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Original Research Paper

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ASSOCIATION OF GLYCATED HEMOGLOBIN WITH ACUTE ISCHEMIC STROKE- A HOSPITAL BASED OBSERVATIONAL STUDY

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ABSTRACT

Background- Tight glucose control (TGC) improves clinical outcomes in critically ill non-stroke patients. However, ICU investigations on rigorous glucose control does not confirm these promising benefits. In some trials, TGC increased the risk of hypoglycaemia and was associated with poor clinical outcomes. The latest findings are being used to discuss TGC's efficacy and safety. Ischemic stroke patients with hyperglycaemia can improve their prognosis with TGC. However, safely delivering TGC to severely ill individuals seems tricky. This study examined the relationship between HbA1c and acute ischemic stroke. HbA1c was estimated at admission to assess glycaemic status and to investigate its prognostic significance in Acute Ischemic Stroke by connecting it with outcome. **Methods-** This was an observational study undertaken from March 2021 to December 2022 in the Department of Medicine at a Maharashtra tertiary care hospital in central India. 100 acute ischemic stroke patients meeting inclusion and exclusion criteria gave written and informed consent. Clinical and radiological examinations revealed acute ischemic stroke. Regular haematology tests were done. HbA1c was taken for all patients. The NIHSS criteria determined stroke severity. The severity was measured on Days 0, 3, and 7. The Modified Rankin Scale examined stroke outcome. Data was examined with SPSS-25. **Results-** There was male preponderance with 72% of the study participants being males. The mean age was 57.86 ± 13.95 years. A total of 31 study participants were diabetic. When assessed according to the NIHSS score, it was observed that the mean score for 100 cases on Day 0 was 11.20 ± 3.87; range: 4.00 to 26.00. Most of the cases had MRS score of 3 to 5 (74%), followed by 0 to 2 (15%) and 6 (11%). HbA1c showed significant weakly positive correlation with NIHSS score at Day 0, Day 3 and Day 7 (P value < 0.001). When assessed for MRS score and HbA1c, HbA1c showed a significant weakly positive correlation with the MRS score. (P value < 0.001) **Conclusion-** The severity of the score (as assessed by the NIHSS score) and the outcome (as assessed by the MRS score) have a significantly positive correlation with HbA1c. Also, assessing according to the known history of diabetes, the outcome is poorer in diabetics as compared to non-diabetics. Thus, chronic hyperglycemia may also be a risk factor for poorer outcome following acute ischemic stroke.

KEYWORDS :

INTRODUCTION

A stroke is characterised as an unexpected neurological eruption brought on by reduced brain blood vessel perfusion. About 85% of stroke victims die as a result of ischemic occlusions. Ischemic occlusion happens as a result of cerebral emboli or thrombotic diseases.[1] Atherosclerosis-related vascular constriction impairs blood flow in thrombosis. Plaque accumulation eventually causes the vascular chamber to narrow and clot, which results in thrombotic stroke. An embolic stroke results in extreme stress and premature cell death (necrosis) due to blockage of blood flow to the affected brain region. Following necrosis, the plasma membrane is disrupted, organelles enlarge and leak cellular contents into extracellular space, and neuronal function is lost.[2] Inflammation, loss of homeostasis, acidosis, elevated intracellular calcium levels, cytokine- and free radical-mediated cytotoxicity, complement activation, disruption of the blood–brain barrier, glial cell activation, oxidative stress, and leukocyte infiltration are additional major events that contribute to stroke pathology. Roughly 10-15% of all strokes are hemorrhagic strokes, which have a high death rate. Blood vessels burst in this illness as a result of internal injuries and stress on the brain tissue. There are two types of haemorrhage: subarachnoid and intracerebral.[3-8]

Most strokes are caused by primary (first-time) haemorrhages, with secondary (second-time) haemorrhages accounting for an estimated 10–25% of cases. Between 1990 and 2016, the incidence of stroke decreased by 42% in high-income nations but doubled in low- and middle-income countries. The Global cost of Disease Study (GBD) reports that while the prevalence of stroke has declined, the socioeconomic cost of the condition has risen over time due to changes in the age, sex, and geographic distribution of the affected population.[9,10]

Numerous studies have demonstrated that increased blood glucose levels can persist for several days after the acute phase of an acute ischemic stroke and are commonly detected in individuals who are hospitalised for the condition.[11,12] High glucose levels are independent of other risk factors for a bad prognosis, such as age, the severity of the stroke, and diabetic status, and they indicate a greater infarct size, poor clinical outcome, and a higher chance of mortality.A number of pathophysiological processes have been postulated to explain the harmful effects of hyperglycemia on the ischemic brain, and numerous mechanisms appear to account for the high tendency of hyperglycemia seen in patients with acute ischemic stroke [13, 14].

Tight hyperglycemia control (TGC) has been demonstrated to improve clinical outcomes in critically sick patients with diseases other than stroke [15]. However, studies examining tight glycemic control in the intensive care unit (ICU) were unable to corroborate these prior encouraging results.[16] In reality, TGC was found to raise the risk of hypoglycemia in patients in subsequent trials, and treatment with TGC was linked to a poor clinical outcome. The effectiveness and safety

of TGC are currently being discussed in light of these most recent findings. TGC is still a viable treatment option for patients with ischemic stroke and concurrent hyperglycemia, which may enhance their clinical prognosis. Nevertheless, successfully and safely administering TGC to critically ill patients appears to be a difficult undertaking.

Therefore, the present study was conducted with the aim to study the association of HbA1c levels with the acute ischemic stroke. The objectives were to assess the glycaemic status by estimation of HbA1c at the time of admission and to determine the prognostic value of HbA1c levels in Acute Ischemic Stroke by correlating its levels with outcome.

MATERIALS AND METHODS

This was an observational study conducted from March 2021 to December 2022 in the Department of Medicine, at a tertiary care hospital of Maharashtra in central India. Written and informed consent was sought and100 patients presenting with acute ischemic stroke and meeting the inclusion and exclusion criteria.

Inclusion Criteria- 1. All patients suffering from acute ischemic stroke. 2. Patients above 18 years and either gender. 3. Patients giving consent for taking part in the study.

Exclusion Criteria- Patients with end stage renal disease, heart failure, haemorrhagic stroke. 2. Patients declining consent.

For the patients/legal guardians who could not read and write, the consent form was explained to them in their vernacular language in the presence of an unbiased, non-related witness, provided the witness was literate. Adequate time was provided to the patients/legal guardians to ensure their proper understanding of the nature of the study and the degree of participation.

Approval from institutional ethical committee was obtained before start of study. Information was collected through a pre-tested and structured proforma for each patient. Patients underwent detailed history, clinical examination and laboratory investigations. Demographic details were recorded. Detailed history of present illness along with personal and past history were recorded. History of comorbidities and medications were noted. General and systemic examinations were performed. Acute ischemic stroke was diagnosed on clinical and radiological examination. Routine hematological investigations were done. HbA1c was recorded for all patients. The severity of stroke was assessed by the National Institute of Health Stroke Severity (NIHSS) criteria. The severity was assessed on Day 0, Day 3 and Day 7. The outcome of the stroke was assessed by the Modified Rankin Scale (MRS)

RESULTS

The data was entered and cleaned using MS-Excel and analyzed statistically using SPSS-25. Quantitative variables were be expressed as mean value + standard deviation or median. Qualitative data was expressed as percentages (%) and proportion. Normality of data was tested using Shapiro-wilk test .Mann-Whitney U test was used to compare between patients with different outcome. There was a total of 100 patients who fulfilled the inclusion criteria and the results were as follows.

Table 1- Distribution of Study participants based on Gender and Presence of Comorbidities

Variables	Frequency (n)	Percentage (%)
Gender		
Males	72	72
Females	28	28
Comorbidity		
Present	64	64
Absent	36	36
Diabetes		
Present	31	31
Absent	69	69
Total	100	100

Table 1 depicts that there was male preponderance with 72% of the study particpants being males. The mean age was 57.86 ± 13.95 years. When comorbidities were observed, 64% of the study participants showed presence of comorbidities. A total of 31 study participants were diabetic.

Table 2- Distribution of the study population according to the NIHSS score

NIHSS Score	N	Mean	Sd
Day 0	100	11.20	3.87
Day 3	99	10.09	3.71
Day 7	89	9.48	3.54

In the present study, when assessed according to the NIHSS score, it was observed that the mean score for 100 cases on Day 0 was 11.20 ± 3.87; range: 4.00 to 26.00. There was one death by Day 3 and the mean score for 99 cases was 10.09 ± 3.71; range: 3.00 to 22.00. By Day 7, death was recorded in 10 more cases and the mean score for 89 cases was 9.48 ± 3.54; range: 3.00 to 18.00.(Table 2)

Table 3- Distribution of the study population according to the MRS score at the time of discharge/death

MRS Score	N	%
0-2	15	15
3-5	74	74
6	11	11
Total	100	100

Table 3 showes that when assessed according to the MRS score, it was observed that most of the cases had MRS score of 3 to 5 (74%), followed by 0 to 2 (15%) and 6 (11%).

Table 4- Correlation between HbA1c and NIHSS and MRS Scores in the study population

NIHSS Score and HbA1c	Correlation Coefficient(R)	P Value	Interpretation
Day 0	0.35	<0.001	Weakly Positive
Day 3	0.35	<0.001	Weakly Positive
Day 7	0.41	<0.001	Weakly Positive
MRS Score and HbA1c	0.40	<0.001	Weakly Positive

When assessed for correlation of the outcomes with laboratory findings, it was observed that HbA1c showed significant weakly positive correlation with NIHSS score at Day 0, Day 3 and Day 7 (P value < 0.001). When assessed for MRS score and HbA1c, HbA1c showed a significant weakly positive correlation with the MRS score. (P value < 0.001) (Table 4)

DISCUSSION

In the present study, it was observed that the mean age of the study population was 57.86 ± 13.95 years; range 25 to 90 years. There was male preponderance (72%). The age distribution between the two genders was similar. In the study by **Subhash A. et al**,[17] they compared a total of 40 cases with diabetes and 40 cases without diabetes. They observed that the mean age of the cases with diabetes was 57 ± 12.7 years and of those without diabetes was 61.3 ± 12.9 years. This was similar to the present study. In the study by **Wang H. et al**,[18] they included a total of 408 cases of first time acute ischemic stroke. They observed that the mean age of the study population was 63.8 ± 11.5 years. There was a male preponderance (64%). These findings were similar to the present study. Thus, it can be effectively concluded from the present study that the cases presenting with acute ischemic

stroke are elderly with a mean age of around 57 years and male preponderance.

In the present study, it was observed that comorbidities were present in 64% of the cases. Amongst the comorbidities, HTN was present in 39% of the cases, followed by DM which was present in 31% of the cases. Rest of the comorbidities, viz., hypothyroidism, CKD, IHD, carcinoma cervix, polycythemia and past history of CVA were present in less than 10% of the cases, each. In the study by Wang H. et al,[143] they observed that hypertension was the most common comorbidity (75%), followed by diabetes (36%), dyslipidemia (32.1%) and atrial fibrillation (13%). The distribution was similar to the present study. Thus, it can be effectively concluded that HTN and DM are the most common comorbidities in cases with acute ischemic stroke.

When assessed for correlation of the outcomes with laboratory findings, it was observed that HbA1c showed significant weakly positive correlation with NIHSS score at Day 0, Day 3 and Day 7 (P value < 0.001). When assessed for MRS score and HbA1c, HbA1c showed a significant weakly positive correlation with the MRS score. (P value < 0.001).

When compared according to the laboratory findings, HbA1c was significantly higher in the cases with diabetes (10.14 ± 1.56%) than in the cases without diabetes (8.08 ± 2.03 %); (P value < 0.001). In the study by **Subhash A. et al**,[17] they compared stroke in diabetic and non-diabetic cases. They included 40 cases of each. They observed that 37.5% of stroke patients with diabetes had poor outcome as compared to 22.5% of the cases without diabetes. In the study by **Wang H. et al**,[18] they observed that the clinical outcome, assessed in terms of MRS score at 3 months, decreased significantly with increase in values of HbA1c. They also observed that the increase in HbA1c was significantly associated with poor outcome in diabetics whereas no such correlation was observed in non-diabetics. These findings were almost similar to the present study.

Hence, it can be effectively concluded from the present study that increase in HbA1c is significantly associated with poor outcome in terms of NIHSS score and MRS score. Also, HbA1c and MRS scores are significantly higher in the cases with diabetes. Thus, chronic hyperglycemia may be associated with poorer outcome. Several underlying pathophysiologic mechanisms may be hypothesized. Persistent hyperglycemia may be associated with increases infarct size. It may also cause significant changes and remodeling of the cerebral vasculature predisposing to significant adverse outcomes. Hyperglycemia may also be associated with increased oxidative stress and a prothrombotic state by increasing the coagulant levels.

CONCLUSION

Like any other research, this study too had its limitations as it was a single centre study and limited by the IPD attendance of the patients. Therefore, the results may not be generalized. It can be effectively concluded from the present study that the affected population is elderly with a mean age of about 57 years and a male preponderance. HTN and DM are the most commonly associated comorbidities. There is a mortality rate of 11%. The severity of the score (as assessed by the NIHSS score) and the outcome (as assessed by the MRS score) have a significantly positive correlation with HbA1c. Also, assessing according to the known history of diabetes, the outcome is poorer in diabetics as compared to non-diabetics. Thus, chronic hyperglycemia may also be a risk factor for poorer outcome following acute ischemic stroke.

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Conflict of Interest- None

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