman WN, Inzucchi SE, Viscoli CM, Brass LM, Bravata DM, Horwitz CI, *et al.* Insulin resistance and risk for stroke, Neurology. 2002;59:809-815.
- D'souza S, Udavant P, Kadam J, Khairnar S, Ahire ED, Sable R, *et al.* Role of Vitamins in Metabolic Diseases. Vitamins as Nutraceuticals: Recent Advances and Applications. 2023 May 26:205-33.
- 10. Poppe AY, Majumdar SR, Jeerakathil T, Ghali W, Buchan AM, Hill MD, *et al.* Admission hyperglycemia predicts a worse outcome in stroke patients treated with intravenous thrombolysis. Diabetes care. 2009;32(4):617-622.
- 11. Masrur S, Cox M, Bhatt DL, Smith EE, Ellrodt G, Fonarow GC, *et al.* Association of acute and chronic hyperglycemia with acute ischemic stroke outcomes post- thrombolysis: findings from get with the guidelines- stroke. Journal of the American Heart Association. 2015 Sep 25;4(10):e002193.
- 12. Ahire ED, Surana KR, Sonawane VN, Talele SG, Talele GS, Kshirsagar SJ, *et al.* The Metabolic Syndrome: A Concerning Area for Future Research. InThe Metabolic Syndrome; c2023. p. 231-249. Apple Academic Press.
- 13. Kawai N, Keep RF, Benz AI. Hyperglycemia and the vascular effects of cerebral ischemia, Stroke. 1997;28:149-154.
- 14. Stead LG, Gilmore RM, Bellolio MF, Mishra S, Bhagra A, Vaidyanathan L, *et al.* Hyperglycemia as an independent predictor of worse outcome in non-diabetic patients presenting with acute ischemic stroke. Neurocritical care. 2009 Apr;10:181-6.
- 15. Ahire ED, Pathan AS, Pandagale PM, Khairnar SJ, Surana KR, Kshirsagar SJ, *et al.* Role of Dietary in the Prevention and Management of Obesity. InThe Metabolic Syndrome 2023 Aug 4 (pp. 139-161). Apple Academic Press.
- 16. Steinberg HO, Tarsh Boy BI, Monestel R, Hook G, Cronin J, Johnson A, Bayazeed B, Boron AD, Elevated circulating free fatty acid levels impair Endothelial dependent vasodilatation J Clinical Invent. 1997;100:1230-1239.
- 17. Koistinaho J, Pasonen S, Yrjanheikki J, Chan P. Spreading depression induced genes expression is regulated by plasma glucose. Stroke. 1999;30:114-119.
- 18. Song E-C, Chu K, Jeong SC, Jung K-H, Kim S-H, Kim M, *et al.* Hyperglycemia exacerbates brain edema and peri hematomal cell death after ICH. Stroke. 2003;34:2215-2220.
- 19. Toni D, De Michele M, Fiorelli M, Bastianello S, Camerlingo M, Sacchetti ML, *et al.* Influence of hyperglycaemia on infarct size and clinical outcome of acute ischemic stroke patients with intracranial arterial occlusion. Journal of the neurological sciences. 1994 May 1;123(1-2):129-33.
- 20. Parsons HW, Borber PA, Desmond PM, Baird TA, Darby DG, Bymer G, *et al.* Acute hyperglycemia adversely affects acute stroke outcome, AMRI and spectroscopy study. Ann. Neurol. 2002;52:20-28.
- 21. Baird TA, Parson MW, Prang T, Butcher KS, Desmond DM, Tress BM, *et al.* Persistent post stoke hyperglycemia Is independently associated with infarct expansion and worse clinical outcome. Stroke. 2003;34:2208-2214.
- 22. Els T, Klisch J, Orszagh M, Hetzel A, Schulte-Mönting J, Schumacher M, *et al.* Hyperglycemia in patients with focal cerebral ischemia after intravenous thrombolysis: influence on clinical outcome and infarct size. Cerebrovascular Diseases. 2002 Feb 27;13(2):89-94.
- 23. Capes SE, Hunt D, Malmburg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in non-diabetes and diabetes patients: A systemic overview, Stroke. 2001;32:2426-2432.
- 24. Bruno A, Biller J, Adams HP, Clarke WR, Woolson RF, Williams LS, *et al.* Acute blood glucose level and outcome from ischemic stroke. Neurology. 1999 Jan 1;52(2):280.

ISSN:0975 -3583,0976-2833 VOL 9, ISSUE 2, 2018

- 25. Scott JF, Robinson GM, French JM, O'Connell JE, Albert KG, Grey CS, *et al.* Glucose insulin potassium infusion in the treatment of acute stroke patients with mild to moderate hyperglycemia: The Glucose Insulin in Stroke Trail(GIST), Stroke. 1999;30:793-799.
- 26. Gilmore RM, Stedd LG. The role of hyperglycemia in acute ischemic stroke. Neurocritical care. 2006 Oct;5:153-8.
- 27. Malmberg K. for the DIGAMI study group. Prospective randomized study of intensive insulin therapy on long term survival after acute MI in patients with diabetes, BMJ. 1997;314:1512-1515.
- 28. Lindsberg PJ, Soinne L, Roine RO, Salomen O, Tatlisumak T, Kallela M, *et al.* community based thrombolytic therapy of acute ischemic stroke in Helsinki, Stroke. 2003;34:1443-1449.
- 29. Bruno A, Levine SR, Frankel MR, Brott TG, Kwiatkowski TG, Fienberg SE, *et al.* And the NINDS rtPA stroke study group. Admission glucose level and clinical outcome in the NINDS rtPA stroke trail, Neurology. 2002;59:669- 674.
- 30. Alvarez-Sabin J, Molina CA, Montaner J, Arenillas JF, Huertas R, Ribo M, *et al.* Effects of admission hyperglycemia on stroke outcome in reperfused tissue plasminogen activator treated patients. Stroke. 2003;34:1235-1241.
- Pulsinelli WA, Levy DE, Sigsbee B, Scherer P, Plum F. Increased damage, After ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus. Am J Med. 1983;74:540-544.
- 32. Adams Jr HP, Olinger CP, Marler JR, Biller J, Brott TG, Barsan WG, *et al.* Comparison of admission serum glucose concentration with neurologic outcome in acute cerebral infarction: a study in patients given naloxone. Stroke. 1988;19:455-458.
- Stephan M, Vinychuk, Volodymyr S, Melnyk, Victor M. Margitich Hyperglycemia after Acute Ischemic Stroke: Prediction, Significance and Immediate Control with Insulin- Potassium- Saline -Magnesium Infusions, Heart Drug. 2005;5:197-204.